Dossier zur Nutzenbewertung gemäß § 35a SGB V

Difelikefalin (Kapruvia®)

Fresenius Medical Care Nephrologica Deutschland GmbH

Separater Anhang 4-H

Erwachsene Hämodialysepatienten mit moderatem bis schwerem Pruritus im Zusammenhang mit einer CKD

Medizinischer Nutzen und medizinischer Zusatznutzen, Patientengruppen mit therapeutisch bedeutsamem Zusatznutzen

Stand: 29.09.2022

Inhaltsverzeichnis Anhang 4-H

Anhang 4-H-1:
Zusatzauswertungen der Studie KALM-1 (DB)

Table AT2WIB_IOA0: Baseline weekly WI-NRS (categorical)
ITT

		CR845		Placebo	
	Category	N	n (%)	N	n (%)
Baseline weekly WI-NRS	< 3 points	189	0 (0.0)	189	0 (0.0)
	3 - < 4 points	189	0 (0.0)	189	0 (0.0)
	4 - 6 points	189	44 (23.3)	189	53 (28.0)
	> 6 - 7 points	189	54 (28.6)	189	30 (15.9)
	> 7 points	189	91 (48.1)	189	106 (56.1)
	Missing	189	0 (0.0)	189	0 (0.0)

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients in category. WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 11FEB2022

Table AT2DTB_IOA0: Baseline 5-D total score (categorical)
ITT

		CR845		Placebo	
	Category	N	n (%)	N	n (%)
Baseline 5-D total score	< 10 points	189	3 (1.6)	189	1 (0.5)
	10 - 20 points	189	149 (78.8)	189	137 (72.5)
	> 20 points	189	33 (17.5)	189	51 (27.0)
	Missing	189	4 (2.1)	189	0 (0.0)

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients in category.
Source Data: afived, created on: 10FEB2022

Table AT2DDB_IOA0: Baseline 5-D degree score (categorical)
ITT

		CR845		Placebo	
	Category	N	n (%)	N	n (%)
Baseline 5-D degree score	1 point	189	0 (0.0)	189	1 (0.5)
	2 - 4 points	189	178 (94.2)	189	164 (86.8)
	5 points	189	8 (4.2)	189	24 (12.7)
	Missing	189	3 (1.6)	189	0 (0.0)

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients in category.
Source Data: afived, created on: 10FEB2022

Table AT2DLB_IOA0: Baseline 5-D duration score (categorical)
ITT

		CR845		Placebo	
	Category	N	n (%)	N	n (%)
Baseline 5-D duration score	1 point	189	36 (19.0)	189	20 (10.6)
	2 - 4 points	189	120 (63.5)	189	114 (60.3)
	5 points	189	29 (15.3)	189	55 (29.1)
	Missing	189	4 (2.1)	189	0 (0.0)

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients in category.
Source Data: afived, created on: 10FEB2022

Table AT2DWB_IOA0: Baseline 5-D direction score (categorical)
ITT

		CR845		Placebo	
	Category	N	n (%)	N	n (%)
Baseline 5-D direction score	1 point	189	0 (0.0)	189	0 (0.0)
	2 - 4 points	189	163 (86.2)	189	166 (87.8)
	5 points	189	23 (12.2)	189	23 (12.2)
	Missing	189	3 (1.6)	189	0 (0.0)

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients in category.
Source Data: afived, created on: 10FEB2022

Table AT2DNB_IOA0: Baseline 5-D disability score (categorical)
ITT

		CR845		Placebo	
	Category	N	n (%)	N	n (%)
Baseline 5-D disability score	1 point	189	11 (5.8)	189	8 (4.2)
	2 - 4 points	189	139 (73.5)	189	124 (65.6)
	5 points	189	36 (19.0)	189	57 (30.2)
	Missing	189	3 (1.6)	189	0 (0.0)

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients in category.
Source Data: afived, created on: 10FEB2022

Table AT2DVB_IOA0: Baseline 5-D distribution score (categorical)
ITT

		CR845		Placebo	
	Category	N	n (%)	N	n (%)
Baseline 5-D distribution score	1 point	189	7 (3.7)	189	6 (3.2)
	2 - 4 points	189	141 (74.6)	189	139 (73.5)
	5 points	189	38 (20.1)	189	44 (23.3)
	Missing	189	3 (1.6)	189	0 (0.0)

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients in category.
Source Data: afived, created on: 10FEB2022

Table AT2DDC_IMH0: Change from baseline in 5-D degree score
ITT

		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
5-D degree score	Baseline	CR845	189	186 (98.4)	3.4 (0.7)	2	3.0	5	
		Placebo	189	189 (100.0)	3.6 (0.8)	1	4.0	5	
	Week 4	CR845	189	169 (89.4)	2.8 (0.8)	1	3.0	5	
		Placebo	189	165 (87.3)	3.2 (0.8)	1	3.0	5	
	Week 8	CR845	189	159 (84.1)	2.7 (0.8)	1	3.0	5	
		Placebo	189	170 (89.9)	2.9 (0.9)	1	3.0	5	
	Week 10	CR845	189	157 (83.1)	2.6 (0.8)	1	3.0	5	
		Placebo	189	167 (88.4)	3.0 (0.9)	1	3.0	5	
	Week 12	CR845	189	160 (84.7)	2.5 (0.8)	1	2.0	5	
		Placebo	189	166 (87.8)	2.8 (0.9)	1	3.0	5	
Change from baseline in 5-D degree score	Week 4	CR845	189	167 (88.4)	-0.6 (0.8)	-3	-1.0	2	-0.29 [-0.51, -0.07]
		Placebo	189	165 (87.3)	-0.3 (0.9)	-3	0.0	2	
	Week 8	CR845	189	157 (83.1)	-0.7 (0.9)	-3	-1.0	2	-0.11 [-0.32, 0.11]
		Placebo	189	170 (89.9)	-0.6 (1.0)	-4	0.0	2	
	Week 10	CR845	189	155 (82.0)	-0.8 (0.9)	-3	-1.0	2	-0.25 [-0.47, -0.03]
		Placebo	189	167 (88.4)	-0.6 (1.0)	-4	-1.0	2	
	Week 12	CR845	189	159 (84.1)	-0.9 (0.9)	-3	-1.0	2	-0.17 [-0.39, 0.05]
		Placebo	189	166 (87.8)	-0.7 (0.9)	-3	-1.0	2	

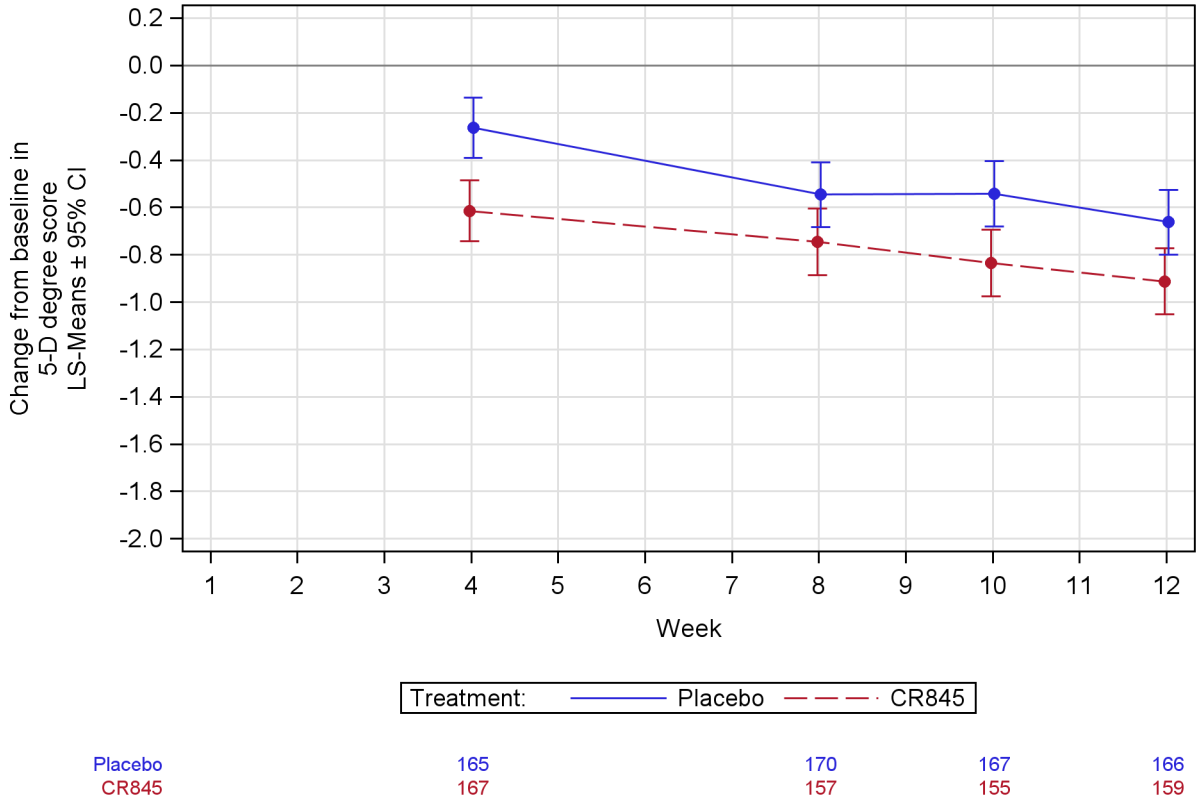
Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DDC_IMC0: Change from baseline in 5-D degree score - MMRM results
ITT

Change from baseline in 5-D degree score				Repeated measures analysis				
				Change from Baseline		Treatment Difference		
Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Week 4	CR845	189	167 (88.4)	-0.6 (0.1)	(-0.7, -0.5)	-0.4 (0.1)	(-0.5, -0.2)	<0.001 *
	Placebo	189	165 (87.3)	-0.3 (0.1)	(-0.4, -0.1)			
Week 8	CR845	189	157 (83.1)	-0.7 (0.1)	(-0.9, -0.6)	-0.2 (0.1)	(-0.4, -0.0)	0.026 *
	Placebo	189	170 (89.9)	-0.5 (0.1)	(-0.7, -0.4)			
Week 10	CR845	189	155 (82.0)	-0.8 (0.1)	(-1.0, -0.7)	-0.3 (0.1)	(-0.5, -0.1)	0.001 *
	Placebo	189	167 (88.4)	-0.5 (0.1)	(-0.7, -0.4)			
Week 12	CR845	189	159 (84.1)	-0.9 (0.1)	(-1.1, -0.8)	-0.2 (0.1)	(-0.4, -0.1)	0.005 *
	Placebo	189	166 (87.8)	-0.7 (0.1)	(-0.8, -0.5)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval . * = significant treatment effect.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Figure AF2DDC_IMG0: Course of change from baseline in 5-D degree score
ITT



Note: ITT = Intent-to-treat Set.
Symbols present least square mean (LS-Mean), bars present 95% confidence intervals (CI).
CR845 = Difelikefalin.
Source Table: AT2DDC_IMC0
Source Data: afived, created on: 17FEB2022

Table AT2DLC_IMH0: Change from baseline in 5-D duration score
ITT

		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
5-D duration score	Baseline	CR845	189	185 (97.9)	2.7 (1.3)	1	2.0	5	
		Placebo	189	189 (100.0)	3.2 (1.4)	1	3.0	5	
	Week 4	CR845	189	169 (89.4)	2.1 (1.2)	1	2.0	5	
		Placebo	189	165 (87.3)	2.7 (1.4)	1	2.0	5	
	Week 8	CR845	189	159 (84.1)	1.8 (1.0)	1	1.0	5	
		Placebo	189	170 (89.9)	2.4 (1.4)	1	2.0	5	
	Week 10	CR845	189	157 (83.1)	1.7 (0.9)	1	2.0	5	
		Placebo	189	167 (88.4)	2.3 (1.4)	1	2.0	5	
	Week 12	CR845	189	160 (84.7)	1.8 (1.0)	1	1.0	5	
		Placebo	189	166 (87.8)	2.2 (1.3)	1	2.0	5	
Change from baseline in 5-D duration score	Week 4	CR845	189	166 (87.8)	-0.7 (1.3)	-4	-1.0	4	-0.09 [-0.31, 0.12]
		Placebo	189	165 (87.3)	-0.5 (1.6)	-4	0.0	4	
	Week 8	CR845	189	156 (82.5)	-0.9 (1.4)	-4	-1.0	3	-0.08 [-0.29, 0.14]
		Placebo	189	170 (89.9)	-0.8 (1.6)	-4	-1.0	4	
	Week 10	CR845	189	154 (81.5)	-1.0 (1.4)	-4	-1.0	4	-0.05 [-0.27, 0.16]
		Placebo	189	167 (88.4)	-0.9 (1.6)	-4	-1.0	4	
	Week 12	CR845	189	158 (83.6)	-1.0 (1.5)	-4	-1.0	3	-0.02 [-0.23, 0.20]
		Placebo	189	166 (87.8)	-1.0 (1.5)	-4	-1.0	4	

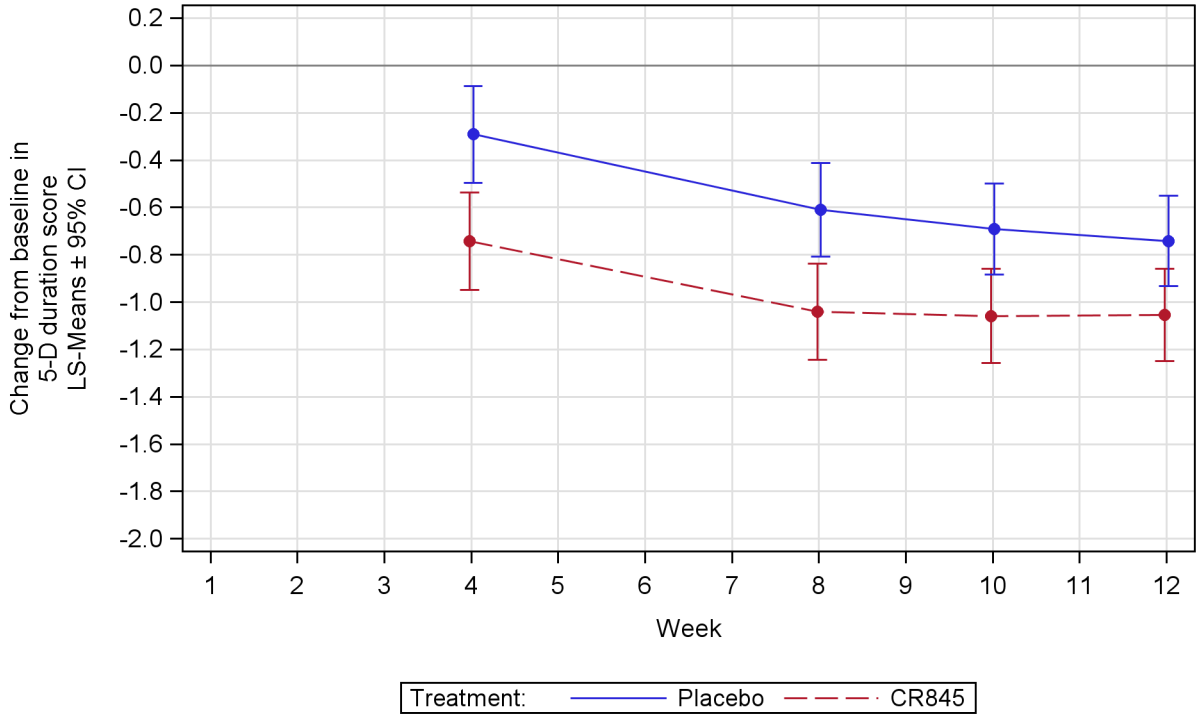
Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DLC_IMC0: Change from baseline in 5-D duration score - MMRM results
ITT

Change from baseline in 5-D duration score				Repeated measures analysis				
				Change from Baseline		Treatment Difference		
Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Week 4	CR845	189	166 (87.8)	-0.7 (0.1)	(-0.9, -0.5)	-0.5 (0.1)	(-0.7, -0.2)	<0.001 *
	Placebo	189	165 (87.3)	-0.3 (0.1)	(-0.5, -0.1)			
Week 8	CR845	189	156 (82.5)	-1.0 (0.1)	(-1.2, -0.8)	-0.4 (0.1)	(-0.7, -0.2)	<0.001 *
	Placebo	189	170 (89.9)	-0.6 (0.1)	(-0.8, -0.4)			
Week 10	CR845	189	154 (81.5)	-1.1 (0.1)	(-1.3, -0.9)	-0.4 (0.1)	(-0.6, -0.1)	0.003 *
	Placebo	189	167 (88.4)	-0.7 (0.1)	(-0.9, -0.5)			
Week 12	CR845	189	158 (83.6)	-1.1 (0.1)	(-1.3, -0.9)	-0.3 (0.1)	(-0.6, -0.1)	0.010 *
	Placebo	189	166 (87.8)	-0.7 (0.1)	(-0.9, -0.6)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval . * = significant treatment effect.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Figure AF2DLC_IMG0: Course of change from baseline in 5-D duration score
ITT



Note: ITT = Intent-to-treat Set.
Symbols present least square mean (LS-Mean), bars present 95% confidence intervals (CI).
CR845 = Difelikefalin.
Source Table: AT2DLC_IMC0
Source Data: afived, created on: 17FEB2022

Table AT2DWC_IMH0: Change from baseline in 5-D direction score
ITT

		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
5-D direction score	Baseline	CR845	189	186 (98.4)	3.9 (0.6)	2	4.0	5	
		Placebo	189	189 (100.0)	3.9 (0.6)	2	4.0	5	
	Week 4	CR845	189	169 (89.4)	2.7 (0.8)	1	3.0	5	
		Placebo	189	165 (87.3)	3.2 (0.9)	1	3.0	5	
	Week 8	CR845	189	159 (84.1)	2.6 (0.8)	1	2.0	5	
		Placebo	189	170 (89.9)	3.0 (1.0)	1	3.0	5	
	Week 10	CR845	189	157 (83.1)	2.5 (0.7)	1	2.0	5	
		Placebo	189	167 (88.4)	2.9 (0.9)	1	3.0	5	
	Week 12	CR845	189	160 (84.7)	2.5 (0.8)	1	2.0	5	
		Placebo	189	166 (87.8)	2.9 (1.0)	1	3.0	5	
Change from baseline in 5-D direction score	Week 4	CR845	189	167 (88.4)	-1.2 (0.9)	-4	-1.0	1	-0.43 [-0.65, -0.21]
		Placebo	189	165 (87.3)	-0.8 (1.0)	-4	-1.0	3	
	Week 8	CR845	189	157 (83.1)	-1.3 (0.9)	-3	-1.0	2	-0.38 [-0.60, -0.16]
		Placebo	189	170 (89.9)	-0.9 (1.1)	-4	-1.0	2	
	Week 10	CR845	189	155 (82.0)	-1.4 (0.9)	-4	-1.0	1	-0.40 [-0.62, -0.18]
		Placebo	189	167 (88.4)	-1.0 (1.0)	-4	-1.0	2	
	Week 12	CR845	189	159 (84.1)	-1.4 (1.0)	-4	-1.0	2	-0.34 [-0.56, -0.12]
		Placebo	189	166 (87.8)	-1.0 (1.1)	-3	-1.0	2	

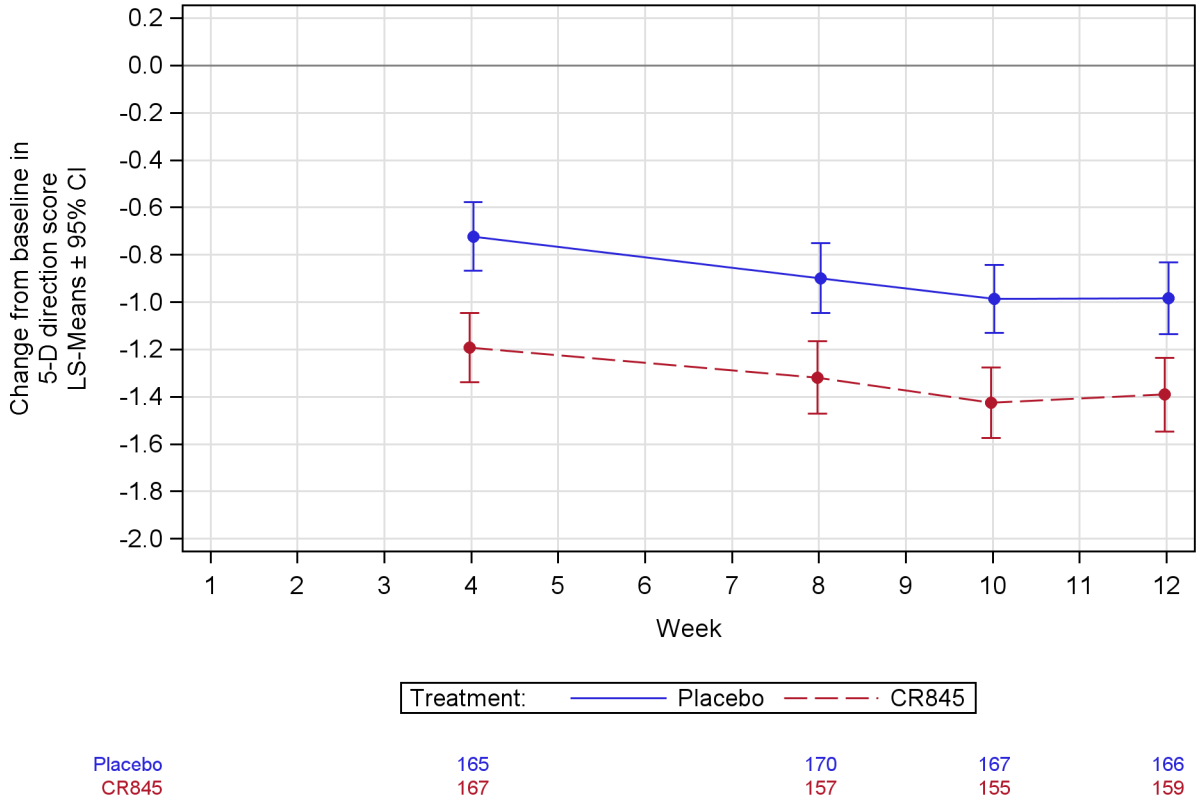
Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DWC_IMC0: Change from baseline in 5-D direction score - MMRM results
ITT

Change from baseline in 5-D direction score				Repeated measures analysis				
				Change from Baseline		Treatment Difference		
Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Week 4	CR845	189	167 (88.4)	-1.2 (0.1)	(-1.3, -1.0)	-0.5 (0.1)	(-0.6, -0.3)	<0.001 *
	Placebo	189	165 (87.3)	-0.7 (0.1)	(-0.9, -0.6)			
Week 8	CR845	189	157 (83.1)	-1.3 (0.1)	(-1.5, -1.2)	-0.4 (0.1)	(-0.6, -0.2)	<0.001 *
	Placebo	189	170 (89.9)	-0.9 (0.1)	(-1.0, -0.8)			
Week 10	CR845	189	155 (82.0)	-1.4 (0.1)	(-1.6, -1.3)	-0.4 (0.1)	(-0.6, -0.3)	<0.001 *
	Placebo	189	167 (88.4)	-1.0 (0.1)	(-1.1, -0.8)			
Week 12	CR845	189	159 (84.1)	-1.4 (0.1)	(-1.5, -1.2)	-0.4 (0.1)	(-0.6, -0.2)	<0.001 *
	Placebo	189	166 (87.8)	-1.0 (0.1)	(-1.1, -0.8)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval . * = significant treatment effect.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Figure AF2DWC_IMG0: Course of change from baseline in 5-D direction score
ITT



Note: ITT = Intent-to-treat Set.
Symbols present least square mean (LS-Mean), bars present 95% confidence intervals (CI).
CR845 = Difelikefalin.
Source Table: AT2DWC_IMC0
Source Data: afived, created on: 17FEB2022

Table AT2DNC_IMH0: Change from baseline in 5-D disability score
ITT

		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
5-D disability score	Baseline	CR845	189	186 (98.4)	3.5 (1.1)	1	4.0	5	
		Placebo	189	189 (100.0)	3.8 (1.1)	1	4.0	5	
	Week 4	CR845	189	169 (89.4)	2.9 (1.1)	1	3.0	5	
		Placebo	189	165 (87.3)	3.3 (1.2)	1	3.0	5	
	Week 8	CR845	189	159 (84.1)	2.8 (1.2)	1	3.0	5	
		Placebo	189	170 (89.9)	3.0 (1.2)	1	3.0	5	
	Week 10	CR845	189	157 (83.1)	2.6 (1.1)	1	2.0	5	
		Placebo	189	167 (88.4)	2.8 (1.2)	1	3.0	5	
	Week 12	CR845	189	160 (84.7)	2.5 (1.2)	1	2.0	5	
		Placebo	189	166 (87.8)	2.7 (1.2)	1	3.0	5	
Change from baseline in 5-D disability score	Week 4	CR845	189	167 (88.4)	-0.6 (1.1)	-4	-1.0	2	-0.08 [-0.29, 0.14]
		Placebo	189	165 (87.3)	-0.5 (1.4)	-4	0.0	4	
	Week 8	CR845	189	157 (83.1)	-0.8 (1.2)	-4	-1.0	4	-0.04 [-0.26, 0.17]
		Placebo	189	170 (89.9)	-0.7 (1.3)	-4	-1.0	3	
	Week 10	CR845	189	155 (82.0)	-1.0 (1.4)	-4	-1.0	3	-0.05 [-0.27, 0.17]
		Placebo	189	167 (88.4)	-0.9 (1.4)	-4	-1.0	2	
	Week 12	CR845	189	159 (84.1)	-1.1 (1.4)	-4	-1.0	3	-0.01 [-0.23, 0.20]
		Placebo	189	166 (87.8)	-1.0 (1.4)	-4	-1.0	2	

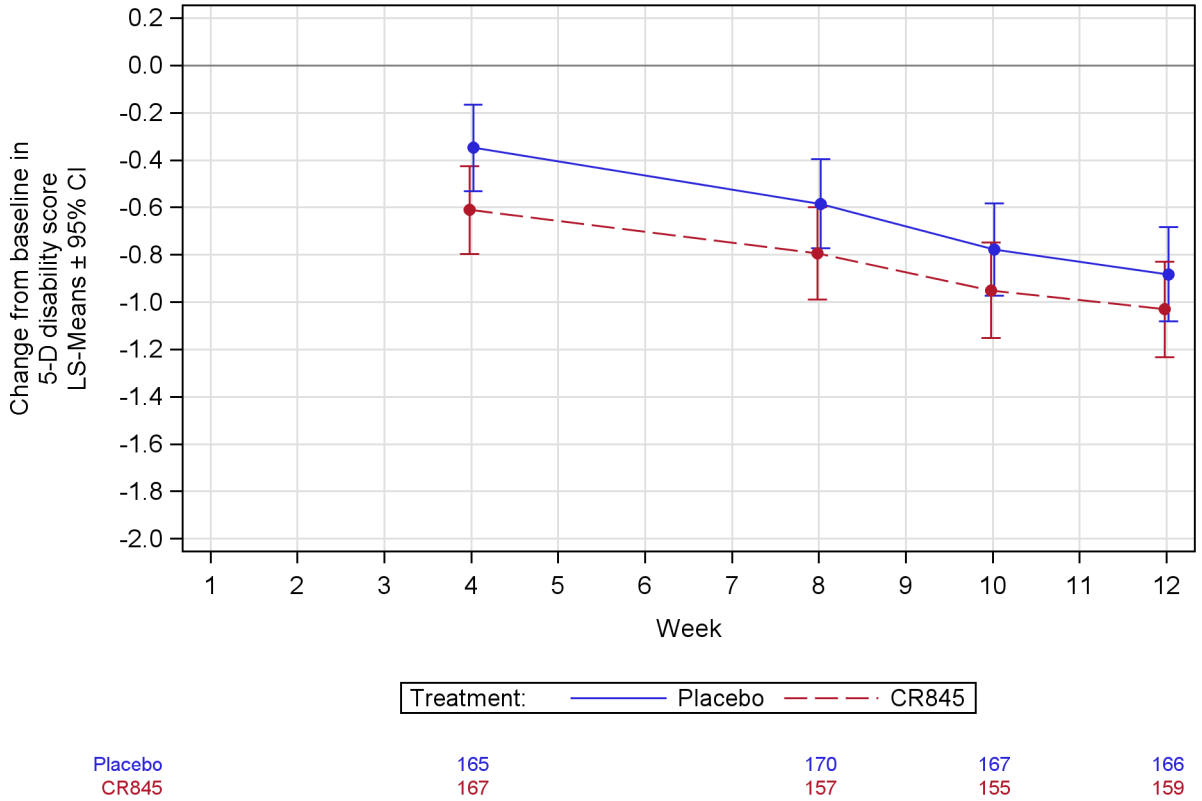
Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DNC_IMC0: Change from baseline in 5-D disability score - MMRM results
ITT

Change from baseline in 5-D disability score				Repeated measures analysis				
				Change from Baseline		Treatment Difference		
Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Week 4	CR845	189	167 (88.4)	-0.6 (0.1)	(-0.8, -0.4)	-0.3 (0.1)	(-0.5, -0.0)	0.024 *
	Placebo	189	165 (87.3)	-0.3 (0.1)	(-0.5, -0.2)			
Week 8	CR845	189	157 (83.1)	-0.8 (0.1)	(-1.0, -0.6)	-0.2 (0.1)	(-0.4, 0.0)	0.083
	Placebo	189	170 (89.9)	-0.6 (0.1)	(-0.8, -0.4)			
Week 10	CR845	189	155 (82.0)	-1.0 (0.1)	(-1.2, -0.7)	-0.2 (0.1)	(-0.4, 0.1)	0.173
	Placebo	189	167 (88.4)	-0.8 (0.1)	(-1.0, -0.6)			
Week 12	CR845	189	159 (84.1)	-1.0 (0.1)	(-1.2, -0.8)	-0.1 (0.1)	(-0.4, 0.1)	0.249
	Placebo	189	166 (87.8)	-0.9 (0.1)	(-1.1, -0.7)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval . * = significant treatment effect.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Figure AF2DNC_IMG0: Course of change from baseline in 5-D disability score
ITT



Note: ITT = Intent-to-treat Set.
Symbols present least square mean (LS-Mean), bars present 95% confidence intervals (CI).
CR845 = Difelikefalin.
Source Table: AT2DNC_IMC0
Source Data: afived, created on: 17FEB2022

Table AT2DVC_IMH0: Change from baseline in 5-D distribution score
ITT

		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
5-D distribution score	Baseline	CR845	189	186 (98.4)	3.3 (1.1)	1	3.0	5	
		Placebo	189	189 (100.0)	3.4 (1.1)	1	3.0	5	
	Week 4	CR845	189	169 (89.4)	2.9 (1.1)	1	3.0	5	
		Placebo	189	165 (87.3)	3.3 (1.2)	1	3.0	5	
	Week 8	CR845	189	159 (84.1)	2.8 (1.1)	1	3.0	5	
		Placebo	189	170 (89.9)	3.1 (1.2)	1	3.0	5	
	Week 10	CR845	189	157 (83.1)	2.7 (1.2)	1	3.0	5	
		Placebo	189	167 (88.4)	3.0 (1.2)	1	3.0	5	
	Week 12	CR845	189	160 (84.7)	2.7 (1.2)	1	3.0	5	
		Placebo	189	166 (87.8)	3.1 (1.2)	1	3.0	5	
Change from baseline in 5-D distribution score	Week 4	CR845	189	167 (88.4)	-0.4 (1.0)	-3	0.0	3	-0.19 [-0.41, 0.02]
		Placebo	189	165 (87.3)	-0.2 (1.1)	-3	0.0	3	
	Week 8	CR845	189	157 (83.1)	-0.5 (1.1)	-3	0.0	4	-0.21 [-0.42, 0.01]
		Placebo	189	170 (89.9)	-0.3 (1.3)	-4	0.0	4	
	Week 10	CR845	189	155 (82.0)	-0.5 (1.2)	-4	0.0	3	-0.12 [-0.34, 0.10]
		Placebo	189	167 (88.4)	-0.4 (1.2)	-4	0.0	3	
	Week 12	CR845	189	159 (84.1)	-0.6 (1.2)	-4	0.0	2	-0.25 [-0.47, -0.03]
		Placebo	189	166 (87.8)	-0.3 (1.2)	-4	0.0	3	

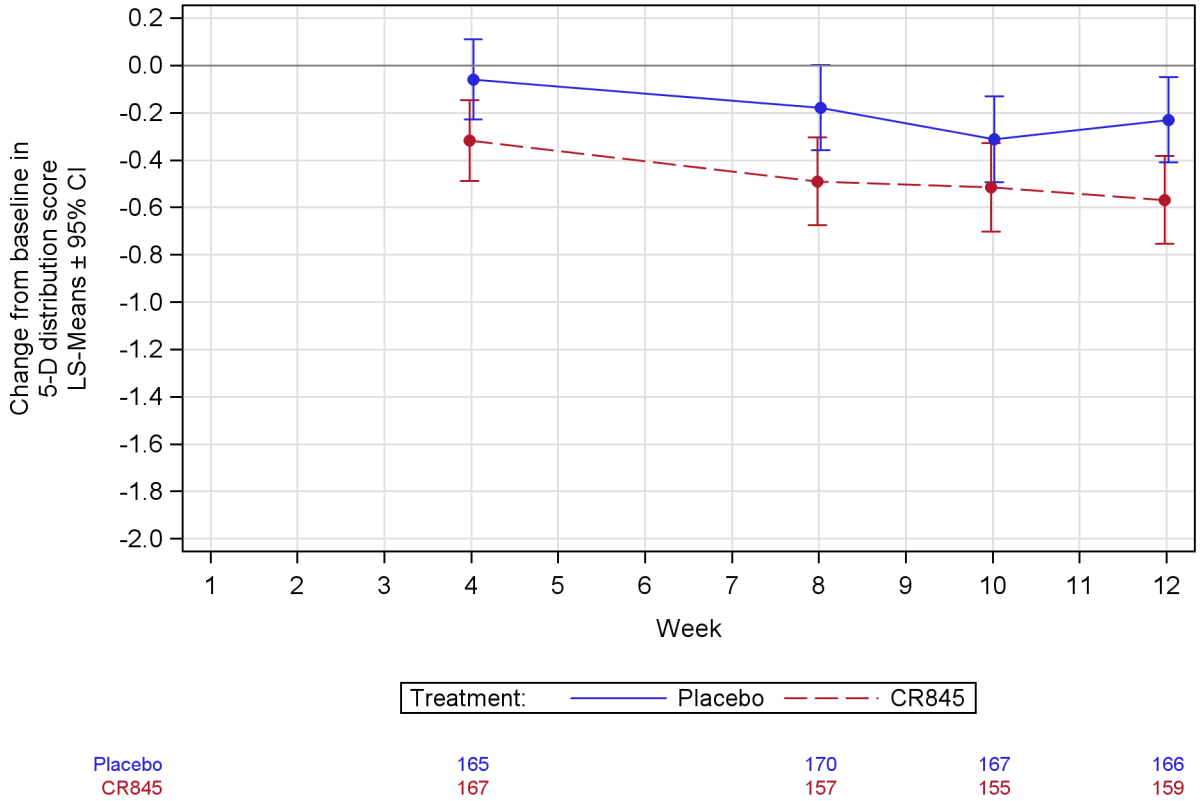
Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DVC_IMC0: Change from baseline in 5-D distribution score - MMRM results
ITT

Change from baseline in 5-D distribution score				Repeated measures analysis				
				Change from Baseline		Treatment Difference		
Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Week 4	CR845	189	167 (88.4)	-0.3 (0.1)	(-0.5, -0.1)	-0.3 (0.1)	(-0.5, -0.1)	0.014 *
	Placebo	189	165 (87.3)	-0.1 (0.1)	(-0.2, 0.1)			
Week 8	CR845	189	157 (83.1)	-0.5 (0.1)	(-0.7, -0.3)	-0.3 (0.1)	(-0.5, -0.1)	0.007 *
	Placebo	189	170 (89.9)	-0.2 (0.1)	(-0.4, 0.0)			
Week 10	CR845	189	155 (82.0)	-0.5 (0.1)	(-0.7, -0.3)	-0.2 (0.1)	(-0.4, 0.0)	0.080
	Placebo	189	167 (88.4)	-0.3 (0.1)	(-0.5, -0.1)			
Week 12	CR845	189	159 (84.1)	-0.6 (0.1)	(-0.8, -0.4)	-0.3 (0.1)	(-0.6, -0.1)	0.003 *
	Placebo	189	166 (87.8)	-0.2 (0.1)	(-0.4, -0.0)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval . * = significant treatment effect.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Figure AF2DVC_IMG0: Course of change from baseline in 5-D distribution score
ITT



Note: ITT = Intent-to-treat Set.
Symbols present least square mean (LS-Mean), bars present 95% confidence intervals (CI).
CR845 = Difelikefalin.
Source Table: AT2DVC_IMC0
Source Data: afived, created on: 17FEB2022

Table AT2DDCD1_IMP0: Decrease of 5-D degree score of at least 1 point
ITT

		CR845			Placebo						
Variable	Time	N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Decrease of 5-D degree score of at least 1 point	Week 12	189	159 (84.1)	108 (57.1) [49.8, 64.3]	189	166 (87.8)	96 (50.8) [43.4, 58.1]	1.125 [0.933, 1.356]	1.292 [0.861, 1.937]	6.3 [-4.2, 16.9]	0.216

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: afived, created on: 10FEB2022

Table AT2DLCD1_IMP0: Decrease of 5-D duration score of at least 1 point
ITT

		CR845			Placebo						
Variable	Time	N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Decrease of 5-D duration score of at least 1 point	Week 12	189	158 (83.6)	96 (50.8) [43.4, 58.1]	189	166 (87.8)	100 (52.9) [45.5, 60.2]	0.960 [0.790, 1.166]	0.919 [0.614, 1.376]	-2.1 [-12.7, 8.5]	0.681

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: afived, created on: 10FEB2022

Table AT2DWCD1_IMP0: Decrease of 5-D direction score of at least 1 point
ITT

		CR845			Placebo						
Variable	Time	N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Decrease of 5-D direction score of at least 1 point	Week 12	189	159 (84.1)	132 (69.8) [62.8, 76.3]	189	166 (87.8)	115 (60.8) [53.5, 67.8]	1.148 [0.990, 1.331]	1.490 [0.973, 2.283]	9.0 [-1.1, 19.1]	0.067

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: afived, created on: 10FEB2022

Table AT2DNCD1_IMP0: Decrease of 5-D disability score of at least 1 point
ITT

		CR845			Placebo						
Variable	Time	N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Decrease of 5-D disability score of at least 1 point	Week 12	189	159 (84.1)	103 (54.5) [47.1, 61.7]	189	166 (87.8)	102 (54.0) [46.6, 61.2]	1.010 [0.839, 1.215]	1.022 [0.682, 1.531]	0.5 [-10.0, 11.1]	0.918

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: afived, created on: 10FEB2022

Table AT2DVCD1_IMP0: Decrease of 5-D distribution score of at least 1 point
ITT

		CR845			Placebo						
Variable	Time	N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Decrease of 5-D distribution score of at least 1 point	Week 12	189	159 (84.1)	74 (39.2) [32.2, 46.5]	189	166 (87.8)	64 (33.9) [27.2, 41.1]	1.156 [0.885, 1.510]	1.257 [0.826, 1.912]	5.3 [-4.9, 15.5]	0.286

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: afived, created on: 10FEB2022

Table AT2STB_IOA0: Baseline Skindex-10 total score (categorical)
ITT

		CR845		Placebo	
	Category	N	n (%)	N	n (%)
Baseline Skindex-10 total score	< 15 points	189	12 (6.3)	189	16 (8.5)
	15 - 45 points	189	117 (61.9)	189	97 (51.3)
	> 45 points	189	54 (28.6)	189	72 (38.1)
	Missing	189	6 (3.2)	189	4 (2.1)

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients in category.
Source Data: askin, created on: 11FEB2022

Table AT2SDB_IOA0: Baseline Skindex-10 disease score (categorical)
ITT

		CR845		Placebo	
	Category	N	n (%)	N	n (%)
Baseline Skindex-10 disease score	< 3 points	189	1 (0.5)	189	1 (0.5)
	3 - 15 points	189	118 (62.4)	189	107 (56.6)
	> 15 points	189	67 (35.4)	189	80 (42.3)
	Missing	189	3 (1.6)	189	1 (0.5)

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients in category.
Source Data: askin, created on: 11FEB2022

Table AT2SMB_IOA0: Baseline Skindex-10 mood/emotional distress score (categorical)
ITT

		CR845		Placebo	
	Category	N	n (%)	N	n (%)
Baseline Skindex-10 mood/emotional distress score	< 3 points	189	7 (3.7)	189	11 (5.8)
	3 - 15 points	189	133 (70.4)	189	120 (63.5)
	> 15 points	189	44 (23.3)	189	56 (29.6)
	Missing	189	5 (2.6)	189	2 (1.1)

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients in category.
Source Data: askin, created on: 11FEB2022

Table AT2SSB_IOA0: Baseline Skindex-10 social functioning score (categorical)
ITT

		CR845		Placebo	
	Category	N	n (%)	N	n (%)
Baseline Skindex-10 social functioning score	< 4 points	189	37 (19.6)	189	33 (17.5)
	4 - 20 points	189	117 (61.9)	189	116 (61.4)
	> 20 points	189	31 (16.4)	189	38 (20.1)
	Missing	189	4 (2.1)	189	2 (1.1)

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients in category.
Source Data: askin, created on: 11FEB2022

Table AT2SDC_IMH0: Change from baseline in Skindex-10 disease score
ITT

		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Skindex-10 disease score	Baseline	CR845	189	186 (98.4)	13.3 (3.9)	2	14.0	18	
		Placebo	189	188 (99.5)	13.8 (3.8)	2	15.0	18	
	Week 4	CR845	189	168 (88.9)	9.9 (4.7)	0	9.0	18	
		Placebo	189	164 (86.8)	11.3 (4.6)	0	11.0	18	
	Week 8	CR845	189	158 (83.6)	8.6 (4.8)	0	8.0	18	
		Placebo	189	168 (88.9)	10.3 (4.9)	0	10.0	18	
	Week 10	CR845	189	156 (82.5)	7.9 (4.8)	0	7.0	18	
		Placebo	189	165 (87.3)	9.6 (5.2)	0	9.0	18	
	Week 12	CR845	189	158 (83.6)	7.2 (4.8)	0	6.0	18	
		Placebo	189	162 (85.7)	9.4 (5.2)	0	9.0	18	
Change from baseline in Skindex-10 disease score	Week 4	CR845	189	166 (87.8)	-3.5 (4.4)	-17	-3.0	10	-0.20 [-0.42, 0.02]
		Placebo	189	163 (86.2)	-2.6 (4.2)	-15	-2.0	7	
	Week 8	CR845	189	156 (82.5)	-4.6 (4.8)	-16	-4.0	11	-0.23 [-0.45, -0.01]
		Placebo	189	167 (88.4)	-3.6 (4.7)	-18	-3.0	7	
	Week 10	CR845	189	154 (81.5)	-5.4 (5.3)	-18	-5.0	9	-0.22 [-0.44, -0.00]
		Placebo	189	164 (86.8)	-4.2 (5.0)	-18	-4.0	7	
	Week 12	CR845	189	157 (83.1)	-6.1 (5.3)	-18	-6.0	9	-0.34 [-0.56, -0.11]
		Placebo	189	161 (85.2)	-4.4 (4.8)	-18	-4.0	9	

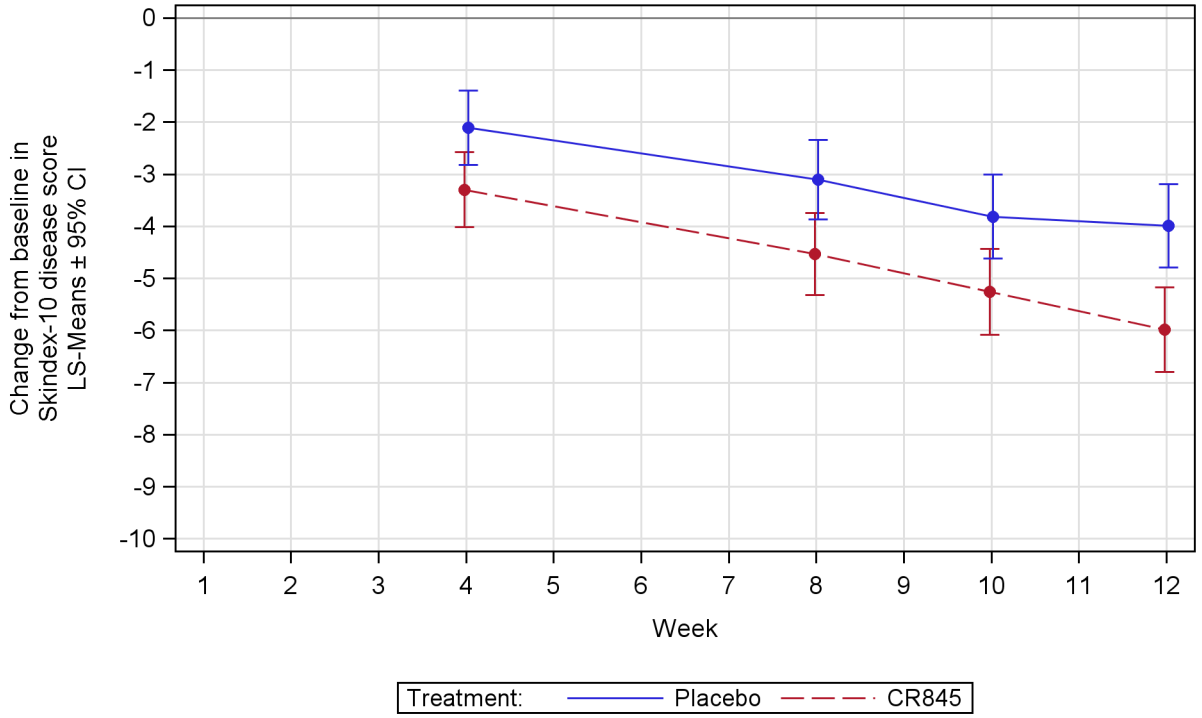
Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SDC_IMC0: Change from baseline in Skindex-10 disease score - MMRM results
ITT

Change from baseline in Skindex-10 disease score				Repeated measures analysis				
				Change from Baseline		Treatment Difference		
Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Week 4	CR845	189	166 (87.8)	-3.3 (0.4)	(-4.0, -2.6)	-1.2 (0.4)	(-2.1, -0.3)	0.006 *
	Placebo	189	163 (86.2)	-2.1 (0.4)	(-2.8, -1.4)			
Week 8	CR845	189	156 (82.5)	-4.5 (0.4)	(-5.3, -3.7)	-1.4 (0.5)	(-2.4, -0.5)	0.003 *
	Placebo	189	167 (88.4)	-3.1 (0.4)	(-3.9, -2.3)			
Week 10	CR845	189	154 (81.5)	-5.3 (0.4)	(-6.1, -4.4)	-1.4 (0.5)	(-2.5, -0.4)	0.006 *
	Placebo	189	164 (86.8)	-3.8 (0.4)	(-4.6, -3.0)			
Week 12	CR845	189	157 (83.1)	-6.0 (0.4)	(-6.8, -5.2)	-2.0 (0.5)	(-3.0, -1.0)	<0.001 *
	Placebo	189	161 (85.2)	-4.0 (0.4)	(-4.8, -3.2)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval . * = significant treatment effect.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Figure AF2SDC_IMG0: Course of change from baseline in Skindex-10 disease score
ITT



Note: ITT = Intent-to-treat Set.
Symbols present least square mean (LS-Mean), bars present 95% confidence intervals (CI).
CR845 = Difelikefalin.
Source Table: AT2SDC_IMC0
Source Data: askin, created on: 17FEB2022

Table AT2SMC_IMH0: Change from baseline in Skindex-10 mood/emotional distress score
ITT

		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Skindex-10 mood/emotional distress score	Baseline	CR845	189	184 (97.4)	11.6 (4.6)	0	12.0	18	
		Placebo	189	187 (98.9)	12.0 (5.0)	0	12.0	18	
	Week 4	CR845	189	169 (89.4)	8.4 (5.2)	0	8.0	18	
		Placebo	189	163 (86.2)	9.6 (5.4)	0	10.0	18	
	Week 8	CR845	189	158 (83.6)	6.8 (5.4)	0	6.0	18	
		Placebo	189	167 (88.4)	8.8 (5.7)	0	9.0	18	
	Week 10	CR845	189	156 (82.5)	6.0 (5.2)	0	5.0	18	
		Placebo	189	166 (87.8)	8.2 (5.7)	0	8.0	18	
	Week 12	CR845	189	159 (84.1)	5.5 (5.0)	0	5.0	18	
		Placebo	189	165 (87.3)	7.8 (5.8)	0	7.0	18	
Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	189	165 (87.3)	-3.2 (5.1)	-18	-3.0	12	-0.14 [-0.36, 0.08]
		Placebo	189	161 (85.2)	-2.6 (4.7)	-17	-2.0	10	
	Week 8	CR845	189	154 (81.5)	-4.8 (5.4)	-18	-4.0	14	-0.29 [-0.51, -0.07]
		Placebo	189	165 (87.3)	-3.3 (4.9)	-18	-3.0	9	
	Week 10	CR845	189	153 (81.0)	-5.7 (5.2)	-17	-6.0	10	-0.33 [-0.55, -0.10]
		Placebo	189	164 (86.8)	-3.9 (5.5)	-18	-3.0	10	
	Week 12	CR845	189	156 (82.5)	-6.1 (5.3)	-18	-6.0	6	-0.34 [-0.56, -0.12]
		Placebo	189	163 (86.2)	-4.2 (5.5)	-18	-4.0	14	

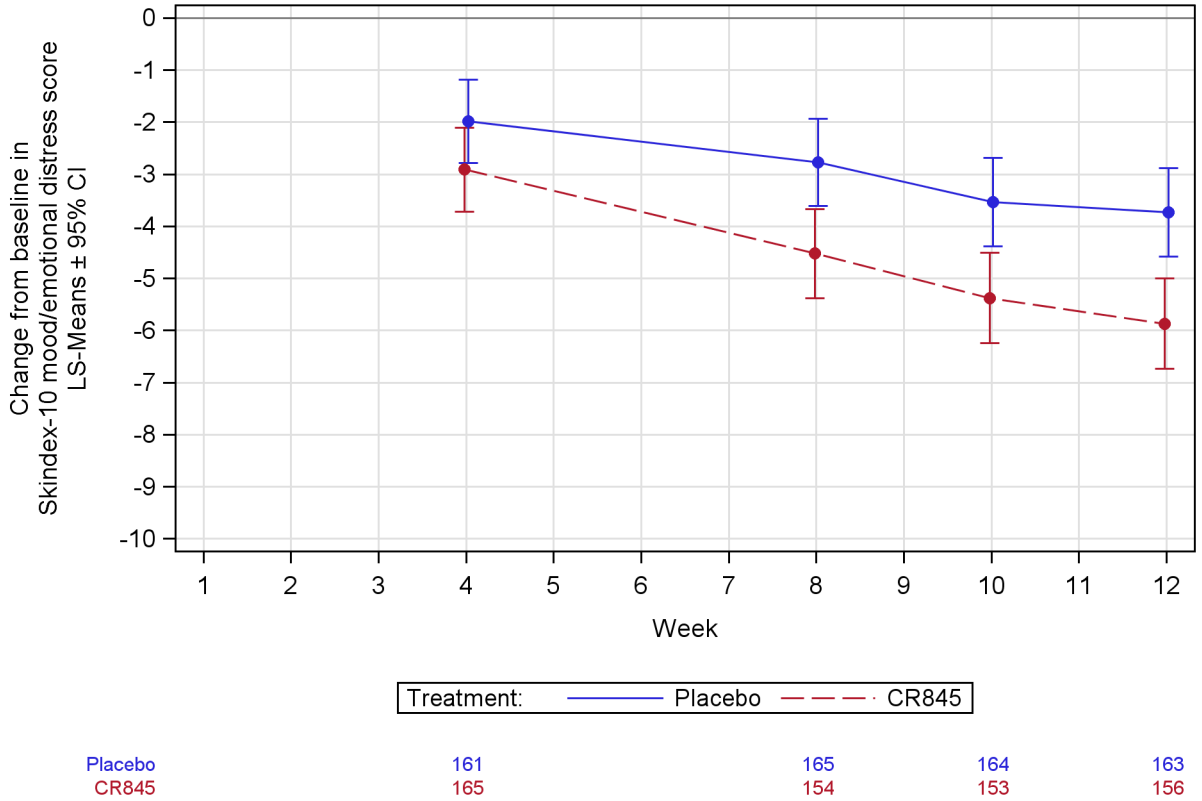
Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SMC_IMC0: Change from baseline in Skindex-10 mood/emotional distress score - MMRM results
ITT

Change from baseline in Skindex-10 mood/emotional distress score				Repeated measures analysis				
				Change from Baseline		Treatment Difference		
Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Week 4	CR845	189	165 (87.3)	-2.9 (0.4)	(-3.7, -2.1)	-0.9 (0.5)	(-1.9, 0.0)	0.059
	Placebo	189	161 (85.2)	-2.0 (0.4)	(-2.8, -1.2)			
Week 8	CR845	189	154 (81.5)	-4.5 (0.4)	(-5.4, -3.7)	-1.8 (0.5)	(-2.8, -0.7)	0.001 *
	Placebo	189	165 (87.3)	-2.8 (0.4)	(-3.6, -1.9)			
Week 10	CR845	189	153 (81.0)	-5.4 (0.4)	(-6.2, -4.5)	-1.8 (0.5)	(-2.9, -0.8)	<0.001 *
	Placebo	189	164 (86.8)	-3.5 (0.4)	(-4.4, -2.7)			
Week 12	CR845	189	156 (82.5)	-5.9 (0.4)	(-6.7, -5.0)	-2.1 (0.5)	(-3.2, -1.1)	<0.001 *
	Placebo	189	163 (86.2)	-3.7 (0.4)	(-4.6, -2.9)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval . * = significant treatment effect.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Figure AF2SMC_IMG0: Course of change from baseline in Skindex-10 mood/emotional distress score
ITT



Note: ITT = Intent-to-treat Set.
Symbols present least square mean (LS-Mean), bars present 95% confidence intervals (CI).
CR845 = Difelikefalin.
Source Table: AT2SMC_IMC0
Source Data: askin, created on: 17FEB2022

Table AT2SSC_IMH0: Change from baseline in Skindex-10 social functioning score
ITT

		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Skindex-10 social functioning score	Baseline	CR845	189	185 (97.9)	11.3 (7.7)	0	11.0	24	
		Placebo	189	187 (98.9)	12.6 (8.1)	0	13.0	24	
	Week 4	CR845	189	168 (88.9)	7.9 (7.4)	0	6.5	24	
		Placebo	189	165 (87.3)	9.9 (7.9)	0	9.0	24	
	Week 8	CR845	189	157 (83.1)	7.0 (7.1)	0	5.0	24	
		Placebo	189	169 (89.4)	9.2 (8.1)	0	8.0	24	
	Week 10	CR845	189	157 (83.1)	6.2 (7.0)	0	4.0	24	
		Placebo	189	166 (87.8)	8.3 (7.9)	0	6.5	24	
	Week 12	CR845	189	159 (84.1)	5.8 (6.7)	0	4.0	24	
		Placebo	189	166 (87.8)	8.0 (7.7)	0	5.0	24	
Change from baseline in Skindex-10 social functioning score	Week 4	CR845	189	165 (87.3)	-3.5 (6.6)	-24	-2.0	11	-0.08 [-0.29, 0.14]
		Placebo	189	163 (86.2)	-3.0 (6.9)	-23	-1.0	20	
	Week 8	CR845	189	154 (81.5)	-4.2 (6.7)	-24	-3.0	11	-0.09 [-0.31, 0.13]
		Placebo	189	167 (88.4)	-3.5 (7.6)	-24	-3.0	20	
	Week 10	CR845	189	155 (82.0)	-4.8 (6.7)	-24	-4.0	12	-0.07 [-0.29, 0.15]
		Placebo	189	164 (86.8)	-4.2 (7.9)	-24	-3.0	20	
	Week 12	CR845	189	157 (83.1)	-5.5 (7.5)	-24	-5.0	16	-0.11 [-0.33, 0.11]
		Placebo	189	164 (86.8)	-4.7 (7.4)	-24	-4.0	20	

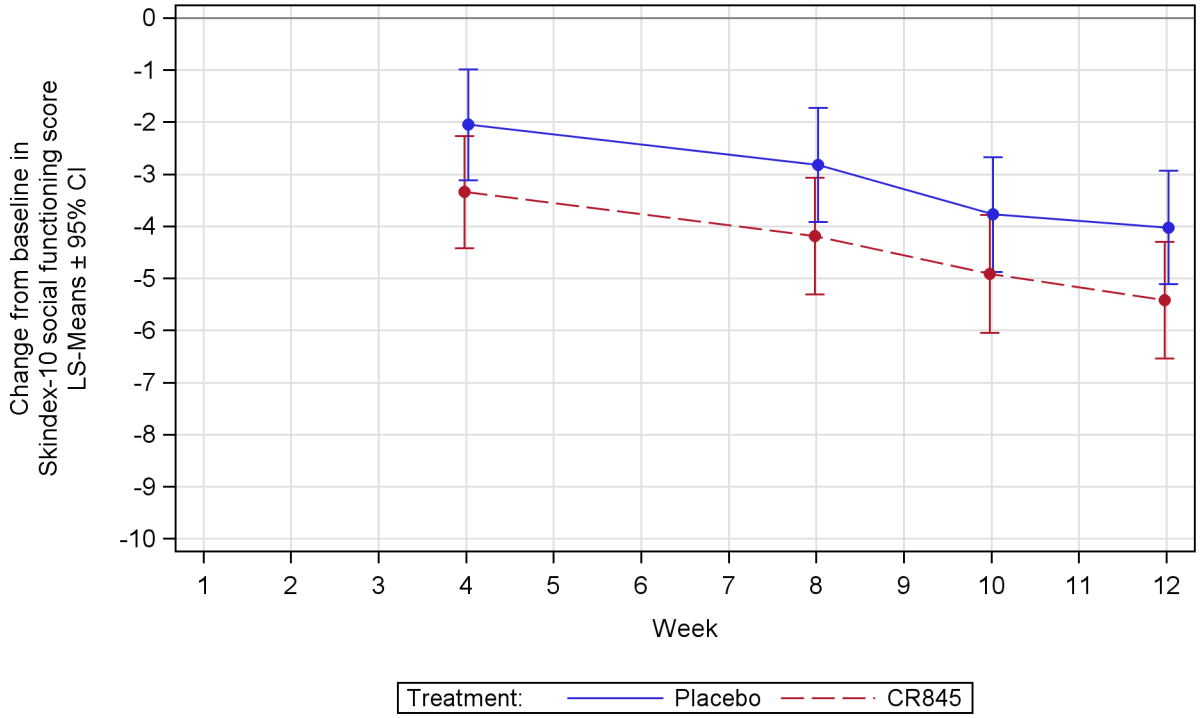
Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SSC_IMC0: Change from baseline in Skindex-10 social functioning score - MMRM results
ITT

Change from baseline in Skindex-10 social functioning score				Repeated measures analysis				
				Change from Baseline		Treatment Difference		
Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Week 4	CR845	189	165 (87.3)	-3.3 (0.5)	(-4.4, -2.3)	-1.3 (0.6)	(-2.6, -0.0)	0.047 *
	Placebo	189	163 (86.2)	-2.0 (0.5)	(-3.1, -1.0)			
Week 8	CR845	189	154 (81.5)	-4.2 (0.6)	(-5.3, -3.1)	-1.4 (0.7)	(-2.7, -0.0)	0.046 *
	Placebo	189	167 (88.4)	-2.8 (0.6)	(-3.9, -1.7)			
Week 10	CR845	189	155 (82.0)	-4.9 (0.6)	(-6.0, -3.8)	-1.1 (0.7)	(-2.5, 0.2)	0.096
	Placebo	189	164 (86.8)	-3.8 (0.6)	(-4.9, -2.7)			
Week 12	CR845	189	157 (83.1)	-5.4 (0.6)	(-6.5, -4.3)	-1.4 (0.7)	(-2.7, -0.1)	0.040 *
	Placebo	189	164 (86.8)	-4.0 (0.6)	(-5.1, -2.9)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval . * = significant treatment effect.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Figure AF2SSC_IMG0: Course of change from baseline in Skindex-10 social functioning score
ITT



Note: ITT = Intent-to-treat Set.
Symbols present least square mean (LS-Mean), bars present 95% confidence intervals (CI).
CR845 = Difelikefalin.
Source Table: AT2SSC_IMC0
Source Data: askin, created on: 17FEB2022

Table AT2SDCD3_IMP0: Decrease of Skindex-10 disease score of at least 3 points
ITT

		CR845			Placebo						
Variable	Time	N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Decrease of Skindex-10 disease score of at least 3 points	Week 12	189	157 (83.1)	114 (60.3) [53.0, 67.3]	189	161 (85.2)	101 (53.4) [46.1, 60.7]	1.129 [0.946, 1.346]	1.324 [0.881, 1.992]	6.9 [-3.6, 17.4]	0.178

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: askin, created on: 11FEB2022

Table AT2SMCD3_IMP0: Decrease of Skindex-10 mood/emotional distress score of at least 3 points
ITT

		CR845			Placebo						
Variable	Time	N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Decrease of Skindex-10 mood/emotional distress score of at least 3 points	Week 12	189	156 (82.5)	113 (59.8) [52.4, 66.8]	189	163 (86.2)	103 (54.5) [47.1, 61.7]	1.097 [0.921, 1.307]	1.241 [0.825, 1.867]	5.3 [-5.2, 15.8]	0.299

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: askin, created on: 11FEB2022

Table AT2SSCD4_IMP0: Decrease of Skindex-10 social functioning score of at least 4 points
ITT

		CR845			Placebo						
Variable	Time	N	nval	n (%) [95 % CI]	N	nval	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Decrease of Skindex-10 social functioning score of at least 4 points	Week 12	189	157 (83.1)	93 (49.2) [41.9, 56.6]	189	164 (86.8)	83 (43.9) [36.7, 51.3]	1.120 [0.902, 1.392]	1.237 [0.825, 1.855]	5.3 [-5.3, 15.9]	0.303

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: askin, created on: 11FEB2022

Table AT2A_SMS0: TEAEs by SOC and PT
SAF-S

	CR845		Placebo					
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
SOC: Cardiac disorders	189	11 (5.8) [2.9, 10.2]	188	8 (4.3) [1.9, 8.2]	1.368 [0.563, 3.324]	1.390 [0.546, 3.538]	1.6 [-3.4, 6.5]	0.488
SOC: Gastrointestinal disorders	189	47 (24.9) [18.9, 31.7]	188	37 (19.7) [14.3, 26.1]	1.264 [0.864, 1.849]	1.351 [0.829, 2.200]	5.2 [-3.7, 14.1]	0.227
Diarrhoea	189	18 (9.5) [5.7, 14.6]	188	7 (3.7) [1.5, 7.5]	2.558 [1.094, 5.981]	2.722 [1.109, 6.679]	5.8 [0.3, 11.3]	0.024 *
Vomiting	189	10 (5.3) [2.6, 9.5]	188	6 (3.2) [1.2, 6.8]	1.658 [0.615, 4.470]	1.695 [0.603, 4.761]	2.1 [-2.5, 6.7]	0.313
SOC: General disorders and administration site conditions	189	27 (14.3) [9.6, 20.1]	188	20 (10.6) [6.6, 16.0]	1.343 [0.781, 2.309]	1.400 [0.755, 2.595]	3.6 [-3.5, 10.8]	0.284
SOC: Infections and infestations	189	43 (22.8) [17.0, 29.4]	188	40 (21.3) [15.7, 27.8]	1.069 [0.731, 1.564]	1.090 [0.669, 1.774]	1.5 [-7.4, 10.4]	0.730
Nasopharyngitis	189	6 (3.2) [1.2, 6.8]	188	10 (5.3) [2.6, 9.6]	0.597 [0.221, 1.609]	0.584 [0.208, 1.640]	-2.1 [-6.7, 2.5]	0.302
SOC: Injury, poisoning and procedural complications	189	13 (6.9) [3.7, 11.5]	188	30 (16.0) [11.0, 22.0]	0.431 [0.232, 0.800]	0.389 [0.196, 0.772]	-9.1 [-16.0, -2.2]	0.006 *
SOC: Metabolism and nutrition disorders	189	15 (7.9) [4.5, 12.8]	188	18 (9.6) [5.8, 14.7]	0.829 [0.431, 1.595]	0.814 [0.397, 1.668]	-1.6 [-7.9, 4.6]	0.574
SOC: Musculoskeletal and connective tissue disorders	189	25 (13.2) [8.7, 18.9]	188	18 (9.6) [5.8, 14.7]	1.382 [0.780, 2.446]	1.440 [0.757, 2.738]	3.7 [-3.3, 10.6]	0.265
SOC: Nervous system disorders	189	34 (18.0) [12.8, 24.2]	188	22 (11.7) [7.5, 17.2]	1.537 [0.935, 2.527]	1.655 [0.927, 2.954]	6.3 [-1.4, 14.0]	0.087
Dizziness	189	13 (6.9) [3.7, 11.5]	188	2 (1.1) [0.1, 3.8]	6.466 [1.479, 28.260]	6.869 [1.528, 30.876]	5.8 [1.4, 10.2]	0.004 *
SOC: Psychiatric disorders	189	15 (7.9) [4.5, 12.8]	188	7 (3.7) [1.5, 7.5]	2.132 [0.889, 5.109]	2.229 [0.887, 5.599]	4.2 [-1.0, 9.5]	0.081

Note: SAF-S = Week 12 Safety Set. Only events are displayed with an incidence of at least 10 percent in a treatment group or 10 patients with an incidence of at least 1 percent in a treatment group.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 31JAN2022

Table AT2A_SMS0: TEAEs by SOC and PT
SAF-S

	CR845		Placebo					
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
SOC: Respiratory, thoracic and mediastinal disorders	189	30 (15.9) [11.0, 21.9]	188	22 (11.7) [7.5, 17.2]	1.356 [0.813, 2.263]	1.424 [0.788, 2.572]	4.2 [-3.3, 11.6]	0.241
SOC: Skin and subcutaneous tissue disorders	189	3 (1.6) [0.3, 4.6]	188	11 (5.9) [3.0, 10.2]	0.271 [0.077, 0.957]	0.260 [0.071, 0.946]	-4.3 [-8.6, 0.1]	0.029 *
SOC: Vascular disorders	189	19 (10.1) [6.2, 15.3]	188	14 (7.4) [4.1, 12.2]	1.350 [0.698, 2.612]	1.389 [0.675, 2.859]	2.6 [-3.6, 8.8]	0.371

Note: SAF-S = Week 12 Safety Set. Only events are displayed with an incidence of at least 10 percent in a treatment group or 10 patients with an incidence of at least 1 percent in a treatment group.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 31JAN2022

Table AT2AD_SMSD: Fatal TEAEs by SOC and PT
SAF-S

	CR845		Placebo	
Fatal TEAEs	N	n (%)	N	n (%)
SOC: Infections and infestations	189	2 (1.1)	188	2 (1.1)
Sepsis	189	1 (0.5)	188	0 (0.0)
Septic shock	189	0 (0.0)	188	2 (1.1)
Staphylococcal sepsis	189	1 (0.5)	188	0 (0.0)

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term.
Source Data: aae, created on: 31JAN2022

Table AT2AEGN_SMI0: Incidence of AESI gait disturbance - non-severe
SAF-S

	CR845		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
AESI gait disturbance - non-severe	189	2 (1.1) [0.1, 3.8]	188	2 (1.1) [0.1, 3.8]	0.995 [0.142, 6.988]	0.995 [0.139, 7.136]	-0.0 [-2.6, 2.6]	1.000 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 31JAN2022

Table AT2AEFN_SMI0: Incidence of AESI falls/injuries - non-severe
SAF-S

	CR845		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
AESI falls/injuries - non-severe	189	7 (3.7) [1.5, 7.5]	188	9 (4.8) [2.2, 8.9]	0.774 [0.294, 2.035]	0.765 [0.279, 2.098]	-1.1 [-5.7, 3.5]	0.602

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 31JAN2022

Table AT2AEVN_SMI0: Incidence of AESI dizziness - non-severe
SAF-S

	CR845		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
AESI dizziness - non-severe	189	13 (6.9) [3.7, 11.5]	188	2 (1.1) [0.1, 3.8]	6.466 [1.479, 28.260]	6.869 [1.528, 30.876]	5.8 [1.4, 10.2]	0.004 *

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 31JAN2022

Table AT2AEYN_SMI0: Incidence of AESI syncope - non-severe
SAF-S

	CR845		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
AESI syncope - non-severe	189	1 (0.5) [0.0, 2.9]	188	1 (0.5) [0.0, 2.9]	0.995 [0.063, 15.786]	0.995 [0.062, 16.020]	-0.0 [-2.0, 2.0]	1.000 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 31JAN2022

Table AT2AEON_SMI0: Incidence of AESI somnolence - non-severe
SAF-S

	CR845		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
AESI somnolence - non-severe	189	6 (3.2) [1.2, 6.8]	188	4 (2.1) [0.6, 5.4]	1.492 [0.428, 5.202]	1.508 [0.419, 5.433]	1.0 [-2.7, 4.8]	0.751 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 31JAN2022

Table AT2AEKN_SMI0: Incidence of AESI seizures - non-severe
SAF-S

	CR845		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
AESI seizures - non-severe	189	0 (0.0) [0.0, 1.9]	188	1 (0.5) [0.0, 2.9]	0.332 + [0.014, 8.088]	0.330 + [0.013, 8.148]	-0.5 [-2.1, 1.0]	0.499 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 31JAN2022

Table AT2AEMN_SMI0: Incidence of AESI mental status change - non-severe
SAF-S

	CR845		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
AESI mental status change - non-severe	189	5 (2.6) [0.9, 6.1]	188	6 (3.2) [1.2, 6.8]	0.829 [0.257, 2.670]	0.824 [0.247, 2.749]	-0.5 [-4.5, 3.4]	0.753

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 31JAN2022

Table AT2AEEN_SMI0: Incidence of AESI mood change - non-severe
SAF-S

	CR845		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
AESI mood change - non-severe	189	4 (2.1) [0.6, 5.3]	188	2 (1.1) [0.1, 3.8]	1.989 [0.369, 10.731]	2.011 [0.364, 11.113]	1.1 [-2.0, 4.1]	0.685 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 31JAN2022

Table AT2AEUN_SMI0: Incidence of AESI unusual feeling/sensation - non-severe
SAF-S

	CR845		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
AESI unusual feeling/sensation - non-severe	189	5 (2.6) [0.9, 6.1]	188	7 (3.7) [1.5, 7.5]	0.711 [0.230, 2.199]	0.703 [0.219, 2.254]	-1.1 [-5.2, 3.0]	0.552

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 31JAN2022

Table AT2AERN_SMI0: Incidence of AESI tachycardia/palpitation - non-severe
SAF-S

	CR845		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
AESI tachycardia/palpitation - non-severe	189	2 (1.1) [0.1, 3.8]	188	3 (1.6) [0.3, 4.6]	0.663 [0.112, 3.924]	0.660 [0.109, 3.993]	-0.5 [-3.4, 2.3]	0.685 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 31JAN2022

Table AT2WIC_ISHA: Change from baseline in weekly WI-NRS by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
< 65 years	Weekly WI-NRS	Baseline	CR845	135	135 (100.0)	7.0 (1.4)	4.3	7.00	10.0	
			Placebo	137	137 (100.0)	7.3 (1.6)	4.1	7.38	10.0	
		Week 1	CR845	135	131 (97.0)	6.0 (1.9)	1.6	6.14	9.9	
			Placebo	137	130 (94.9)	6.8 (2.0)	1.3	7.00	10.0	
		Week 2	CR845	135	129 (95.6)	5.4 (2.0)	0.4	5.29	10.0	
			Placebo	137	127 (92.7)	6.5 (2.0)	1.4	6.57	10.0	
		Week 3	CR845	135	127 (94.1)	5.0 (2.2)	0.0	5.00	10.0	
			Placebo	137	127 (92.7)	6.4 (2.1)	1.7	6.50	10.0	
		Week 4	CR845	135	126 (93.3)	4.8 (2.3)	0.0	4.93	10.0	
			Placebo	137	127 (92.7)	6.2 (2.3)	1.1	6.29	10.0	
		Week 5	CR845	135	123 (91.1)	4.6 (2.3)	0.0	4.71	10.0	
			Placebo	137	126 (92.0)	5.9 (2.3)	0.3	5.79	10.0	
		Week 6	CR845	135	122 (90.4)	4.3 (2.2)	0.0	4.29	9.1	
			Placebo	137	126 (92.0)	5.8 (2.5)	0.0	5.64	10.0	
		Week 7	CR845	135	118 (87.4)	4.1 (2.2)	0.0	4.00	10.0	
			Placebo	137	123 (89.8)	5.6 (2.6)	0.0	5.57	10.0	
		Week 8	CR845	135	118 (87.4)	4.2 (2.2)	0.0	4.21	9.4	
			Placebo	137	124 (90.5)	5.5 (2.6)	0.0	5.57	10.0	
		Week 9	CR845	135	118 (87.4)	3.9 (2.2)	0.0	3.93	8.9	
			Placebo	137	125 (91.2)	5.4 (2.6)	0.0	5.14	10.0	
		Week 10	CR845	135	117 (86.7)	3.7 (2.3)	0.0	3.71	9.0	
			Placebo	137	125 (91.2)	5.4 (2.7)	0.0	5.57	10.0	
		Week 11	CR845	135	112 (83.0)	3.6 (2.3)	0.0	3.14	9.1	
			Placebo	137	120 (87.6)	5.4 (2.6)	0.0	5.29	10.0	
		Week 12	CR845	135	112 (83.0)	3.6 (2.3)	0.0	3.14	9.2	
			Placebo	137	116 (84.7)	5.4 (2.6)	0.0	5.34	10.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	135	131 (97.0)	-1.0 (1.3)	-7.8	-0.75	2.1	-0.37 [-0.62, -0.13]
			Placebo	137	130 (94.9)	-0.5 (1.1)	-4.7	-0.14	1.9	
		Week 2	CR845	135	129 (95.6)	-1.5 (1.6)	-7.3	-1.18	1.6	-0.49 [-0.74, -0.24]
			Placebo	137	127 (92.7)	-0.8 (1.4)	-5.4	-0.39	2.4	
		Week 3	CR845	135	127 (94.1)	-2.0 (1.9)	-8.1	-1.43	1.4	-0.60 [-0.85, -0.35]
			Placebo	137	127 (92.7)	-0.9 (1.6)	-5.2	-0.41	2.5	
		Week 4	CR845	135	126 (93.3)	-2.2 (2.1)	-8.4	-1.84	1.4	-0.56 [-0.81, -0.31]
			Placebo	137	127 (92.7)	-1.1 (1.9)	-7.4	-0.57	3.2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table AT2WIC_ISHA: Change from baseline in weekly WI-NRS by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 5	CR845	135	123 (91.1)	-2.4 (2.1)	-8.7	-2.20	1.0	-0.54 [-0.80, -0.29]
			Placebo	137	126 (92.0)	-1.3 (1.9)	-7.7	-0.82	2.8	
		Week 6	CR845	135	122 (90.4)	-2.7 (2.1)	-8.9	-2.56	1.7	-0.59 [-0.84, -0.34]
			Placebo	137	126 (92.0)	-1.5 (2.1)	-9.0	-1.10	3.0	
		Week 7	CR845	135	118 (87.4)	-2.8 (2.1)	-8.2	-2.45	1.7	-0.55 [-0.81, -0.29]
			Placebo	137	123 (89.8)	-1.6 (2.2)	-9.0	-1.00	2.7	
		Week 8	CR845	135	118 (87.4)	-2.8 (2.2)	-8.1	-2.55	1.2	-0.48 [-0.73, -0.22]
			Placebo	137	124 (90.5)	-1.7 (2.3)	-9.0	-1.19	2.8	
		Week 9	CR845	135	118 (87.4)	-3.1 (2.1)	-8.1	-3.09	1.9	-0.56 [-0.81, -0.30]
			Placebo	137	125 (91.2)	-1.8 (2.3)	-9.0	-1.38	2.2	
		Week 10	CR845	135	117 (86.7)	-3.3 (2.3)	-8.7	-3.14	1.3	-0.63 [-0.89, -0.37]
			Placebo	137	125 (91.2)	-1.8 (2.3)	-9.0	-1.25	2.3	
		Week 11	CR845	135	112 (83.0)	-3.3 (2.4)	-8.3	-3.40	1.9	-0.66 [-0.92, -0.40]
			Placebo	137	120 (87.6)	-1.8 (2.2)	-9.0	-1.33	2.6	
		Week 12	CR845	135	112 (83.0)	-3.3 (2.4)	-8.3	-3.40	1.4	-0.63 [-0.89, -0.36]
			Placebo	137	116 (84.7)	-1.9 (2.2)	-9.0	-1.31	3.6	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table AT2WIC_ISHA: Change from baseline in weekly WI-NRS by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 65 years	Weekly WI-NRS	Baseline	CR845	54	54 (100.0)	7.2 (1.4)	4.2	7.25	10.0	
			Placebo	52	52 (100.0)	7.2 (1.7)	4.1	7.63	10.0	
		Week 1	CR845	54	52 (96.3)	6.3 (2.1)	1.4	6.93	10.0	
			Placebo	52	51 (98.1)	6.3 (1.9)	2.0	7.00	10.0	
		Week 2	CR845	54	50 (92.6)	5.9 (2.2)	1.0	6.43	9.2	
			Placebo	52	51 (98.1)	5.7 (2.2)	0.3	5.86	9.6	
		Week 3	CR845	54	51 (94.4)	5.4 (2.6)	0.3	6.14	9.4	
			Placebo	52	49 (94.2)	5.7 (2.2)	1.0	5.67	9.7	
		Week 4	CR845	54	50 (92.6)	5.0 (2.7)	0.0	5.64	9.5	
			Placebo	52	51 (98.1)	5.3 (2.1)	0.4	5.29	9.9	
		Week 5	CR845	54	49 (90.7)	5.1 (2.6)	0.0	5.14	9.3	
			Placebo	52	50 (96.2)	5.3 (2.1)	0.1	5.07	8.9	
		Week 6	CR845	54	48 (88.9)	5.0 (2.6)	0.0	5.07	9.6	
			Placebo	52	50 (96.2)	5.2 (2.1)	0.6	5.07	10.0	
		Week 7	CR845	54	48 (88.9)	4.9 (2.7)	0.0	4.79	9.4	
			Placebo	52	50 (96.2)	5.1 (2.2)	1.0	5.00	10.0	
		Week 8	CR845	54	49 (90.7)	4.8 (2.7)	0.0	4.67	9.9	
			Placebo	52	49 (94.2)	5.2 (2.3)	1.0	5.00	10.0	
		Week 9	CR845	54	47 (87.0)	4.6 (2.6)	0.0	4.57	9.4	
			Placebo	52	49 (94.2)	5.2 (2.4)	0.7	5.00	10.0	
		Week 10	CR845	54	48 (88.9)	4.6 (2.5)	0.0	4.64	9.4	
			Placebo	52	48 (92.3)	4.9 (2.4)	0.0	4.86	10.0	
		Week 11	CR845	54	45 (83.3)	4.6 (2.5)	0.0	4.29	9.3	
			Placebo	52	48 (92.3)	4.9 (2.2)	0.1	4.79	10.0	
		Week 12	CR845	54	45 (83.3)	4.6 (2.6)	0.3	4.43	9.4	
			Placebo	52	49 (94.2)	4.7 (2.6)	0.0	4.43	10.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	54	52 (96.3)	-0.9 (1.3)	-5.0	-0.61	2.1	-0.10 [-0.49, 0.29]
			Placebo	52	51 (98.1)	-0.8 (1.1)	-4.1	-0.77	1.5	
		Week 2	CR845	54	50 (92.6)	-1.3 (1.4)	-5.6	-1.04	1.6	0.11 [-0.28, 0.50]
			Placebo	52	51 (98.1)	-1.5 (1.8)	-8.7	-1.20	1.5	
		Week 3	CR845	54	51 (94.4)	-1.8 (1.8)	-6.6	-1.89	1.6	-0.21 [-0.60, 0.19]
			Placebo	52	49 (94.2)	-1.5 (1.8)	-7.4	-1.17	1.5	
		Week 4	CR845	54	50 (92.6)	-2.2 (2.0)	-7.3	-1.75	2.0	-0.19 [-0.58, 0.20]
			Placebo	52	51 (98.1)	-1.8 (2.0)	-8.6	-1.20	1.0	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table AT2WIC_ISHA: Change from baseline in weekly WI-NRS by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 5	CR845	54	49 (90.7)	-2.2 (2.0)	-7.3	-2.11	1.8	-0.14 [-0.53, 0.26]
			Placebo	52	50 (96.2)	-1.9 (2.1)	-8.7	-1.36	1.6	
		Week 6	CR845	54	48 (88.9)	-2.2 (2.1)	-8.9	-2.03	1.8	-0.09 [-0.49, 0.30]
			Placebo	52	50 (96.2)	-2.0 (2.1)	-8.3	-1.60	2.1	
		Week 7	CR845	54	48 (88.9)	-2.4 (2.2)	-8.9	-2.22	1.9	-0.12 [-0.51, 0.28]
			Placebo	52	50 (96.2)	-2.2 (2.1)	-7.8	-1.68	2.6	
		Week 8	CR845	54	49 (90.7)	-2.4 (2.2)	-8.9	-2.17	2.1	-0.16 [-0.56, 0.23]
			Placebo	52	49 (94.2)	-2.1 (2.2)	-7.5	-1.71	3.2	
		Week 9	CR845	54	47 (87.0)	-2.7 (2.2)	-8.9	-2.27	1.6	-0.27 [-0.68, 0.13]
			Placebo	52	49 (94.2)	-2.0 (2.4)	-8.1	-1.63	2.3	
		Week 10	CR845	54	48 (88.9)	-2.7 (2.1)	-8.9	-2.12	1.9	-0.19 [-0.59, 0.21]
			Placebo	52	48 (92.3)	-2.2 (2.5)	-9.0	-1.71	2.5	
		Week 11	CR845	54	45 (83.3)	-2.7 (2.0)	-6.6	-2.45	1.8	-0.21 [-0.61, 0.20]
			Placebo	52	48 (92.3)	-2.2 (2.3)	-7.2	-1.89	2.5	
		Week 12	CR845	54	45 (83.3)	-2.8 (2.3)	-7.0	-2.00	1.4	-0.12 [-0.53, 0.28]
			Placebo	52	49 (94.2)	-2.5 (2.6)	-8.7	-2.00	2.5	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table AT2WIC_ISHB: Change from baseline in weekly WI-NRS by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Male	Weekly WI-NRS	Baseline	CR845	112	112 (100.0)	7.03 (1.51)	4.2	7.00	10.0	
			Placebo	119	119 (100.0)	7.16 (1.63)	4.1	7.25	10.0	
		Week 1	CR845	112	109 (97.3)	6.11 (1.91)	1.6	6.43	9.9	
			Placebo	119	114 (95.8)	6.72 (1.91)	2.1	7.00	10.0	
		Week 2	CR845	112	106 (94.6)	5.60 (2.04)	1.0	5.79	10.0	
			Placebo	119	112 (94.1)	6.33 (2.10)	0.8	6.43	10.0	
		Week 3	CR845	112	103 (92.0)	5.19 (2.20)	0.3	5.86	10.0	
			Placebo	119	110 (92.4)	6.34 (2.23)	1.0	6.24	10.0	
		Week 4	CR845	112	102 (91.1)	4.84 (2.38)	0.0	4.93	10.0	
			Placebo	119	113 (95.0)	6.12 (2.26)	1.0	6.00	10.0	
		Week 5	CR845	112	99 (88.4)	4.66 (2.35)	0.0	4.57	10.0	
			Placebo	119	111 (93.3)	5.94 (2.31)	0.1	5.71	10.0	
		Week 6	CR845	112	98 (87.5)	4.31 (2.28)	0.0	4.14	9.5	
			Placebo	119	110 (92.4)	5.85 (2.32)	0.0	5.43	10.0	
		Week 7	CR845	112	95 (84.8)	4.23 (2.43)	0.0	4.00	10.0	
			Placebo	119	110 (92.4)	5.75 (2.41)	0.0	5.43	10.0	
		Week 8	CR845	112	96 (85.7)	4.30 (2.34)	0.0	4.24	9.9	
			Placebo	119	110 (92.4)	5.69 (2.45)	0.0	5.43	10.0	
		Week 9	CR845	112	93 (83.0)	4.13 (2.34)	0.0	4.00	9.1	
			Placebo	119	109 (91.6)	5.63 (2.45)	0.0	5.14	10.0	
		Week 10	CR845	112	95 (84.8)	3.96 (2.43)	0.0	4.00	9.0	
			Placebo	119	109 (91.6)	5.51 (2.47)	0.0	5.29	10.0	
		Week 11	CR845	112	89 (79.5)	3.93 (2.36)	0.0	3.57	9.1	
			Placebo	119	107 (89.9)	5.39 (2.46)	0.0	5.14	10.0	
		Week 12	CR845	112	90 (80.4)	3.90 (2.42)	0.0	3.57	9.4	
			Placebo	119	102 (85.7)	5.40 (2.52)	0.0	5.00	10.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	112	109 (97.3)	-0.93 (1.37)	-7.8	-0.66	2.1	-0.36 [-0.63, -0.10]
			Placebo	119	114 (95.8)	-0.48 (1.11)	-4.7	-0.28	1.9	
		Week 2	CR845	112	106 (94.6)	-1.42 (1.59)	-7.3	-1.07	1.6	-0.38 [-0.65, -0.11]
			Placebo	119	112 (94.1)	-0.84 (1.47)	-6.3	-0.61	2.2	
		Week 3	CR845	112	103 (92.0)	-1.85 (1.69)	-7.3	-1.39	1.4	-0.64 [-0.91, -0.36]
			Placebo	119	110 (92.4)	-0.82 (1.54)	-5.7	-0.41	2.5	
		Week 4	CR845	112	102 (91.1)	-2.19 (1.96)	-8.1	-1.88	1.4	-0.61 [-0.89, -0.34]
			Placebo	119	113 (95.0)	-1.05 (1.76)	-7.8	-0.63	2.6	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table AT2WIC_ISHB: Change from baseline in weekly WI-NRS by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 5	CR845	112	99 (88.4)	-2.41 (2.01)	-7.3	-2.25	1.0	-0.60 [-0.88, -0.32]
			Placebo	119	111 (93.3)	-1.25 (1.87)	-8.7	-1.03	2.8	
		Week 6	CR845	112	98 (87.5)	-2.75 (2.06)	-8.9	-2.59	1.7	-0.72 [-1.00, -0.44]
			Placebo	119	110 (92.4)	-1.32 (1.92)	-9.0	-1.08	2.3	
		Week 7	CR845	112	95 (84.8)	-2.80 (2.25)	-8.9	-2.54	1.7	-0.65 [-0.93, -0.36]
			Placebo	119	110 (92.4)	-1.43 (2.00)	-9.0	-1.17	2.6	
		Week 8	CR845	112	96 (85.7)	-2.72 (2.23)	-8.9	-2.76	1.2	-0.58 [-0.86, -0.30]
			Placebo	119	110 (92.4)	-1.48 (2.05)	-9.0	-1.13	3.2	
		Week 9	CR845	112	93 (83.0)	-2.90 (2.25)	-8.9	-3.13	1.9	-0.61 [-0.90, -0.33]
			Placebo	119	109 (91.6)	-1.57 (2.10)	-9.0	-1.36	2.3	
		Week 10	CR845	112	95 (84.8)	-3.08 (2.36)	-8.9	-3.14	1.3	-0.64 [-0.92, -0.36]
			Placebo	119	109 (91.6)	-1.64 (2.15)	-9.0	-1.30	2.5	
		Week 11	CR845	112	89 (79.5)	-3.07 (2.31)	-8.3	-3.25	1.9	-0.61 [-0.90, -0.33]
			Placebo	119	107 (89.9)	-1.71 (2.14)	-9.0	-1.38	2.6	
		Week 12	CR845	112	90 (80.4)	-3.10 (2.45)	-8.3	-3.21	1.4	-0.57 [-0.86, -0.28]
			Placebo	119	102 (85.7)	-1.78 (2.21)	-9.0	-1.46	3.6	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table AT2WIC_ISHB: Change from baseline in weekly WI-NRS by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Female	Weekly WI-NRS	Baseline	CR845	77	77 (100.0)	7.09 (1.34)	4.3	7.20	10.0	
			Placebo	70	70 (100.0)	7.38 (1.56)	4.1	7.81	10.0	
		Week 1	CR845	77	74 (96.1)	6.09 (1.96)	1.4	6.43	10.0	
			Placebo	70	67 (95.7)	6.61 (2.00)	1.3	7.00	10.0	
		Week 2	CR845	77	73 (94.8)	5.53 (2.10)	0.4	6.14	9.6	
			Placebo	70	66 (94.3)	6.16 (2.05)	0.3	6.50	10.0	
		Week 3	CR845	77	75 (97.4)	5.00 (2.40)	0.0	5.43	9.4	
			Placebo	70	66 (94.3)	5.90 (1.99)	1.6	6.00	10.0	
		Week 4	CR845	77	74 (96.1)	4.86 (2.46)	0.0	5.21	9.7	
			Placebo	70	65 (92.9)	5.65 (2.23)	0.4	5.57	10.0	
		Week 5	CR845	77	73 (94.8)	4.76 (2.43)	0.0	5.00	9.4	
			Placebo	70	65 (92.9)	5.43 (2.25)	0.3	5.29	10.0	
		Week 6	CR845	77	72 (93.5)	4.71 (2.42)	0.0	4.86	9.6	
			Placebo	70	66 (94.3)	5.15 (2.47)	0.3	5.36	10.0	
		Week 7	CR845	77	71 (92.2)	4.53 (2.30)	0.0	4.57	9.4	
			Placebo	70	63 (90.0)	4.99 (2.60)	0.0	5.14	10.0	
		Week 8	CR845	77	71 (92.2)	4.45 (2.41)	0.0	4.43	9.6	
			Placebo	70	63 (90.0)	4.99 (2.65)	0.0	5.14	10.0	
		Week 9	CR845	77	72 (93.5)	4.10 (2.35)	0.0	4.00	9.4	
			Placebo	70	65 (92.9)	4.97 (2.71)	0.1	5.14	10.0	
		Week 10	CR845	77	70 (90.9)	3.99 (2.35)	0.0	3.93	9.4	
			Placebo	70	64 (91.4)	4.91 (2.82)	0.0	5.36	10.0	
		Week 11	CR845	77	68 (88.3)	3.92 (2.48)	0.0	3.71	9.3	
			Placebo	70	61 (87.1)	5.06 (2.63)	0.0	5.14	10.0	
		Week 12	CR845	77	67 (87.0)	3.86 (2.50)	0.0	3.29	9.0	
			Placebo	70	63 (90.0)	4.84 (2.74)	0.0	5.00	10.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	77	74 (96.1)	-1.00 (1.26)	-5.0	-0.73	2.1	-0.18 [-0.51, 0.15]
			Placebo	70	67 (95.7)	-0.77 (1.20)	-3.9	-0.46	1.2	
		Week 2	CR845	77	73 (94.8)	-1.53 (1.60)	-5.8	-1.18	1.6	-0.19 [-0.52, 0.14]
			Placebo	70	66 (94.3)	-1.21 (1.76)	-8.7	-0.79	2.4	
		Week 3	CR845	77	75 (97.4)	-2.05 (2.06)	-8.1	-1.88	1.6	-0.29 [-0.62, 0.05]
			Placebo	70	66 (94.3)	-1.49 (1.83)	-7.4	-0.96	2.5	
		Week 4	CR845	77	74 (96.1)	-2.23 (2.20)	-8.4	-1.69	2.0	-0.22 [-0.55, 0.11]
			Placebo	70	65 (92.9)	-1.75 (2.12)	-8.6	-1.09	3.2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table AT2WIC_ISHB: Change from baseline in weekly WI-NRS by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 5	CR845	77	73 (94.8)	-2.32 (2.13)	-8.7	-2.11	1.8	-0.16 [-0.50, 0.17]
			Placebo	70	65 (92.9)	-1.97 (2.14)	-7.7	-1.38	2.4	
		Week 6	CR845	77	72 (93.5)	-2.42 (2.16)	-8.9	-2.03	1.8	-0.08 [-0.42, 0.25]
			Placebo	70	66 (94.3)	-2.23 (2.30)	-8.3	-1.90	3.0	
		Week 7	CR845	77	71 (92.2)	-2.57 (2.07)	-8.1	-2.27	1.9	-0.09 [-0.43, 0.25]
			Placebo	70	63 (90.0)	-2.38 (2.40)	-8.5	-1.91	2.7	
		Week 8	CR845	77	71 (92.2)	-2.64 (2.17)	-8.1	-2.33	2.1	-0.09 [-0.43, 0.25]
			Placebo	70	63 (90.0)	-2.43 (2.47)	-8.5	-1.79	2.8	
		Week 9	CR845	77	72 (93.5)	-2.99 (2.08)	-8.1	-2.76	1.6	-0.26 [-0.60, 0.08]
			Placebo	70	65 (92.9)	-2.39 (2.58)	-8.4	-1.80	2.2	
		Week 10	CR845	77	70 (90.9)	-3.12 (2.14)	-8.1	-2.86	1.9	-0.28 [-0.63, 0.06]
			Placebo	70	64 (91.4)	-2.43 (2.70)	-9.0	-1.71	1.7	
		Week 11	CR845	77	68 (88.3)	-3.17 (2.23)	-7.8	-3.18	1.8	-0.40 [-0.75, -0.05]
			Placebo	70	61 (87.1)	-2.25 (2.40)	-8.5	-1.79	2.0	
		Week 12	CR845	77	67 (87.0)	-3.29 (2.35)	-7.1	-3.13	1.4	-0.32 [-0.67, 0.03]
			Placebo	70	63 (90.0)	-2.51 (2.54)	-8.7	-2.02	1.7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table AT2WIC_ISHC: Change from baseline in weekly WI-NRS by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Black/African American	Weekly WI-NRS	Baseline	CR845	82	82 (100.0)	6.95 (1.35)	4.3	7.00	10.0	
			Placebo	76	76 (100.0)	7.18 (1.57)	4.3	7.38	10.0	
		Week 1	CR845	82	80 (97.6)	6.02 (1.92)	1.4	6.43	9.6	
			Placebo	76	70 (92.1)	6.63 (1.93)	2.0	6.86	10.0	
		Week 2	CR845	82	77 (93.9)	5.40 (2.01)	0.4	5.86	9.1	
			Placebo	76	68 (89.5)	6.25 (1.93)	1.0	6.36	10.0	
		Week 3	CR845	82	75 (91.5)	4.88 (2.23)	0.3	5.29	9.4	
			Placebo	76	70 (92.1)	6.03 (2.05)	1.0	6.00	10.0	
		Week 4	CR845	82	74 (90.2)	4.67 (2.44)	0.0	5.00	9.7	
			Placebo	76	71 (93.4)	5.81 (2.21)	1.0	5.57	10.0	
		Week 5	CR845	82	71 (86.6)	4.58 (2.42)	0.0	4.80	9.6	
			Placebo	76	71 (93.4)	5.72 (2.27)	0.3	5.57	10.0	
		Week 6	CR845	82	70 (85.4)	4.36 (2.41)	0.0	4.61	9.6	
			Placebo	76	70 (92.1)	5.38 (2.32)	0.0	5.21	10.0	
		Week 7	CR845	82	69 (84.1)	4.25 (2.35)	0.0	4.57	9.4	
			Placebo	76	70 (92.1)	5.31 (2.39)	0.0	5.38	10.0	
		Week 8	CR845	82	71 (86.6)	4.36 (2.40)	0.0	4.57	9.6	
			Placebo	76	69 (90.8)	5.23 (2.40)	0.0	5.14	10.0	
		Week 9	CR845	82	70 (85.4)	3.91 (2.34)	0.0	4.00	9.4	
			Placebo	76	71 (93.4)	5.14 (2.40)	0.0	5.00	10.0	
		Week 10	CR845	82	70 (85.4)	3.69 (2.34)	0.0	3.29	9.4	
			Placebo	76	71 (93.4)	5.08 (2.49)	0.0	5.00	10.0	
		Week 11	CR845	82	63 (76.8)	3.72 (2.42)	0.0	3.14	9.3	
			Placebo	76	69 (90.8)	5.07 (2.40)	0.0	5.00	10.0	
		Week 12	CR845	82	65 (79.3)	3.62 (2.46)	0.0	3.00	8.9	
			Placebo	76	67 (88.2)	4.99 (2.47)	0.0	4.86	10.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	82	80 (97.6)	-0.95 (1.51)	-7.8	-0.68	2.1	-0.26 [-0.58, 0.06]
			Placebo	76	70 (92.1)	-0.60 (1.10)	-3.5	-0.37	1.9	
		Week 2	CR845	82	77 (93.9)	-1.55 (1.77)	-7.3	-1.20	1.6	-0.39 [-0.72, -0.06]
			Placebo	76	68 (89.5)	-0.92 (1.38)	-5.4	-0.83	2.2	
		Week 3	CR845	82	75 (91.5)	-2.04 (1.89)	-8.1	-1.75	1.6	-0.48 [-0.81, -0.15]
			Placebo	76	70 (92.1)	-1.18 (1.65)	-5.2	-0.96	2.5	
		Week 4	CR845	82	74 (90.2)	-2.25 (2.23)	-8.4	-1.84	2.0	-0.41 [-0.73, -0.08]
			Placebo	76	71 (93.4)	-1.39 (1.99)	-7.4	-1.00	2.6	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table AT2WIC_ISHC: Change from baseline in weekly WI-NRS by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 5	CR845	82	71 (86.6)	-2.39 (2.23)	-8.7	-2.13	1.8	-0.42 [-0.75, -0.09]
			Placebo	76	71 (93.4)	-1.48 (2.07)	-7.7	-1.16	2.8	
		Week 6	CR845	82	70 (85.4)	-2.66 (2.30)	-8.9	-2.27	1.8	-0.37 [-0.71, -0.04]
			Placebo	76	70 (92.1)	-1.80 (2.25)	-9.0	-1.46	2.3	
		Week 7	CR845	82	69 (84.1)	-2.76 (2.23)	-8.9	-2.39	1.9	-0.37 [-0.71, -0.04]
			Placebo	76	70 (92.1)	-1.90 (2.35)	-9.0	-1.38	2.3	
		Week 8	CR845	82	71 (86.6)	-2.65 (2.30)	-8.9	-2.17	2.1	-0.27 [-0.61, 0.06]
			Placebo	76	69 (90.8)	-2.01 (2.36)	-9.0	-1.48	2.0	
		Week 9	CR845	82	70 (85.4)	-3.10 (2.19)	-8.9	-3.04	1.6	-0.46 [-0.79, -0.12]
			Placebo	76	71 (93.4)	-2.06 (2.33)	-9.0	-1.43	2.2	
		Week 10	CR845	82	70 (85.4)	-3.31 (2.31)	-8.9	-3.31	1.9	-0.50 [-0.84, -0.17]
			Placebo	76	71 (93.4)	-2.12 (2.45)	-9.0	-1.57	2.3	
		Week 11	CR845	82	63 (76.8)	-3.27 (2.34)	-8.3	-3.25	1.8	-0.52 [-0.87, -0.18]
			Placebo	76	69 (90.8)	-2.05 (2.33)	-9.0	-1.71	2.6	
		Week 12	CR845	82	65 (79.3)	-3.38 (2.42)	-8.3	-3.25	1.4	-0.51 [-0.85, -0.16]
			Placebo	76	67 (88.2)	-2.16 (2.38)	-9.0	-1.58	3.6	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table AT2WIC_ISHC: Change from baseline in weekly WI-NRS by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
White	Weekly WI-NRS	Baseline	CR845	91	91 (100.0)	7.15 (1.52)	4.2	7.13	10.0	
			Placebo	93	93 (100.0)	7.22 (1.62)	4.1	7.25	10.0	
		Week 1	CR845	91	87 (95.6)	6.10 (1.93)	1.6	6.29	9.9	
			Placebo	93	91 (97.8)	6.55 (1.93)	1.3	6.86	10.0	
		Week 2	CR845	91	86 (94.5)	5.65 (2.07)	1.0	5.86	9.6	
			Placebo	93	90 (96.8)	6.12 (2.20)	0.3	6.14	10.0	
		Week 3	CR845	91	88 (96.7)	5.24 (2.27)	0.4	5.79	9.4	
			Placebo	93	86 (92.5)	6.18 (2.23)	1.0	6.46	10.0	
		Week 4	CR845	91	87 (95.6)	4.95 (2.35)	0.0	5.57	9.7	
			Placebo	93	87 (93.5)	5.92 (2.29)	0.4	6.00	10.0	
		Week 5	CR845	91	85 (93.4)	4.71 (2.25)	0.0	4.86	9.4	
			Placebo	93	85 (91.4)	5.67 (2.34)	0.1	5.29	10.0	
		Week 6	CR845	91	85 (93.4)	4.51 (2.17)	0.1	4.43	9.5	
			Placebo	93	86 (92.5)	5.71 (2.42)	0.6	5.50	10.0	
		Week 7	CR845	91	82 (90.1)	4.31 (2.27)	0.0	4.14	9.4	
			Placebo	93	84 (90.3)	5.58 (2.50)	0.1	5.43	10.0	
		Week 8	CR845	91	81 (89.0)	4.26 (2.23)	0.0	4.14	9.9	
			Placebo	93	84 (90.3)	5.61 (2.58)	0.3	5.36	10.0	
		Week 9	CR845	91	81 (89.0)	4.16 (2.30)	0.0	4.00	9.1	
			Placebo	93	83 (89.2)	5.60 (2.59)	0.3	5.29	10.0	
		Week 10	CR845	91	80 (87.9)	4.08 (2.29)	0.1	4.00	9.0	
			Placebo	93	82 (88.2)	5.48 (2.63)	0.0	5.57	10.0	
		Week 11	CR845	91	80 (87.9)	3.98 (2.30)	0.0	3.86	9.1	
			Placebo	93	80 (86.0)	5.38 (2.57)	0.0	5.20	10.0	
		Week 12	CR845	91	78 (85.7)	3.98 (2.34)	0.0	3.73	9.4	
			Placebo	93	79 (84.9)	5.39 (2.65)	0.0	5.00	10.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	91	87 (95.6)	-1.04 (1.17)	-5.0	-0.79	0.9	-0.31 [-0.60, -0.01]
			Placebo	93	91 (97.8)	-0.66 (1.24)	-4.7	-0.38	1.5	
		Week 2	CR845	91	86 (94.5)	-1.46 (1.40)	-5.6	-1.19	1.6	-0.22 [-0.52, 0.08]
			Placebo	93	90 (96.8)	-1.10 (1.82)	-8.7	-0.63	2.4	
		Week 3	CR845	91	88 (96.7)	-1.91 (1.76)	-6.6	-1.60	1.4	-0.50 [-0.80, -0.20]
			Placebo	93	86 (92.5)	-1.01 (1.81)	-7.4	-0.46	2.5	
		Week 4	CR845	91	87 (95.6)	-2.23 (1.90)	-7.0	-1.88	1.4	-0.48 [-0.78, -0.18]
			Placebo	93	87 (93.5)	-1.30 (1.98)	-8.6	-0.88	3.2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table AT2WIC_ISHC: Change from baseline in weekly WI-NRS by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 5	CR845	91	85 (93.4)	-2.44 (1.88)	-7.0	-2.30	1.0	-0.44 [-0.74, -0.13]
			Placebo	93	85 (91.4)	-1.57 (2.08)	-8.7	-1.11	2.4	
		Week 6	CR845	91	85 (93.4)	-2.62 (1.93)	-6.9	-2.61	1.7	-0.55 [-0.86, -0.25]
			Placebo	93	86 (92.5)	-1.51 (2.07)	-8.3	-1.32	3.0	
		Week 7	CR845	91	82 (90.1)	-2.76 (2.10)	-7.1	-2.76	1.7	-0.55 [-0.86, -0.24]
			Placebo	93	84 (90.3)	-1.61 (2.08)	-7.8	-1.34	2.7	
		Week 8	CR845	91	81 (89.0)	-2.81 (2.11)	-7.0	-2.84	1.2	-0.57 [-0.88, -0.26]
			Placebo	93	84 (90.3)	-1.58 (2.17)	-7.5	-1.30	3.2	
		Week 9	CR845	91	81 (89.0)	-2.92 (2.16)	-7.0	-2.96	1.9	-0.59 [-0.90, -0.27]
			Placebo	93	83 (89.2)	-1.62 (2.26)	-8.1	-1.32	2.3	
		Week 10	CR845	91	80 (87.9)	-3.03 (2.20)	-7.5	-3.00	1.3	-0.60 [-0.91, -0.28]
			Placebo	93	82 (88.2)	-1.67 (2.33)	-9.0	-1.13	2.5	
		Week 11	CR845	91	80 (87.9)	-3.09 (2.26)	-7.6	-3.40	1.9	-0.60 [-0.91, -0.28]
			Placebo	93	80 (86.0)	-1.76 (2.21)	-7.2	-1.27	2.5	
		Week 12	CR845	91	78 (85.7)	-3.14 (2.43)	-8.2	-3.41	1.4	-0.56 [-0.88, -0.24]
			Placebo	93	79 (84.9)	-1.82 (2.30)	-8.7	-1.33	2.5	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table AT2WIC_ISHC: Change from baseline in weekly WI-NRS by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Other	Weekly WI-NRS	Baseline	CR845	15	15 (100.0)	7.14 (1.48)	4.8	7.00	10.0	
			Placebo	18	18 (100.0)	7.45 (1.68)	4.4	7.94	10.0	
		Week 1	CR845	15	15 (100.0)	6.64 (2.04)	2.7	6.86	10.0	
			Placebo	18	18 (100.0)	7.23 (1.96)	2.4	7.50	10.0	
		Week 2	CR845	15	15 (100.0)	6.14 (2.31)	2.3	6.50	10.0	
			Placebo	18	18 (100.0)	6.78 (1.90)	2.0	6.93	10.0	
		Week 3	CR845	15	14 (93.3)	5.66 (2.69)	0.0	6.00	10.0	
			Placebo	18	18 (100.0)	6.38 (2.05)	2.0	6.64	10.0	
		Week 4	CR845	15	14 (93.3)	5.25 (2.73)	0.0	5.39	10.0	
			Placebo	18	18 (100.0)	6.23 (2.11)	1.8	6.24	10.0	
		Week 5	CR845	15	15 (100.0)	5.25 (2.97)	0.0	5.17	10.0	
			Placebo	18	18 (100.0)	5.90 (2.20)	1.3	5.45	10.0	
		Week 6	CR845	15	14 (93.3)	4.96 (3.07)	0.0	5.08	9.1	
			Placebo	18	18 (100.0)	5.44 (2.52)	1.0	5.50	10.0	
		Week 7	CR845	15	14 (93.3)	5.20 (3.11)	0.0	5.24	10.0	
			Placebo	18	17 (94.4)	5.26 (2.90)	1.0	5.29	10.0	
		Week 8	CR845	15	14 (93.3)	5.01 (3.02)	0.0	5.93	9.0	
			Placebo	18	18 (100.0)	5.13 (2.83)	1.0	5.36	10.0	
		Week 9	CR845	15	13 (86.7)	4.91 (2.68)	0.0	5.57	9.0	
			Placebo	18	18 (100.0)	5.04 (2.97)	0.7	5.29	10.0	
		Week 10	CR845	15	14 (93.3)	4.76 (3.12)	0.0	5.64	8.5	
			Placebo	18	18 (100.0)	4.96 (2.96)	0.5	4.64	10.0	
		Week 11	CR845	15	13 (86.7)	4.59 (3.01)	0.3	4.60	9.0	
			Placebo	18	17 (94.4)	5.25 (2.73)	1.4	5.29	10.0	
		Week 12	CR845	15	13 (86.7)	4.59 (3.06)	0.0	4.80	9.0	
			Placebo	18	17 (94.4)	4.76 (2.98)	0.7	4.71	10.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	15	15 (100.0)	-0.49 (1.03)	-3.0	-0.17	0.8	-0.29 [-0.98, 0.40]
			Placebo	18	18 (100.0)	-0.22 (0.87)	-2.0	0.00	1.2	
		Week 2	CR845	15	15 (100.0)	-0.99 (1.71)	-5.8	-0.67	0.9	-0.24 [-0.93, 0.45]
			Placebo	18	18 (100.0)	-0.67 (1.05)	-3.3	-0.33	0.8	
		Week 3	CR845	15	14 (93.3)	-1.41 (2.24)	-8.1	-0.82	0.9	-0.20 [-0.90, 0.50]
			Placebo	18	18 (100.0)	-1.07 (1.10)	-3.4	-0.47	0.1	
		Week 4	CR845	15	14 (93.3)	-1.82 (2.22)	-8.1	-1.36	0.9	-0.34 [-1.04, 0.36]
			Placebo	18	18 (100.0)	-1.22 (1.31)	-3.7	-0.82	0.6	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table AT2WIC_ISHC: Change from baseline in weekly WI-NRS by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 5	CR845	15	15 (100.0)	-1.88 (2.24)	-8.1	-1.88	0.9	-0.19 [-0.87, 0.50]
			Placebo	18	18 (100.0)	-1.55 (1.34)	-4.0	-1.36	0.1	
		Week 6	CR845	15	14 (93.3)	-2.27 (2.28)	-8.1	-2.03	0.0	-0.13 [-0.82, 0.57]
			Placebo	18	18 (100.0)	-2.01 (1.86)	-6.3	-1.65	0.1	
		Week 7	CR845	15	14 (93.3)	-2.03 (2.37)	-8.1	-1.45	0.9	0.06 [-0.65, 0.76]
			Placebo	18	17 (94.4)	-2.16 (2.25)	-6.3	-1.86	0.6	
		Week 8	CR845	15	14 (93.3)	-2.22 (2.33)	-8.1	-1.67	0.0	0.04 [-0.66, 0.74]
			Placebo	18	18 (100.0)	-2.31 (2.25)	-6.6	-1.63	0.1	
		Week 9	CR845	15	13 (86.7)	-2.25 (2.17)	-8.1	-1.55	0.0	0.07 [-0.65, 0.78]
			Placebo	18	18 (100.0)	-2.41 (2.57)	-7.4	-1.79	1.1	
		Week 10	CR845	15	14 (93.3)	-2.46 (2.42)	-8.1	-2.03	0.5	0.01 [-0.69, 0.71]
			Placebo	18	18 (100.0)	-2.49 (2.53)	-7.6	-1.68	0.0	
		Week 11	CR845	15	13 (86.7)	-2.58 (2.19)	-7.8	-2.25	0.0	-0.19 [-0.91, 0.54]
			Placebo	18	17 (94.4)	-2.16 (2.24)	-5.6	-1.59	0.8	
		Week 12	CR845	15	13 (86.7)	-2.49 (2.30)	-7.1	-1.96	0.3	0.14 [-0.58, 0.86]
			Placebo	18	17 (94.4)	-2.84 (2.63)	-7.5	-1.86	0.3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table AT2WIC_ISHD: Change from baseline in weekly WI-NRS by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 4 to < 7	Weekly WI-NRS	Baseline	CR845	83	83 (100.0)	5.75 (0.78)	4.2	6.00	6.9	
			Placebo	80	80 (100.0)	5.64 (0.79)	4.1	5.63	6.9	
		Week 1	CR845	83	80 (96.4)	4.68 (1.47)	1.4	4.71	7.7	
			Placebo	80	75 (93.8)	5.12 (1.46)	1.3	5.00	8.6	
		Week 2	CR845	83	79 (95.2)	4.23 (1.59)	0.4	4.29	7.7	
			Placebo	80	75 (93.8)	4.92 (1.56)	0.8	5.00	8.9	
		Week 3	CR845	83	79 (95.2)	3.78 (1.80)	0.3	3.75	7.6	
			Placebo	80	75 (93.8)	4.85 (1.77)	1.0	4.86	9.1	
		Week 4	CR845	83	76 (91.6)	3.52 (1.85)	0.0	3.57	7.6	
			Placebo	80	75 (93.8)	4.74 (1.71)	1.0	5.00	9.3	
		Week 5	CR845	83	74 (89.2)	3.45 (1.81)	0.0	3.64	7.1	
			Placebo	80	74 (92.5)	4.59 (1.70)	1.0	4.71	9.4	
		Week 6	CR845	83	71 (85.5)	3.33 (1.80)	0.0	3.29	7.9	
			Placebo	80	75 (93.8)	4.48 (1.74)	0.7	4.43	9.0	
		Week 7	CR845	83	71 (85.5)	3.33 (1.86)	0.0	3.14	7.9	
			Placebo	80	74 (92.5)	4.35 (1.88)	0.1	4.43	9.0	
		Week 8	CR845	83	72 (86.7)	3.38 (1.89)	0.0	3.29	7.3	
			Placebo	80	73 (91.3)	4.35 (2.00)	0.3	4.43	9.6	
		Week 9	CR845	83	71 (85.5)	3.18 (1.86)	0.0	2.71	8.0	
			Placebo	80	74 (92.5)	4.37 (1.90)	0.3	4.57	8.9	
		Week 10	CR845	83	70 (84.3)	3.16 (1.86)	0.0	2.93	7.4	
			Placebo	80	75 (93.8)	4.30 (1.97)	0.1	4.57	9.0	
		Week 11	CR845	83	69 (83.1)	3.12 (1.80)	0.0	3.00	8.0	
			Placebo	80	74 (92.5)	4.18 (2.02)	0.0	4.43	8.3	
		Week 12	CR845	83	67 (80.7)	3.06 (1.88)	0.0	2.75	7.6	
			Placebo	80	70 (87.5)	4.16 (1.99)	0.0	4.27	9.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	83	80 (96.4)	-1.07 (1.28)	-4.4	-0.73	1.5	-0.43 [-0.75, -0.11]
			Placebo	80	75 (93.8)	-0.53 (1.19)	-3.9	-0.29	1.9	
		Week 2	CR845	83	79 (95.2)	-1.50 (1.40)	-5.3	-1.25	1.6	-0.56 [-0.88, -0.23]
			Placebo	80	75 (93.8)	-0.72 (1.43)	-5.9	-0.59	2.4	
		Week 3	CR845	83	79 (95.2)	-1.96 (1.64)	-5.8	-2.33	1.4	-0.72 [-1.04, -0.39]
			Placebo	80	75 (93.8)	-0.79 (1.62)	-5.7	-0.52	2.5	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table AT2WIC_ISHD: Change from baseline in weekly WI-NRS by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 4	CR845	83	76 (91.6)	-2.19 (1.79)	-6.3	-1.97	1.4	-0.78 [-1.11, -0.45]
			Placebo	80	75 (93.8)	-0.89 (1.54)	-5.3	-0.63	3.2	
		Week 5	CR845	83	74 (89.2)	-2.28 (1.73)	-6.3	-2.25	1.0	-0.74 [-1.08, -0.41]
			Placebo	80	74 (92.5)	-1.05 (1.59)	-5.2	-0.96	2.8	
		Week 6	CR845	83	71 (85.5)	-2.41 (1.73)	-6.3	-2.54	1.7	-0.74 [-1.08, -0.41]
			Placebo	80	75 (93.8)	-1.17 (1.63)	-6.2	-0.96	3.0	
		Week 7	CR845	83	71 (85.5)	-2.41 (1.78)	-5.8	-2.50	1.7	-0.63 [-0.96, -0.30]
			Placebo	80	74 (92.5)	-1.29 (1.77)	-6.2	-1.04	2.7	
		Week 8	CR845	83	72 (86.7)	-2.37 (1.83)	-6.9	-2.19	1.2	-0.58 [-0.91, -0.25]
			Placebo	80	73 (91.3)	-1.30 (1.87)	-6.0	-0.98	3.2	
		Week 9	CR845	83	71 (85.5)	-2.56 (1.80)	-6.3	-2.68	1.9	-0.71 [-1.05, -0.38]
			Placebo	80	74 (92.5)	-1.29 (1.79)	-6.3	-1.20	2.3	
		Week 10	CR845	83	70 (84.3)	-2.59 (1.74)	-6.3	-2.76	1.3	-0.69 [-1.03, -0.36]
			Placebo	80	75 (93.8)	-1.35 (1.86)	-6.7	-0.98	2.3	
		Week 11	CR845	83	69 (83.1)	-2.61 (1.70)	-6.3	-2.86	1.9	-0.63 [-0.96, -0.29]
			Placebo	80	74 (92.5)	-1.46 (1.96)	-6.6	-1.11	2.6	
		Week 12	CR845	83	67 (80.7)	-2.68 (1.91)	-6.3	-2.96	1.4	-0.60 [-0.94, -0.25]
			Placebo	80	70 (87.5)	-1.52 (1.95)	-6.7	-1.20	3.6	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table AT2WIC_ISHD: Change from baseline in weekly WI-NRS by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 7	Weekly WI-NRS	Baseline	CR845	106	106 (100.0)	8.08 (0.91)	7.0	8.00	10.0	
			Placebo	109	109 (100.0)	8.42 (0.86)	7.0	8.25	10.0	
		Week 1	CR845	106	103 (97.2)	7.20 (1.45)	1.9	7.14	10.0	
			Placebo	109	106 (97.2)	7.78 (1.40)	3.3	7.93	10.0	
		Week 2	CR845	106	100 (94.3)	6.63 (1.75)	1.4	7.00	10.0	
			Placebo	109	103 (94.5)	7.25 (1.85)	0.3	7.43	10.0	
		Week 3	CR845	106	99 (93.4)	6.18 (2.06)	0.0	6.43	10.0	
			Placebo	109	101 (92.7)	7.16 (1.86)	1.6	7.14	10.0	
		Week 4	CR845	106	100 (94.3)	5.86 (2.30)	0.0	6.14	10.0	
			Placebo	109	103 (94.5)	6.82 (2.20)	0.4	7.00	10.0	
		Week 5	CR845	106	98 (92.5)	5.64 (2.33)	0.0	5.71	10.0	
			Placebo	109	102 (93.6)	6.59 (2.31)	0.1	6.86	10.0	
		Week 6	CR845	106	99 (93.4)	5.31 (2.34)	0.0	5.71	9.6	
			Placebo	109	101 (92.7)	6.41 (2.49)	0.0	6.71	10.0	
		Week 7	CR845	106	95 (89.6)	5.12 (2.44)	0.0	5.00	10.0	
			Placebo	109	99 (90.8)	6.31 (2.58)	0.0	6.71	10.0	
		Week 8	CR845	106	95 (89.6)	5.11 (2.42)	0.0	5.14	9.9	
			Placebo	109	100 (91.7)	6.23 (2.60)	0.0	6.50	10.0	
		Week 9	CR845	106	94 (88.7)	4.82 (2.42)	0.0	5.00	9.4	
			Placebo	109	100 (91.7)	6.13 (2.73)	0.0	6.36	10.0	
		Week 10	CR845	106	95 (89.6)	4.57 (2.56)	0.0	4.57	9.4	
			Placebo	109	98 (89.9)	6.05 (2.80)	0.0	6.50	10.0	
		Week 11	CR845	106	88 (83.0)	4.56 (2.63)	0.0	4.43	9.3	
			Placebo	109	94 (86.2)	6.13 (2.55)	0.0	6.07	10.0	
		Week 12	CR845	106	90 (84.9)	4.49 (2.64)	0.0	4.42	9.4	
			Placebo	109	95 (87.2)	5.95 (2.76)	0.0	6.14	10.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	106	103 (97.2)	-0.87 (1.35)	-7.8	-0.68	2.1	-0.20 [-0.47, 0.08]
			Placebo	109	106 (97.2)	-0.63 (1.12)	-4.7	-0.33	1.6	
		Week 2	CR845	106	100 (94.3)	-1.44 (1.73)	-7.3	-1.04	1.6	-0.16 [-0.43, 0.12]
			Placebo	109	103 (94.5)	-1.17 (1.68)	-8.7	-0.75	1.5	
		Week 3	CR845	106	99 (93.4)	-1.91 (2.01)	-8.1	-1.25	1.6	-0.34 [-0.62, -0.06]
			Placebo	109	101 (92.7)	-1.27 (1.70)	-7.4	-0.86	1.7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table AT2WIC_ISHD: Change from baseline in weekly WI-NRS by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 4	CR845	106	100 (94.3)	-2.22 (2.25)	-8.4	-1.77	2.0	-0.28 [-0.56, -0.00]
			Placebo	109	103 (94.5)	-1.61 (2.11)	-8.6	-0.98	2.0	
		Week 5	CR845	106	98 (92.5)	-2.44 (2.27)	-8.7	-2.03	1.8	-0.26 [-0.54, 0.02]
			Placebo	109	102 (93.6)	-1.86 (2.19)	-8.7	-1.31	2.0	
		Week 6	CR845	106	99 (93.4)	-2.75 (2.34)	-8.9	-2.39	1.8	-0.30 [-0.58, -0.02]
			Placebo	109	101 (92.7)	-2.04 (2.35)	-9.0	-1.57	2.0	
		Week 7	CR845	106	95 (89.6)	-2.92 (2.41)	-8.9	-2.29	1.9	-0.33 [-0.61, -0.04]
			Placebo	109	99 (90.8)	-2.13 (2.41)	-9.0	-1.73	2.0	
		Week 8	CR845	106	95 (89.6)	-2.93 (2.42)	-8.9	-2.68	2.1	-0.29 [-0.58, -0.01]
			Placebo	109	100 (91.7)	-2.21 (2.43)	-9.0	-1.78	2.0	
		Week 9	CR845	106	94 (88.7)	-3.22 (2.38)	-8.9	-3.13	1.6	-0.37 [-0.65, -0.09]
			Placebo	109	100 (91.7)	-2.31 (2.56)	-9.0	-1.77	2.0	
		Week 10	CR845	106	95 (89.6)	-3.47 (2.52)	-8.9	-3.25	1.9	-0.42 [-0.70, -0.13]
			Placebo	109	98 (89.9)	-2.38 (2.66)	-9.0	-1.77	2.5	
		Week 11	CR845	106	88 (83.0)	-3.51 (2.57)	-8.3	-3.93	1.8	-0.50 [-0.80, -0.21]
			Placebo	109	94 (86.2)	-2.27 (2.39)	-9.0	-2.00	2.5	
		Week 12	CR845	106	90 (84.9)	-3.56 (2.66)	-8.3	-3.84	1.4	-0.42 [-0.71, -0.13]
			Placebo	109	95 (87.2)	-2.45 (2.56)	-9.0	-1.84	2.5	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table AT2WIC_ISHE: Change from baseline in weekly WI-NRS by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	Weekly WI-NRS	Baseline	CR845	164	164 (100.0)	6.99 (1.46)	4.2	7.00	10.0	
			Placebo	161	161 (100.0)	7.17 (1.58)	4.1	7.25	10.0	
		Week 1	CR845	164	160 (97.6)	6.07 (1.99)	1.4	6.43	10.0	
			Placebo	161	153 (95.0)	6.56 (1.93)	1.3	6.86	10.0	
		Week 2	CR845	164	156 (95.1)	5.52 (2.11)	0.4	5.86	10.0	
			Placebo	161	151 (93.8)	6.13 (2.08)	0.3	6.33	10.0	
		Week 3	CR845	164	153 (93.3)	5.05 (2.33)	0.0	5.57	10.0	
			Placebo	161	150 (93.2)	6.07 (2.14)	1.0	6.00	10.0	
		Week 4	CR845	164	152 (92.7)	4.81 (2.44)	0.0	5.00	10.0	
			Placebo	161	151 (93.8)	5.76 (2.25)	0.4	6.00	10.0	
		Week 5	CR845	164	148 (90.2)	4.65 (2.41)	0.0	4.85	10.0	
			Placebo	161	149 (92.5)	5.59 (2.28)	0.1	5.29	10.0	
		Week 6	CR845	164	146 (89.0)	4.45 (2.34)	0.0	4.43	9.5	
			Placebo	161	150 (93.2)	5.48 (2.37)	0.0	5.29	10.0	
		Week 7	CR845	164	142 (86.6)	4.31 (2.41)	0.0	4.29	10.0	
			Placebo	161	146 (90.7)	5.35 (2.46)	0.0	5.29	10.0	
		Week 8	CR845	164	143 (87.2)	4.32 (2.40)	0.0	4.43	9.9	
			Placebo	161	146 (90.7)	5.32 (2.52)	0.0	5.14	10.0	
		Week 9	CR845	164	141 (86.0)	4.07 (2.35)	0.0	4.00	9.1	
			Placebo	161	147 (91.3)	5.26 (2.52)	0.0	5.00	10.0	
		Week 10	CR845	164	141 (86.0)	3.96 (2.38)	0.0	4.00	9.4	
			Placebo	161	146 (90.7)	5.16 (2.61)	0.0	5.14	10.0	
		Week 11	CR845	164	135 (82.3)	3.96 (2.39)	0.0	3.71	9.3	
			Placebo	161	144 (89.4)	5.13 (2.53)	0.0	5.00	10.0	
		Week 12	CR845	164	133 (81.1)	3.92 (2.45)	0.0	3.57	9.4	
			Placebo	161	141 (87.6)	5.02 (2.61)	0.0	4.71	10.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	164	160 (97.6)	-0.93 (1.34)	-7.8	-0.62	2.1	-0.24 [-0.46, -0.02]
			Placebo	161	153 (95.0)	-0.63 (1.16)	-4.7	-0.36	1.9	
		Week 2	CR845	164	156 (95.1)	-1.45 (1.58)	-7.3	-1.13	1.6	-0.25 [-0.48, -0.03]
			Placebo	161	151 (93.8)	-1.05 (1.66)	-8.7	-0.63	2.4	
		Week 3	CR845	164	153 (93.3)	-1.91 (1.89)	-8.1	-1.39	1.6	-0.44 [-0.67, -0.21]
			Placebo	161	150 (93.2)	-1.11 (1.74)	-7.4	-0.59	2.5	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table AT2WIC_ISHE: Change from baseline in weekly WI-NRS by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 4	CR845	164	152 (92.7)	-2.18 (2.08)	-8.4	-1.80	2.0	-0.38 [-0.61, -0.15]
			Placebo	161	151 (93.8)	-1.41 (1.99)	-8.6	-1.00	3.2	
		Week 5	CR845	164	148 (90.2)	-2.36 (2.07)	-8.7	-2.07	1.8	-0.37 [-0.60, -0.14]
			Placebo	161	149 (92.5)	-1.60 (2.03)	-8.7	-1.25	2.8	
		Week 6	CR845	164	146 (89.0)	-2.58 (2.11)	-8.9	-2.45	1.8	-0.41 [-0.64, -0.18]
			Placebo	161	150 (93.2)	-1.70 (2.14)	-9.0	-1.45	3.0	
		Week 7	CR845	164	142 (86.6)	-2.68 (2.20)	-8.9	-2.33	1.9	-0.39 [-0.62, -0.16]
			Placebo	161	146 (90.7)	-1.81 (2.21)	-9.0	-1.61	2.7	
		Week 8	CR845	164	143 (87.2)	-2.66 (2.24)	-8.9	-2.49	2.1	-0.36 [-0.59, -0.13]
			Placebo	161	146 (90.7)	-1.85 (2.27)	-9.0	-1.41	3.2	
		Week 9	CR845	164	141 (86.0)	-2.92 (2.19)	-8.9	-2.86	1.9	-0.45 [-0.68, -0.21]
			Placebo	161	147 (91.3)	-1.91 (2.32)	-9.0	-1.57	2.3	
		Week 10	CR845	164	141 (86.0)	-3.05 (2.25)	-8.9	-2.95	1.9	-0.46 [-0.70, -0.23]
			Placebo	161	146 (90.7)	-1.97 (2.43)	-9.0	-1.43	2.5	
		Week 11	CR845	164	135 (82.3)	-3.01 (2.25)	-8.3	-2.96	1.9	-0.44 [-0.68, -0.21]
			Placebo	161	144 (89.4)	-2.00 (2.31)	-9.0	-1.60	2.6	
		Week 12	CR845	164	133 (81.1)	-3.07 (2.42)	-8.3	-3.04	1.4	-0.39 [-0.63, -0.15]
			Placebo	161	141 (87.6)	-2.12 (2.40)	-9.0	-1.54	3.6	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table AT2WIC_ISHE: Change from baseline in weekly WI-NRS by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	Weekly WI-NRS	Baseline	CR845	25	25 (100.0)	7.53 (1.21)	5.3	7.50	10.0	
			Placebo	28	28 (100.0)	7.68 (1.68)	4.3	8.06	10.0	
		Week 1	CR845	25	23 (92.0)	6.33 (1.37)	3.0	6.43	9.3	
			Placebo	28	28 (100.0)	7.33 (1.90)	2.3	7.57	10.0	
		Week 2	CR845	25	23 (92.0)	5.90 (1.72)	3.0	6.14	9.1	
			Placebo	28	27 (96.4)	7.08 (1.91)	3.7	6.86	10.0	
		Week 3	CR845	25	25 (100.0)	5.47 (1.96)	1.6	5.86	9.4	
			Placebo	28	26 (92.9)	6.82 (2.12)	2.3	7.00	10.0	
		Week 4	CR845	25	24 (96.0)	5.11 (2.21)	0.9	5.43	9.0	
			Placebo	28	27 (96.4)	6.97 (2.04)	3.1	6.86	10.0	
		Week 5	CR845	25	24 (96.0)	5.00 (2.21)	1.1	4.86	9.1	
			Placebo	28	27 (96.4)	6.65 (2.22)	2.0	6.86	10.0	
		Week 6	CR845	25	24 (96.0)	4.66 (2.40)	1.1	4.21	9.6	
			Placebo	28	26 (92.9)	6.24 (2.48)	1.3	6.54	10.0	
		Week 7	CR845	25	24 (96.0)	4.62 (2.21)	0.7	4.71	9.0	
			Placebo	28	27 (96.4)	6.15 (2.63)	0.6	6.71	10.0	
		Week 8	CR845	25	24 (96.0)	4.62 (2.11)	1.6	4.21	9.3	
			Placebo	28	27 (96.4)	6.04 (2.59)	1.0	6.00	10.0	
		Week 9	CR845	25	24 (96.0)	4.39 (2.31)	0.9	4.29	9.4	
			Placebo	28	27 (96.4)	6.04 (2.72)	0.3	6.29	10.0	
		Week 10	CR845	25	24 (96.0)	4.07 (2.46)	0.0	4.21	8.5	
			Placebo	28	27 (96.4)	5.98 (2.59)	0.5	5.86	10.0	
		Week 11	CR845	25	22 (88.0)	3.70 (2.52)	0.0	3.07	8.6	
			Placebo	28	24 (85.7)	6.14 (2.32)	1.9	5.86	10.0	
		Week 12	CR845	25	24 (96.0)	3.68 (2.48)	0.0	3.21	8.1	
			Placebo	28	24 (85.7)	6.19 (2.45)	0.7	6.00	10.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	25	23 (92.0)	-1.11 (1.23)	-4.3	-1.25	1.0	-0.67 [-1.23, -0.10]
			Placebo	28	28 (100.0)	-0.36 (1.05)	-3.4	-0.10	1.3	
		Week 2	CR845	25	23 (92.0)	-1.54 (1.70)	-6.3	-1.21	0.6	-0.69 [-1.26, -0.11]
			Placebo	28	27 (96.4)	-0.59 (1.04)	-3.3	-0.57	1.5	
		Week 3	CR845	25	25 (100.0)	-2.06 (1.57)	-5.6	-2.46	0.9	-0.85 [-1.42, -0.27]
			Placebo	28	26 (92.9)	-0.85 (1.28)	-3.4	-0.61	1.4	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table AT2WIC_ISHE: Change from baseline in weekly WI-NRS by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 4	CR845	25	24 (96.0)	-2.35 (1.93)	-6.4	-1.88	0.6	-0.96 [-1.54, -0.38]
			Placebo	28	27 (96.4)	-0.74 (1.41)	-3.7	-0.43	1.9	
		Week 5	CR845	25	24 (96.0)	-2.46 (1.96)	-7.3	-2.26	0.1	-0.74 [-1.31, -0.17]
			Placebo	28	27 (96.4)	-1.07 (1.79)	-5.8	-0.83	1.7	
		Week 6	CR845	25	24 (96.0)	-2.79 (2.10)	-7.1	-2.68	0.9	-0.65 [-1.22, -0.08]
			Placebo	28	26 (92.9)	-1.46 (1.99)	-6.3	-0.78	1.3	
		Week 7	CR845	25	24 (96.0)	-2.84 (2.01)	-7.2	-2.51	0.6	-0.62 [-1.18, -0.05]
			Placebo	28	27 (96.4)	-1.56 (2.13)	-6.7	-0.79	0.8	
		Week 8	CR845	25	24 (96.0)	-2.84 (1.97)	-7.5	-2.97	0.6	-0.56 [-1.12, 0.00]
			Placebo	28	27 (96.4)	-1.68 (2.18)	-7.3	-1.00	0.4	
		Week 9	CR845	25	24 (96.0)	-3.07 (2.07)	-7.8	-3.01	1.0	-0.63 [-1.20, -0.07]
			Placebo	28	27 (96.4)	-1.67 (2.34)	-7.4	-1.00	0.9	
		Week 10	CR845	25	24 (96.0)	-3.39 (2.36)	-8.7	-3.18	0.7	-0.72 [-1.29, -0.15]
			Placebo	28	27 (96.4)	-1.74 (2.22)	-7.6	-1.07	0.6	
		Week 11	CR845	25	22 (88.0)	-3.74 (2.35)	-8.0	-3.78	0.4	-1.15 [-1.77, -0.52]
			Placebo	28	24 (85.7)	-1.37 (1.77)	-5.8	-1.04	1.1	
		Week 12	CR845	25	24 (96.0)	-3.78 (2.29)	-8.1	-4.15	1.1	-0.95 [-1.55, -0.35]
			Placebo	28	24 (85.7)	-1.67 (2.13)	-7.5	-1.51	1.1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table AT2WIC_ISHF: Change from baseline in weekly WI-NRS by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	Weekly WI-NRS	Baseline	CR845	117	117 (100.0)	6.92 (1.47)	4.2	6.88	10.0	
			Placebo	111	111 (100.0)	7.20 (1.58)	4.1	7.38	10.0	
		Week 1	CR845	117	113 (96.6)	5.99 (2.00)	1.4	6.29	10.0	
			Placebo	111	105 (94.6)	6.78 (1.85)	1.3	7.00	10.0	
		Week 2	CR845	117	112 (95.7)	5.47 (2.17)	0.4	5.71	10.0	
			Placebo	111	103 (92.8)	6.30 (2.04)	0.3	6.50	10.0	
		Week 3	CR845	117	114 (97.4)	5.00 (2.35)	0.0	5.29	10.0	
			Placebo	111	100 (90.1)	6.29 (2.01)	1.0	6.31	10.0	
		Week 4	CR845	117	112 (95.7)	4.68 (2.43)	0.0	4.93	10.0	
			Placebo	111	104 (93.7)	6.04 (2.15)	0.4	6.00	10.0	
		Week 5	CR845	117	109 (93.2)	4.49 (2.40)	0.0	4.33	10.0	
			Placebo	111	103 (92.8)	5.88 (2.21)	0.1	5.71	10.0	
		Week 6	CR845	117	108 (92.3)	4.30 (2.35)	0.0	4.29	9.6	
			Placebo	111	103 (92.8)	5.63 (2.38)	0.0	5.43	10.0	
		Week 7	CR845	117	105 (89.7)	4.17 (2.40)	0.0	4.00	10.0	
			Placebo	111	104 (93.7)	5.59 (2.43)	0.0	5.43	10.0	
		Week 8	CR845	117	107 (91.5)	4.08 (2.40)	0.0	4.14	9.9	
			Placebo	111	103 (92.8)	5.58 (2.44)	0.0	5.57	10.0	
		Week 9	CR845	117	105 (89.7)	3.91 (2.35)	0.0	3.86	9.4	
			Placebo	111	104 (93.7)	5.52 (2.47)	0.0	5.21	10.0	
		Week 10	CR845	117	104 (88.9)	3.81 (2.32)	0.0	3.86	8.7	
			Placebo	111	103 (92.8)	5.40 (2.59)	0.0	5.57	10.0	
		Week 11	CR845	117	100 (85.5)	3.79 (2.39)	0.0	3.29	9.0	
			Placebo	111	102 (91.9)	5.37 (2.45)	0.0	5.14	10.0	
		Week 12	CR845	117	99 (84.6)	3.67 (2.39)	0.0	3.14	9.4	
			Placebo	111	99 (89.2)	5.26 (2.68)	0.0	5.00	10.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	117	113 (96.6)	-0.94 (1.20)	-5.0	-0.71	2.1	-0.39 [-0.66, -0.13]
			Placebo	111	105 (94.6)	-0.48 (1.13)	-4.3	-0.25	1.9	
		Week 2	CR845	117	112 (95.7)	-1.41 (1.43)	-5.8	-1.11	1.6	-0.32 [-0.59, -0.05]
			Placebo	111	103 (92.8)	-0.91 (1.68)	-8.7	-0.57	2.4	
		Week 3	CR845	117	114 (97.4)	-1.93 (1.78)	-8.1	-1.41	1.4	-0.58 [-0.86, -0.31]
			Placebo	111	100 (90.1)	-0.92 (1.66)	-7.4	-0.43	2.5	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table AT2WIC_ISHF: Change from baseline in weekly WI-NRS by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 4	CR845	117	112 (95.7)	-2.26 (1.91)	-8.1	-1.88	1.4	-0.55 [-0.82, -0.28]
			Placebo	111	104 (93.7)	-1.19 (1.94)	-8.6	-0.88	3.2	
		Week 5	CR845	117	109 (93.2)	-2.45 (1.91)	-8.1	-2.20	1.0	-0.56 [-0.83, -0.28]
			Placebo	111	103 (92.8)	-1.36 (2.02)	-8.7	-0.84	2.8	
		Week 6	CR845	117	108 (92.3)	-2.66 (1.96)	-8.1	-2.56	1.7	-0.52 [-0.79, -0.24]
			Placebo	111	103 (92.8)	-1.59 (2.22)	-9.0	-1.30	3.0	
		Week 7	CR845	117	105 (89.7)	-2.76 (2.03)	-8.1	-2.55	1.7	-0.52 [-0.80, -0.25]
			Placebo	111	104 (93.7)	-1.64 (2.24)	-9.0	-1.18	2.7	
		Week 8	CR845	117	107 (91.5)	-2.84 (2.12)	-8.1	-2.84	1.2	-0.54 [-0.81, -0.26]
			Placebo	111	103 (92.8)	-1.66 (2.26)	-9.0	-1.30	3.2	
		Week 9	CR845	117	105 (89.7)	-3.02 (2.04)	-8.1	-2.96	1.9	-0.60 [-0.88, -0.32]
			Placebo	111	104 (93.7)	-1.71 (2.32)	-9.0	-1.26	2.3	
		Week 10	CR845	117	104 (88.9)	-3.13 (2.05)	-8.1	-3.14	1.3	-0.58 [-0.86, -0.30]
			Placebo	111	103 (92.8)	-1.81 (2.47)	-9.0	-1.25	2.5	
		Week 11	CR845	117	100 (85.5)	-3.13 (2.14)	-7.8	-3.35	1.9	-0.57 [-0.85, -0.29]
			Placebo	111	102 (91.9)	-1.86 (2.32)	-9.0	-1.48	2.6	
		Week 12	CR845	117	99 (84.6)	-3.27 (2.25)	-8.2	-3.38	1.4	-0.54 [-0.82, -0.25]
			Placebo	111	99 (89.2)	-1.97 (2.55)	-9.0	-1.34	3.6	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table AT2WIC_ISHF: Change from baseline in weekly WI-NRS by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	Weekly WI-NRS	Baseline	CR845	72	72 (100.0)	7.27 (1.36)	4.3	7.31	10.0	
			Placebo	78	78 (100.0)	7.30 (1.65)	4.1	7.79	10.0	
		Week 1	CR845	72	70 (97.2)	6.28 (1.79)	1.9	6.64	9.6	
			Placebo	78	76 (97.4)	6.54 (2.06)	2.1	6.71	10.0	
		Week 2	CR845	72	67 (93.1)	5.73 (1.87)	1.0	6.14	9.1	
			Placebo	78	75 (96.2)	6.22 (2.15)	1.0	6.29	10.0	
		Week 3	CR845	72	64 (88.9)	5.31 (2.16)	0.3	5.86	9.1	
			Placebo	78	76 (97.4)	6.02 (2.32)	1.0	6.00	10.0	
		Week 4	CR845	72	64 (88.9)	5.14 (2.36)	0.0	5.39	9.7	
			Placebo	78	74 (94.9)	5.82 (2.41)	1.0	5.79	10.0	
		Week 5	CR845	72	63 (87.5)	5.06 (2.32)	0.0	5.00	9.6	
			Placebo	78	73 (93.6)	5.57 (2.42)	0.3	5.14	10.0	
		Week 6	CR845	72	62 (86.1)	4.79 (2.30)	0.0	4.79	9.3	
			Placebo	78	73 (93.6)	5.53 (2.44)	0.7	5.29	10.0	
		Week 7	CR845	72	61 (84.7)	4.69 (2.32)	0.0	4.57	9.4	
			Placebo	78	69 (88.5)	5.30 (2.62)	0.4	5.29	10.0	
		Week 8	CR845	72	60 (83.3)	4.87 (2.23)	0.0	4.70	9.6	
			Placebo	78	70 (89.7)	5.23 (2.69)	0.1	5.14	10.0	
		Week 9	CR845	72	60 (83.3)	4.47 (2.30)	0.0	4.21	9.1	
			Placebo	78	70 (89.7)	5.18 (2.70)	0.3	4.93	10.0	
		Week 10	CR845	72	61 (84.7)	4.25 (2.49)	0.0	4.00	9.4	
			Placebo	78	70 (89.7)	5.13 (2.66)	0.1	5.21	10.0	
		Week 11	CR845	72	57 (79.2)	4.16 (2.42)	0.0	3.86	9.3	
			Placebo	78	66 (84.6)	5.12 (2.63)	0.0	5.15	10.0	
		Week 12	CR845	72	58 (80.6)	4.24 (2.52)	0.0	4.00	9.2	
			Placebo	78	66 (84.6)	5.08 (2.52)	0.0	4.86	10.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	72	70 (97.2)	-0.98 (1.51)	-7.8	-0.68	2.1	-0.18 [-0.51, 0.14]
			Placebo	78	76 (97.4)	-0.73 (1.17)	-4.7	-0.48	1.3	
		Week 2	CR845	72	67 (93.1)	-1.56 (1.83)	-7.3	-1.18	1.6	-0.30 [-0.63, 0.03]
			Placebo	78	75 (96.2)	-1.06 (1.46)	-5.4	-0.71	1.4	
		Week 3	CR845	72	64 (88.9)	-1.93 (1.98)	-8.1	-1.69	1.6	-0.36 [-0.70, -0.03]
			Placebo	78	76 (97.4)	-1.26 (1.70)	-5.0	-1.00	1.5	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table AT2WIC_ISHF: Change from baseline in weekly WI-NRS by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 4	CR845	72	64 (88.9)	-2.11 (2.30)	-8.4	-1.69	2.0	-0.31 [-0.65, 0.03]
			Placebo	78	74 (94.9)	-1.46 (1.90)	-6.1	-0.99	1.7	
		Week 5	CR845	72	63 (87.5)	-2.23 (2.29)	-8.7	-2.00	1.8	-0.23 [-0.57, 0.10]
			Placebo	78	73 (93.6)	-1.74 (1.96)	-6.8	-1.29	1.7	
		Week 6	CR845	72	62 (86.1)	-2.51 (2.36)	-8.9	-2.20	1.8	-0.34 [-0.68, -0.00]
			Placebo	78	73 (93.6)	-1.78 (1.96)	-6.4	-1.43	1.3	
		Week 7	CR845	72	61 (84.7)	-2.60 (2.40)	-8.9	-2.25	1.9	-0.28 [-0.62, 0.07]
			Placebo	78	69 (88.5)	-1.98 (2.14)	-6.8	-1.73	1.1	
		Week 8	CR845	72	60 (83.3)	-2.42 (2.32)	-8.9	-2.19	2.1	-0.16 [-0.50, 0.19]
			Placebo	78	70 (89.7)	-2.06 (2.23)	-7.3	-1.72	1.0	
		Week 9	CR845	72	60 (83.3)	-2.81 (2.39)	-8.9	-2.65	1.6	-0.29 [-0.64, 0.06]
			Placebo	78	70 (89.7)	-2.12 (2.31)	-7.4	-1.58	1.6	
		Week 10	CR845	72	61 (84.7)	-3.03 (2.59)	-8.9	-2.82	1.9	-0.38 [-0.73, -0.04]
			Placebo	78	70 (89.7)	-2.11 (2.27)	-7.9	-1.77	2.0	
		Week 11	CR845	72	57 (79.2)	-3.09 (2.50)	-8.3	-3.11	1.8	-0.48 [-0.84, -0.12]
			Placebo	78	66 (84.6)	-1.99 (2.13)	-6.8	-1.50	2.0	
		Week 12	CR845	72	58 (80.6)	-3.04 (2.66)	-8.3	-2.78	1.4	-0.36 [-0.72, -0.00]
			Placebo	78	66 (84.6)	-2.19 (2.07)	-7.5	-1.67	1.1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table AT2WIC_ISCA: Change from baseline in weekly WI-NRS - MMRM results by age
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
A: Age									0.058
< 65 years	Week 1	CR845	135	131 (97.0)	-0.99 (0.14)	(-1.26, -0.72)	-0.51 (0.15)	(-0.81, -0.20)	0.001 *
		Placebo	137	130 (94.9)	-0.49 (0.14)	(-0.76, -0.21)			
>= 65 years	Week 1	CR845	54	52 (96.3)	-0.80 (0.22)	(-1.24, -0.37)	-0.09 (0.24)	(-0.58, 0.39)	0.707
		Placebo	52	51 (98.1)	-0.71 (0.20)	(-1.12, -0.31)			
< 65 years	Week 2	CR845	135	129 (95.6)	-1.58 (0.16)	(-1.89, -1.27)	-0.86 (0.19)	(-1.23, -0.49)	<0.001 *
		Placebo	137	127 (92.7)	-0.72 (0.16)	(-1.03, -0.41)			
>= 65 years	Week 2	CR845	54	50 (92.6)	-1.17 (0.27)	(-1.70, -0.65)	0.20 (0.33)	(-0.45, 0.84)	0.542
		Placebo	52	51 (98.1)	-1.37 (0.25)	(-1.88, -0.87)			
< 65 years	Week 3	CR845	135	127 (94.1)	-2.02 (0.17)	(-2.36, -1.68)	-1.07 (0.22)	(-1.50, -0.64)	<0.001 *
		Placebo	137	127 (92.7)	-0.95 (0.18)	(-1.29, -0.60)			
>= 65 years	Week 3	CR845	54	51 (94.4)	-1.62 (0.30)	(-2.21, -1.04)	-0.20 (0.38)	(-0.95, 0.54)	0.589
		Placebo	52	49 (94.2)	-1.42 (0.29)	(-1.99, -0.85)			
< 65 years	Week 4	CR845	135	126 (93.3)	-2.29 (0.19)	(-2.67, -1.91)	-1.16 (0.25)	(-1.64, -0.67)	<0.001 *
		Placebo	137	127 (92.7)	-1.13 (0.19)	(-1.51, -0.75)			
>= 65 years	Week 4	CR845	54	50 (92.6)	-2.02 (0.31)	(-2.63, -1.42)	-0.31 (0.39)	(-1.08, 0.47)	0.432
		Placebo	52	51 (98.1)	-1.72 (0.30)	(-2.31, -1.13)			
< 65 years	Week 5	CR845	135	123 (91.1)	-2.48 (0.19)	(-2.86, -2.10)	-1.10 (0.25)	(-1.59, -0.61)	<0.001 *
		Placebo	137	126 (92.0)	-1.38 (0.20)	(-1.76, -0.99)			
>= 65 years	Week 5	CR845	54	49 (90.7)	-2.14 (0.31)	(-2.76, -1.52)	-0.30 (0.40)	(-1.10, 0.50)	0.461
		Placebo	52	50 (96.2)	-1.84 (0.31)	(-2.45, -1.23)			
< 65 years	Week 6	CR845	135	122 (90.4)	-2.85 (0.20)	(-3.25, -2.46)	-1.32 (0.26)	(-1.84, -0.81)	<0.001 *
		Placebo	137	126 (92.0)	-1.53 (0.20)	(-1.93, -1.13)			
>= 65 years	Week 6	CR845	54	48 (88.9)	-2.21 (0.32)	(-2.85, -1.58)	-0.27 (0.41)	(-1.09, 0.55)	0.517
		Placebo	52	50 (96.2)	-1.94 (0.31)	(-2.56, -1.32)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: aweek, created on: 17FEB2022

Table AT2WIC_ISCA: Change from baseline in weekly WI-NRS - MMRM results by age
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
< 65 years	Week 7	CR845	135	118 (87.4)	-2.90 (0.21)	(-3.31, -2.49)	-1.26 (0.27)	(-1.79, -0.73)	<0.001 *
		Placebo	137	123 (89.8)	-1.64 (0.21)	(-2.06, -1.23)			
>= 65 years	Week 7	CR845	54	48 (88.9)	-2.37 (0.33)	(-3.02, -1.72)	-0.32 (0.42)	(-1.16, 0.51)	0.444
		Placebo	52	50 (96.2)	-2.05 (0.32)	(-2.68, -1.42)			
< 65 years	Week 8	CR845	135	118 (87.4)	-2.91 (0.21)	(-3.33, -2.49)	-1.16 (0.28)	(-1.71, -0.61)	<0.001 *
		Placebo	137	124 (90.5)	-1.75 (0.21)	(-2.17, -1.33)			
>= 65 years	Week 8	CR845	54	49 (90.7)	-2.37 (0.34)	(-3.04, -1.70)	-0.43 (0.44)	(-1.31, 0.45)	0.331
		Placebo	52	49 (94.2)	-1.94 (0.33)	(-2.59, -1.28)			
< 65 years	Week 9	CR845	135	118 (87.4)	-3.13 (0.21)	(-3.55, -2.71)	-1.28 (0.28)	(-1.83, -0.74)	<0.001 *
		Placebo	137	125 (91.2)	-1.85 (0.21)	(-2.27, -1.43)			
>= 65 years	Week 9	CR845	54	47 (87.0)	-2.54 (0.35)	(-3.23, -1.85)	-0.60 (0.45)	(-1.50, 0.30)	0.190
		Placebo	52	49 (94.2)	-1.94 (0.34)	(-2.62, -1.27)			
< 65 years	Week 10	CR845	135	117 (86.7)	-3.34 (0.22)	(-3.77, -2.90)	-1.48 (0.29)	(-2.05, -0.91)	<0.001 *
		Placebo	137	125 (91.2)	-1.85 (0.22)	(-2.29, -1.42)			
>= 65 years	Week 10	CR845	54	48 (88.9)	-2.62 (0.35)	(-3.32, -1.93)	-0.49 (0.46)	(-1.40, 0.43)	0.292
		Placebo	52	48 (92.3)	-2.13 (0.34)	(-2.82, -1.45)			
< 65 years	Week 11	CR845	135	112 (83.0)	-3.38 (0.22)	(-3.81, -2.95)	-1.56 (0.29)	(-2.12, -0.99)	<0.001 *
		Placebo	137	120 (87.6)	-1.83 (0.22)	(-2.25, -1.40)			
>= 65 years	Week 11	CR845	54	45 (83.3)	-2.53 (0.33)	(-3.19, -1.87)	-0.36 (0.43)	(-1.22, 0.49)	0.400
		Placebo	52	48 (92.3)	-2.17 (0.32)	(-2.81, -1.53)			
< 65 years	Week 12	CR845	135	112 (83.0)	-3.38 (0.22)	(-3.82, -2.95)	-1.50 (0.29)	(-2.07, -0.92)	<0.001 *
		Placebo	137	116 (84.7)	-1.89 (0.22)	(-2.32, -1.45)			
>= 65 years	Week 12	CR845	54	45 (83.3)	-2.80 (0.37)	(-3.53, -2.08)	-0.37 (0.48)	(-1.32, 0.59)	0.448
		Placebo	52	49 (94.2)	-2.44 (0.36)	(-3.14, -1.73)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: aweek, created on: 17FEB2022

Table AT2WIC_ISCB: Change from baseline in weekly WI-NRS - MMRM results by sex
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
B: Sex									0.366
Male	Week 1	CR845	112	109 (97.3)	-0.86 (0.16)	(-1.17, -0.55)	-0.46 (0.17)	(-0.79, -0.14)	0.005 *
		Placebo	119	114 (95.8)	-0.39 (0.15)	(-0.69, -0.10)			
Female	Week 1	CR845	77	74 (96.1)	-1.09 (0.17)	(-1.42, -0.75)	-0.23 (0.21)	(-0.64, 0.19)	0.281
		Placebo	70	67 (95.7)	-0.86 (0.18)	(-1.21, -0.51)			
Male	Week 2	CR845	112	106 (94.6)	-1.39 (0.18)	(-1.74, -1.03)	-0.66 (0.20)	(-1.06, -0.26)	0.001 *
		Placebo	119	112 (94.1)	-0.73 (0.17)	(-1.06, -0.39)			
Female	Week 2	CR845	77	73 (94.8)	-1.59 (0.22)	(-2.02, -1.16)	-0.31 (0.29)	(-0.87, 0.26)	0.286
		Placebo	70	66 (94.3)	-1.28 (0.23)	(-1.73, -0.83)			
Male	Week 3	CR845	112	103 (92.0)	-1.77 (0.19)	(-2.15, -1.39)	-0.95 (0.23)	(-1.39, -0.50)	<0.001 *
		Placebo	119	110 (92.4)	-0.82 (0.18)	(-1.18, -0.46)			
Female	Week 3	CR845	77	75 (97.4)	-2.11 (0.25)	(-2.60, -1.63)	-0.57 (0.34)	(-1.23, 0.10)	0.093
		Placebo	70	66 (94.3)	-1.55 (0.26)	(-2.07, -1.03)			
Male	Week 4	CR845	112	102 (91.1)	-2.12 (0.21)	(-2.53, -1.70)	-1.11 (0.25)	(-1.60, -0.61)	<0.001 *
		Placebo	119	113 (95.0)	-1.01 (0.20)	(-1.40, -0.62)			
Female	Week 4	CR845	77	74 (96.1)	-2.37 (0.27)	(-2.90, -1.84)	-0.56 (0.37)	(-1.28, 0.17)	0.133
		Placebo	70	65 (92.9)	-1.82 (0.28)	(-2.38, -1.25)			
Male	Week 5	CR845	112	99 (88.4)	-2.34 (0.22)	(-2.77, -1.92)	-1.14 (0.26)	(-1.65, -0.62)	<0.001 *
		Placebo	119	111 (93.3)	-1.21 (0.20)	(-1.61, -0.81)			
Female	Week 5	CR845	77	73 (94.8)	-2.45 (0.26)	(-2.97, -1.93)	-0.41 (0.36)	(-1.12, 0.31)	0.265
		Placebo	70	65 (92.9)	-2.05 (0.28)	(-2.60, -1.49)			
Male	Week 6	CR845	112	98 (87.5)	-2.73 (0.22)	(-3.17, -2.30)	-1.46 (0.27)	(-1.99, -0.93)	<0.001 *
		Placebo	119	110 (92.4)	-1.27 (0.21)	(-1.68, -0.86)			
Female	Week 6	CR845	77	72 (93.5)	-2.61 (0.27)	(-3.16, -2.07)	-0.30 (0.38)	(-1.05, 0.45)	0.429
		Placebo	70	66 (94.3)	-2.31 (0.29)	(-2.89, -1.74)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: aweek, created on: 17FEB2022

Table AT2WIC_ISCB: Change from baseline in weekly WI-NRS - MMRM results by sex
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Male	Week 7	CR845	112	95 (84.8)	-2.78 (0.23)	(-3.23, -2.32)	-1.39 (0.29)	(-1.96, -0.83)	<0.001 *
		Placebo	119	110 (92.4)	-1.38 (0.22)	(-1.81, -0.95)			
Female	Week 7	CR845	77	71 (92.2)	-2.74 (0.27)	(-3.28, -2.21)	-0.31 (0.38)	(-1.06, 0.43)	0.405
		Placebo	70	63 (90.0)	-2.43 (0.29)	(-3.00, -1.86)			
Male	Week 8	CR845	112	96 (85.7)	-2.71 (0.23)	(-3.17, -2.24)	-1.28 (0.29)	(-1.85, -0.71)	<0.001 *
		Placebo	119	110 (92.4)	-1.43 (0.22)	(-1.86, -0.99)			
Female	Week 8	CR845	77	71 (92.2)	-2.84 (0.28)	(-3.40, -2.28)	-0.37 (0.39)	(-1.15, 0.41)	0.348
		Placebo	70	63 (90.0)	-2.47 (0.30)	(-3.07, -1.87)			
Male	Week 9	CR845	112	93 (83.0)	-2.83 (0.24)	(-3.30, -2.37)	-1.29 (0.29)	(-1.87, -0.72)	<0.001 *
		Placebo	119	109 (91.6)	-1.54 (0.22)	(-1.98, -1.10)			
Female	Week 9	CR845	77	72 (93.5)	-3.14 (0.29)	(-3.71, -2.58)	-0.65 (0.40)	(-1.44, 0.13)	0.100
		Placebo	70	65 (92.9)	-2.49 (0.30)	(-3.09, -1.89)			
Male	Week 10	CR845	112	95 (84.8)	-3.07 (0.24)	(-3.54, -2.59)	-1.47 (0.30)	(-2.07, -0.87)	<0.001 *
		Placebo	119	109 (91.6)	-1.59 (0.23)	(-2.05, -1.14)			
Female	Week 10	CR845	77	70 (90.9)	-3.23 (0.30)	(-3.81, -2.64)	-0.66 (0.41)	(-1.48, 0.15)	0.110
		Placebo	70	64 (91.4)	-2.57 (0.31)	(-3.19, -1.95)			
Male	Week 11	CR845	112	89 (79.5)	-3.07 (0.24)	(-3.54, -2.59)	-1.41 (0.30)	(-2.00, -0.82)	<0.001 *
		Placebo	119	107 (89.9)	-1.65 (0.23)	(-2.10, -1.21)			
Female	Week 11	CR845	77	68 (88.3)	-3.26 (0.29)	(-3.83, -2.70)	-0.81 (0.40)	(-1.60, -0.03)	0.042 *
		Placebo	70	61 (87.1)	-2.45 (0.30)	(-3.05, -1.85)			
Male	Week 12	CR845	112	90 (80.4)	-3.13 (0.25)	(-3.62, -2.63)	-1.40 (0.31)	(-2.02, -0.78)	<0.001 *
		Placebo	119	102 (85.7)	-1.73 (0.24)	(-2.19, -1.26)			
Female	Week 12	CR845	77	67 (87.0)	-3.37 (0.30)	(-3.96, -2.78)	-0.71 (0.41)	(-1.53, 0.11)	0.087
		Placebo	70	63 (90.0)	-2.66 (0.31)	(-3.28, -2.04)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: aweek, created on: 17FEB2022

Table AT2WIC_ISCC: Change from baseline in weekly WI-NRS - MMRM results by race
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
C: Race									0.944
Black/African American	Week 1	CR845	82	80 (97.6)	-0.87 (0.18)	(-1.22, -0.51)	-0.36 (0.22)	(-0.78, 0.07)	0.100
		Placebo	76	70 (92.1)	-0.51 (0.19)	(-0.89, -0.14)			
White	Week 1	CR845	91	87 (95.6)	-0.97 (0.17)	(-1.31, -0.63)	-0.35 (0.18)	(-0.71, 0.01)	0.060
		Placebo	93	91 (97.8)	-0.62 (0.16)	(-0.94, -0.31)			
Other	Week 1	CR845	15	15 (100.0)	-0.53 (0.36)	(-1.26, 0.20)	-0.32 (0.37)	(-1.09, 0.45)	0.400
		Placebo	18	18 (100.0)	-0.21 (0.33)	(-0.88, 0.46)			
Black/African American	Week 2	CR845	82	77 (93.9)	-1.51 (0.20)	(-1.91, -1.11)	-0.73 (0.26)	(-1.23, -0.22)	0.005 *
		Placebo	76	68 (89.5)	-0.79 (0.21)	(-1.21, -0.36)			
White	Week 2	CR845	91	86 (94.5)	-1.38 (0.21)	(-1.79, -0.97)	-0.34 (0.25)	(-0.82, 0.14)	0.168
		Placebo	93	90 (96.8)	-1.04 (0.20)	(-1.43, -0.65)			
Other	Week 2	CR845	15	15 (100.0)	-1.03 (0.45)	(-1.94, -0.12)	-0.37 (0.52)	(-1.44, 0.69)	0.479
		Placebo	18	18 (100.0)	-0.65 (0.41)	(-1.49, 0.18)			
Black/African American	Week 3	CR845	82	75 (91.5)	-1.96 (0.22)	(-2.40, -1.52)	-0.89 (0.29)	(-1.45, -0.32)	0.002 *
		Placebo	76	70 (92.1)	-1.08 (0.23)	(-1.54, -0.61)			
White	Week 3	CR845	91	88 (96.7)	-1.85 (0.23)	(-2.29, -1.40)	-0.77 (0.28)	(-1.32, -0.21)	0.007 *
		Placebo	93	86 (92.5)	-1.08 (0.22)	(-1.51, -0.65)			
Other	Week 3	CR845	15	14 (93.3)	-1.33 (0.51)	(-2.36, -0.31)	-0.27 (0.61)	(-1.52, 0.97)	0.658
		Placebo	18	18 (100.0)	-1.06 (0.46)	(-1.99, -0.12)			
Black/African American	Week 4	CR845	82	74 (90.2)	-2.23 (0.26)	(-2.74, -1.72)	-0.93 (0.34)	(-1.61, -0.26)	0.007 *
		Placebo	76	71 (93.4)	-1.29 (0.27)	(-1.82, -0.77)			
White	Week 4	CR845	91	87 (95.6)	-2.18 (0.24)	(-2.65, -1.72)	-0.87 (0.29)	(-1.45, -0.29)	0.003 *
		Placebo	93	87 (93.5)	-1.31 (0.23)	(-1.76, -0.86)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: aweek, created on: 17FEB2022

Table AT2WIC_ISCC: Change from baseline in weekly WI-NRS - MMRM results by race
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Other	Week 4	CR845	15	14 (93.3)	-1.69 (0.53)	(-2.76, -0.62)	-0.48 (0.64)	(-1.79, 0.83)	0.462
		Placebo	18	18 (100.0)	-1.21 (0.48)	(-2.19, -0.24)			
Black/African American	Week 5	CR845	82	71 (86.6)	-2.36 (0.26)	(-2.88, -1.84)	-0.97 (0.35)	(-1.66, -0.29)	0.006 *
		Placebo	76	71 (93.4)	-1.39 (0.27)	(-1.92, -0.85)			
White	Week 5	CR845	91	85 (93.4)	-2.37 (0.24)	(-2.84, -1.90)	-0.79 (0.30)	(-1.38, -0.20)	0.009 *
		Placebo	93	85 (91.4)	-1.58 (0.23)	(-2.04, -1.13)			
Other	Week 5	CR845	15	15 (100.0)	-1.92 (0.51)	(-2.95, -0.88)	-0.38 (0.62)	(-1.64, 0.88)	0.541
		Placebo	18	18 (100.0)	-1.54 (0.47)	(-2.48, -0.59)			
Black/African American	Week 6	CR845	82	70 (85.4)	-2.70 (0.28)	(-3.24, -2.15)	-1.01 (0.37)	(-1.74, -0.29)	0.007 *
		Placebo	76	70 (92.1)	-1.68 (0.29)	(-2.25, -1.12)			
White	Week 6	CR845	91	85 (93.4)	-2.63 (0.24)	(-3.11, -2.15)	-1.10 (0.30)	(-1.70, -0.50)	<0.001 *
		Placebo	93	86 (92.5)	-1.52 (0.23)	(-1.99, -1.06)			
Other	Week 6	CR845	15	14 (93.3)	-2.30 (0.56)	(-3.44, -1.16)	-0.31 (0.69)	(-1.72, 1.11)	0.662
		Placebo	18	18 (100.0)	-2.00 (0.51)	(-3.03, -0.96)			
Black/African American	Week 7	CR845	82	69 (84.1)	-2.79 (0.28)	(-3.34, -2.24)	-1.00 (0.37)	(-1.73, -0.27)	0.008 *
		Placebo	76	70 (92.1)	-1.79 (0.29)	(-2.35, -1.22)			
White	Week 7	CR845	91	82 (90.1)	-2.75 (0.25)	(-3.24, -2.26)	-1.11 (0.32)	(-1.74, -0.49)	<0.001 *
		Placebo	93	84 (90.3)	-1.64 (0.24)	(-2.11, -1.16)			
Other	Week 7	CR845	15	14 (93.3)	-2.11 (0.62)	(-3.36, -0.86)	-0.00 (0.77)	(-1.58, 1.58)	0.999
		Placebo	18	17 (94.4)	-2.11 (0.56)	(-3.25, -0.97)			
Black/African American	Week 8	CR845	82	71 (86.6)	-2.66 (0.28)	(-3.22, -2.10)	-0.78 (0.38)	(-1.53, -0.03)	0.042 *
		Placebo	76	69 (90.8)	-1.88 (0.29)	(-2.46, -1.30)			
White	Week 8	CR845	91	81 (89.0)	-2.83 (0.26)	(-3.34, -2.32)	-1.23 (0.33)	(-1.88, -0.59)	<0.001 *
		Placebo	93	84 (90.3)	-1.60 (0.25)	(-2.09, -1.11)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: aweek, created on: 17FEB2022

Table AT2WIC_ISCC: Change from baseline in weekly WI-NRS - MMRM results by race
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Other	Week 8	CR845	15	14 (93.3)	-2.26 (0.62)	(-3.52, -1.00)	0.05 (0.78)	(-1.54, 1.63)	0.951
		Placebo	18	18 (100.0)	-2.30 (0.56)	(-3.45, -1.16)			
Black/African American	Week 9	CR845	82	70 (85.4)	-3.09 (0.28)	(-3.64, -2.55)	-1.13 (0.37)	(-1.86, -0.40)	0.003 *
		Placebo	76	71 (93.4)	-1.97 (0.29)	(-2.53, -1.40)			
White	Week 9	CR845	91	81 (89.0)	-2.91 (0.26)	(-3.42, -2.39)	-1.25 (0.33)	(-1.91, -0.59)	<0.001 *
		Placebo	93	83 (89.2)	-1.66 (0.25)	(-2.16, -1.16)			
Other	Week 9	CR845	15	13 (86.7)	-2.12 (0.68)	(-3.49, -0.75)	0.28 (0.85)	(-1.46, 2.02)	0.747
		Placebo	18	18 (100.0)	-2.40 (0.61)	(-3.64, -1.16)			
Black/African American	Week 10	CR845	82	70 (85.4)	-3.32 (0.29)	(-3.89, -2.75)	-1.30 (0.39)	(-2.06, -0.53)	0.001 *
		Placebo	76	71 (93.4)	-2.03 (0.30)	(-2.61, -1.44)			
White	Week 10	CR845	91	80 (87.9)	-3.00 (0.27)	(-3.53, -2.47)	-1.28 (0.34)	(-1.96, -0.61)	<0.001 *
		Placebo	93	82 (88.2)	-1.71 (0.26)	(-2.23, -1.20)			
Other	Week 10	CR845	15	14 (93.3)	-2.51 (0.68)	(-3.88, -1.14)	-0.03 (0.86)	(-1.77, 1.72)	0.976
		Placebo	18	18 (100.0)	-2.48 (0.61)	(-3.72, -1.24)			
Black/African American	Week 11	CR845	82	63 (76.8)	-3.32 (0.29)	(-3.89, -2.75)	-1.35 (0.38)	(-2.11, -0.59)	<0.001 *
		Placebo	76	69 (90.8)	-1.97 (0.29)	(-2.55, -1.39)			
White	Week 11	CR845	91	80 (87.9)	-3.07 (0.26)	(-3.59, -2.56)	-1.32 (0.34)	(-1.98, -0.65)	<0.001 *
		Placebo	93	80 (86.0)	-1.76 (0.25)	(-2.26, -1.25)			
Other	Week 11	CR845	15	13 (86.7)	-2.46 (0.62)	(-3.73, -1.19)	-0.12 (0.78)	(-1.72, 1.48)	0.878
		Placebo	18	17 (94.4)	-2.34 (0.57)	(-3.50, -1.18)			
Black/African American	Week 12	CR845	82	65 (79.3)	-3.44 (0.30)	(-4.02, -2.85)	-1.43 (0.40)	(-2.22, -0.65)	<0.001 *
		Placebo	76	67 (88.2)	-2.00 (0.30)	(-2.60, -1.41)			
White	Week 12	CR845	91	78 (85.7)	-3.14 (0.28)	(-3.68, -2.59)	-1.23 (0.36)	(-1.93, -0.52)	<0.001 *
		Placebo	93	79 (84.9)	-1.91 (0.27)	(-2.44, -1.38)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: aweek, created on: 17FEB2022

Table AT2WIC_ISCC: Change from baseline in weekly WI-NRS - MMRM results by race
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Other	Week 12	CR845	15	13 (86.7)	-2.37 (0.67)	(-3.74, -1.00)	0.40 (0.85)	(-1.34, 2.13)	0.644
		Placebo	18	17 (94.4)	-2.77 (0.61)	(-4.00, -1.53)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: aweek, created on: 17FEB2022

Table AT2WIC_ISCD: Change from baseline in weekly WI-NRS - MMRM results by baseline WI-NRS
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
D: Baseline worst itching NRS score (WI-NRS)									0.471
>= 4 to < 7	Week 1	CR845	83	80 (96.4)	-0.90 (0.19)	(-1.28, -0.51)	-0.50 (0.20)	(-0.90, -0.10)	0.015 *
		Placebo	80	75 (93.8)	-0.40 (0.18)	(-0.77, -0.04)			
>= 7	Week 1	CR845	106	103 (97.2)	-0.94 (0.15)	(-1.23, -0.65)	-0.31 (0.17)	(-0.65, 0.03)	0.075
		Placebo	109	106 (97.2)	-0.63 (0.15)	(-0.91, -0.34)			
>= 4 to < 7	Week 2	CR845	83	79 (95.2)	-1.38 (0.21)	(-1.79, -0.97)	-0.83 (0.23)	(-1.28, -0.38)	<0.001 *
		Placebo	80	75 (93.8)	-0.55 (0.20)	(-0.95, -0.15)			
>= 7	Week 2	CR845	106	100 (94.3)	-1.49 (0.18)	(-1.85, -1.13)	-0.36 (0.24)	(-0.83, 0.10)	0.123
		Placebo	109	103 (94.5)	-1.13 (0.18)	(-1.49, -0.76)			
>= 4 to < 7	Week 3	CR845	83	79 (95.2)	-1.81 (0.23)	(-2.27, -1.36)	-1.15 (0.26)	(-1.68, -0.63)	<0.001 *
		Placebo	80	75 (93.8)	-0.66 (0.22)	(-1.10, -0.22)			
>= 7	Week 3	CR845	106	99 (93.4)	-1.94 (0.20)	(-2.35, -1.54)	-0.60 (0.27)	(-1.13, -0.08)	0.025 *
		Placebo	109	101 (92.7)	-1.34 (0.20)	(-1.74, -0.94)			
>= 4 to < 7	Week 4	CR845	83	76 (91.6)	-2.06 (0.23)	(-2.52, -1.60)	-1.34 (0.27)	(-1.87, -0.80)	<0.001 *
		Placebo	80	75 (93.8)	-0.72 (0.23)	(-1.17, -0.28)			
>= 7	Week 4	CR845	106	100 (94.3)	-2.29 (0.23)	(-2.74, -1.84)	-0.63 (0.30)	(-1.23, -0.03)	0.041 *
		Placebo	109	103 (94.5)	-1.67 (0.23)	(-2.12, -1.22)			
>= 4 to < 7	Week 5	CR845	83	74 (89.2)	-2.16 (0.23)	(-2.62, -1.70)	-1.26 (0.27)	(-1.79, -0.73)	<0.001 *
		Placebo	80	74 (92.5)	-0.90 (0.22)	(-1.35, -0.46)			
>= 7	Week 5	CR845	106	98 (92.5)	-2.51 (0.23)	(-2.97, -2.05)	-0.61 (0.31)	(-1.22, -0.00)	0.049 *
		Placebo	109	102 (93.6)	-1.90 (0.23)	(-2.35, -1.44)			
>= 4 to < 7	Week 6	CR845	83	71 (85.5)	-2.34 (0.24)	(-2.80, -1.87)	-1.32 (0.28)	(-1.86, -0.77)	<0.001 *
		Placebo	80	75 (93.8)	-1.02 (0.23)	(-1.47, -0.57)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: aweek, created on: 17FEB2022

Table AT2WIC_ISCD: Change from baseline in weekly WI-NRS - MMRM results by baseline WI-NRS
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
>= 7	Week 6	CR845	106	99 (93.4)	-2.89 (0.25)	(-3.37, -2.40)	-0.83 (0.33)	(-1.48, -0.19)	0.012 *
		Placebo	109	101 (92.7)	-2.05 (0.24)	(-2.54, -1.57)			
>= 4 to < 7	Week 7	CR845	83	71 (85.5)	-2.33 (0.25)	(-2.82, -1.85)	-1.20 (0.29)	(-1.78, -0.62)	<0.001 *
		Placebo	80	74 (92.5)	-1.13 (0.24)	(-1.60, -0.67)			
>= 7	Week 7	CR845	106	95 (89.6)	-3.03 (0.25)	(-3.53, -2.54)	-0.87 (0.33)	(-1.53, -0.21)	0.010 *
		Placebo	109	99 (90.8)	-2.17 (0.25)	(-2.65, -1.68)			
>= 4 to < 7	Week 8	CR845	83	72 (86.7)	-2.26 (0.25)	(-2.76, -1.76)	-1.14 (0.31)	(-1.74, -0.53)	<0.001 *
		Placebo	80	73 (91.3)	-1.13 (0.25)	(-1.61, -0.64)			
>= 7	Week 8	CR845	106	95 (89.6)	-3.08 (0.25)	(-3.58, -2.59)	-0.83 (0.34)	(-1.50, -0.17)	0.015 *
		Placebo	109	100 (91.7)	-2.25 (0.25)	(-2.75, -1.76)			
>= 4 to < 7	Week 9	CR845	83	71 (85.5)	-2.47 (0.25)	(-2.96, -1.98)	-1.31 (0.30)	(-1.89, -0.73)	<0.001 *
		Placebo	80	74 (92.5)	-1.16 (0.24)	(-1.63, -0.69)			
>= 7	Week 9	CR845	106	94 (88.7)	-3.30 (0.26)	(-3.81, -2.79)	-0.94 (0.35)	(-1.62, -0.26)	0.007 *
		Placebo	109	100 (91.7)	-2.35 (0.26)	(-2.86, -1.85)			
>= 4 to < 7	Week 10	CR845	83	70 (84.3)	-2.48 (0.25)	(-2.97, -1.99)	-1.28 (0.30)	(-1.87, -0.69)	<0.001 *
		Placebo	80	75 (93.8)	-1.20 (0.24)	(-1.68, -0.73)			
>= 7	Week 10	CR845	106	95 (89.6)	-3.58 (0.27)	(-4.11, -3.06)	-1.15 (0.36)	(-1.86, -0.44)	0.002 *
		Placebo	109	98 (89.9)	-2.43 (0.27)	(-2.96, -1.91)			
>= 4 to < 7	Week 11	CR845	83	69 (83.1)	-2.51 (0.25)	(-3.01, -2.01)	-1.17 (0.30)	(-1.77, -0.57)	<0.001 *
		Placebo	80	74 (92.5)	-1.34 (0.24)	(-1.83, -0.86)			
>= 7	Week 11	CR845	106	88 (83.0)	-3.59 (0.26)	(-4.10, -3.08)	-1.28 (0.35)	(-1.97, -0.60)	<0.001 *
		Placebo	109	94 (86.2)	-2.31 (0.26)	(-2.82, -1.80)			
>= 4 to < 7	Week 12	CR845	83	67 (80.7)	-2.59 (0.26)	(-3.11, -2.07)	-1.15 (0.32)	(-1.78, -0.52)	<0.001 *
		Placebo	80	70 (87.5)	-1.44 (0.25)	(-1.94, -0.94)			
>= 7	Week 12	CR845	106	90 (84.9)	-3.69 (0.27)	(-4.22, -3.15)	-1.23 (0.36)	(-1.95, -0.51)	<0.001 *
		Placebo	109	95 (87.2)	-2.46 (0.27)	(-2.99, -1.93)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: aweek, created on: 17FEB2022

Table AT2WIC_ISCE: Change from baseline in weekly WI-NRS - MMRM results by specific medical condition
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
E: Presence of specific medical conditions									0.257
No	Week 1	CR845	164	160 (97.6)	-0.94 (0.10)	(-1.14, -0.74)	-0.32 (0.14)	(-0.60, -0.04)	0.026 *
		Placebo	161	153 (95.0)	-0.62 (0.10)	(-0.82, -0.42)			
Yes	Week 1	CR845	25	23 (92.0)	-1.12 (0.23)	(-1.57, -0.66)	-0.77 (0.31)	(-1.40, -0.15)	0.016 *
		Placebo	28	28 (100.0)	-0.34 (0.21)	(-0.76, 0.08)			
No	Week 2	CR845	164	156 (95.1)	-1.48 (0.13)	(-1.74, -1.23)	-0.47 (0.18)	(-0.83, -0.11)	0.010 *
		Placebo	161	151 (93.8)	-1.01 (0.13)	(-1.27, -0.75)			
Yes	Week 2	CR845	25	23 (92.0)	-1.56 (0.28)	(-2.12, -0.99)	-1.05 (0.39)	(-1.82, -0.27)	0.009 *
		Placebo	28	27 (96.4)	-0.51 (0.26)	(-1.04, 0.02)			
No	Week 3	CR845	164	153 (93.3)	-1.91 (0.15)	(-2.20, -1.61)	-0.72 (0.21)	(-1.14, -0.31)	<0.001 *
		Placebo	161	150 (93.2)	-1.18 (0.15)	(-1.48, -0.89)			
Yes	Week 3	CR845	25	25 (100.0)	-2.06 (0.29)	(-2.65, -1.48)	-1.32 (0.40)	(-2.13, -0.52)	0.002 *
		Placebo	28	26 (92.9)	-0.74 (0.28)	(-1.30, -0.19)			
No	Week 4	CR845	164	152 (92.7)	-2.20 (0.16)	(-2.53, -1.88)	-0.77 (0.23)	(-1.22, -0.31)	0.001 *
		Placebo	161	151 (93.8)	-1.44 (0.16)	(-1.76, -1.11)			
Yes	Week 4	CR845	25	24 (96.0)	-2.42 (0.34)	(-3.09, -1.74)	-1.71 (0.46)	(-2.64, -0.79)	<0.001 *
		Placebo	28	27 (96.4)	-0.70 (0.32)	(-1.34, -0.07)			
No	Week 5	CR845	164	148 (90.2)	-2.38 (0.16)	(-2.70, -2.06)	-0.75 (0.23)	(-1.21, -0.30)	0.001 *
		Placebo	161	149 (92.5)	-1.63 (0.17)	(-1.95, -1.30)			
Yes	Week 5	CR845	25	24 (96.0)	-2.54 (0.37)	(-3.29, -1.79)	-1.53 (0.51)	(-2.56, -0.50)	0.004 *
		Placebo	28	27 (96.4)	-1.01 (0.35)	(-1.72, -0.31)			
No	Week 6	CR845	164	146 (89.0)	-2.67 (0.17)	(-3.00, -2.33)	-0.94 (0.24)	(-1.41, -0.46)	<0.001 *
		Placebo	161	150 (93.2)	-1.73 (0.17)	(-2.07, -1.39)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor previous use of anti-itch medication is also included in the model.
Source Data: aweek, created on: 17FEB2022

Table AT2WIC_ISCE: Change from baseline in weekly WI-NRS - MMRM results by specific medical condition
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Yes	Week 6	CR845	25	24 (96.0)	-2.88 (0.41)	(-3.69, -2.06)	-1.52 (0.56)	(-2.64, -0.39)	0.009 *
		Placebo	28	26 (92.9)	-1.36 (0.38)	(-2.13, -0.59)			
No	Week 7	CR845	164	142 (86.6)	-2.75 (0.18)	(-3.10, -2.40)	-0.92 (0.25)	(-1.41, -0.43)	<0.001 *
		Placebo	161	146 (90.7)	-1.83 (0.18)	(-2.18, -1.48)			
Yes	Week 7	CR845	25	24 (96.0)	-2.92 (0.41)	(-3.76, -2.09)	-1.42 (0.57)	(-2.56, -0.27)	0.016 *
		Placebo	28	27 (96.4)	-1.51 (0.39)	(-2.29, -0.72)			
No	Week 8	CR845	164	143 (87.2)	-2.75 (0.18)	(-3.11, -2.39)	-0.89 (0.26)	(-1.40, -0.39)	<0.001 *
		Placebo	161	146 (90.7)	-1.86 (0.18)	(-2.22, -1.50)			
Yes	Week 8	CR845	25	24 (96.0)	-2.93 (0.42)	(-3.76, -2.09)	-1.31 (0.57)	(-2.45, -0.16)	0.027 *
		Placebo	28	27 (96.4)	-1.62 (0.39)	(-2.41, -0.84)			
No	Week 9	CR845	164	141 (86.0)	-2.96 (0.18)	(-3.32, -2.60)	-1.01 (0.26)	(-1.51, -0.50)	<0.001 *
		Placebo	161	147 (91.3)	-1.95 (0.18)	(-2.31, -1.59)			
Yes	Week 9	CR845	25	24 (96.0)	-3.16 (0.44)	(-4.05, -2.27)	-1.56 (0.61)	(-2.78, -0.33)	0.014 *
		Placebo	28	27 (96.4)	-1.60 (0.42)	(-2.44, -0.76)			
No	Week 10	CR845	164	141 (86.0)	-3.10 (0.19)	(-3.47, -2.73)	-1.09 (0.27)	(-1.62, -0.57)	<0.001 *
		Placebo	161	146 (90.7)	-2.01 (0.19)	(-2.38, -1.64)			
Yes	Week 10	CR845	25	24 (96.0)	-3.48 (0.46)	(-4.39, -2.56)	-1.81 (0.63)	(-3.07, -0.54)	0.006 *
		Placebo	28	27 (96.4)	-1.67 (0.43)	(-2.54, -0.80)			
No	Week 11	CR845	164	135 (82.3)	-3.08 (0.18)	(-3.45, -2.72)	-1.08 (0.26)	(-1.59, -0.57)	<0.001 *
		Placebo	161	144 (89.4)	-2.01 (0.18)	(-2.37, -1.65)			
Yes	Week 11	CR845	25	22 (88.0)	-3.66 (0.44)	(-4.55, -2.77)	-2.02 (0.61)	(-3.25, -0.80)	0.002 *
		Placebo	28	24 (85.7)	-1.64 (0.42)	(-2.48, -0.79)			
No	Week 12	CR845	164	133 (81.1)	-3.14 (0.20)	(-3.53, -2.76)	-0.97 (0.27)	(-1.51, -0.43)	<0.001 *
		Placebo	161	141 (87.6)	-2.18 (0.19)	(-2.56, -1.80)			
Yes	Week 12	CR845	25	24 (96.0)	-3.85 (0.43)	(-4.72, -2.98)	-2.32 (0.60)	(-3.52, -1.12)	<0.001 *
		Placebo	28	24 (85.7)	-1.53 (0.41)	(-2.36, -0.70)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor previous use of anti-itch medication is also included in the model.
Source Data: aweek, created on: 17FEB2022

Table AT2WIC_ISCF: Change from baseline in weekly WI-NRS - MMRM results by use of concomitant itch medication
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
F: Use of concomitant itch medication									0.537
No	Week 1	CR845	117	113 (96.6)	-0.85 (0.15)	(-1.14, -0.56)	-0.46 (0.16)	(-0.77, -0.14)	0.004 *
		Placebo	111	105 (94.6)	-0.39 (0.15)	(-0.68, -0.10)			
Yes	Week 1	CR845	72	70 (97.2)	-0.97 (0.19)	(-1.34, -0.60)	-0.25 (0.22)	(-0.69, 0.19)	0.260
		Placebo	78	76 (97.4)	-0.72 (0.18)	(-1.08, -0.36)			
No	Week 2	CR845	117	112 (95.7)	-1.30 (0.18)	(-1.65, -0.95)	-0.51 (0.21)	(-0.93, -0.10)	0.015 *
		Placebo	111	103 (92.8)	-0.78 (0.18)	(-1.13, -0.44)			
Yes	Week 2	CR845	72	67 (93.1)	-1.61 (0.22)	(-2.04, -1.18)	-0.59 (0.27)	(-1.13, -0.05)	0.031 *
		Placebo	78	75 (96.2)	-1.02 (0.21)	(-1.43, -0.60)			
No	Week 3	CR845	117	114 (97.4)	-1.83 (0.19)	(-2.21, -1.45)	-0.96 (0.24)	(-1.43, -0.48)	<0.001 *
		Placebo	111	100 (90.1)	-0.87 (0.20)	(-1.26, -0.49)			
Yes	Week 3	CR845	72	64 (88.9)	-1.90 (0.24)	(-2.38, -1.42)	-0.60 (0.31)	(-1.21, 0.01)	0.053
		Placebo	78	76 (97.4)	-1.30 (0.23)	(-1.76, -0.84)			
No	Week 4	CR845	117	112 (95.7)	-2.17 (0.21)	(-2.57, -1.76)	-1.04 (0.26)	(-1.55, -0.52)	<0.001 *
		Placebo	111	104 (93.7)	-1.13 (0.21)	(-1.54, -0.72)			
Yes	Week 4	CR845	72	64 (88.9)	-2.15 (0.27)	(-2.69, -1.62)	-0.69 (0.35)	(-1.38, 0.01)	0.052
		Placebo	78	74 (94.9)	-1.47 (0.26)	(-1.98, -0.96)			
No	Week 5	CR845	117	109 (93.2)	-2.32 (0.21)	(-2.74, -1.91)	-1.04 (0.27)	(-1.56, -0.51)	<0.001 *
		Placebo	111	103 (92.8)	-1.29 (0.21)	(-1.71, -0.87)			
Yes	Week 5	CR845	72	63 (87.5)	-2.34 (0.27)	(-2.88, -1.80)	-0.59 (0.35)	(-1.29, 0.11)	0.096
		Placebo	78	73 (93.6)	-1.75 (0.26)	(-2.26, -1.24)			
No	Week 6	CR845	117	108 (92.3)	-2.59 (0.22)	(-3.02, -2.15)	-1.09 (0.28)	(-1.65, -0.54)	<0.001 *
		Placebo	111	103 (92.8)	-1.49 (0.22)	(-1.93, -1.05)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor presence of medical condition is also included in the model.
Source Data: aweek, created on: 17FEB2022

Table AT2WIC_ISCF: Change from baseline in weekly WI-NRS - MMRM results by use of concomitant itch medication
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Yes	Week 6	CR845	72	62 (86.1)	-2.69 (0.28)	(-3.24, -2.14)	-0.89 (0.36)	(-1.61, -0.18)	0.014 *
		Placebo	78	73 (93.6)	-1.79 (0.27)	(-2.32, -1.27)			
No	Week 7	CR845	117	105 (89.7)	-2.66 (0.22)	(-3.10, -2.22)	-1.10 (0.29)	(-1.67, -0.53)	<0.001 *
		Placebo	111	104 (93.7)	-1.56 (0.23)	(-2.00, -1.11)			
Yes	Week 7	CR845	72	61 (84.7)	-2.78 (0.29)	(-3.35, -2.21)	-0.81 (0.38)	(-1.55, -0.07)	0.033 *
		Placebo	78	69 (88.5)	-1.97 (0.28)	(-2.51, -1.43)			
No	Week 8	CR845	117	107 (91.5)	-2.73 (0.23)	(-3.18, -2.28)	-1.16 (0.30)	(-1.75, -0.58)	<0.001 *
		Placebo	111	103 (92.8)	-1.56 (0.23)	(-2.02, -1.11)			
Yes	Week 8	CR845	72	60 (83.3)	-2.65 (0.30)	(-3.23, -2.07)	-0.59 (0.38)	(-1.34, 0.17)	0.129
		Placebo	78	70 (89.7)	-2.07 (0.28)	(-2.62, -1.51)			
No	Week 9	CR845	117	105 (89.7)	-2.90 (0.23)	(-3.35, -2.45)	-1.28 (0.29)	(-1.86, -0.70)	<0.001 *
		Placebo	111	104 (93.7)	-1.62 (0.23)	(-2.08, -1.17)			
Yes	Week 9	CR845	72	60 (83.3)	-2.92 (0.30)	(-3.52, -2.33)	-0.75 (0.39)	(-1.53, 0.02)	0.057
		Placebo	78	70 (89.7)	-2.17 (0.29)	(-2.73, -1.60)			
No	Week 10	CR845	117	104 (88.9)	-3.01 (0.24)	(-3.48, -2.55)	-1.24 (0.31)	(-1.85, -0.63)	<0.001 *
		Placebo	111	103 (92.8)	-1.77 (0.24)	(-2.25, -1.30)			
Yes	Week 10	CR845	72	61 (84.7)	-3.20 (0.31)	(-3.81, -2.58)	-1.10 (0.41)	(-1.91, -0.30)	0.008 *
		Placebo	78	70 (89.7)	-2.10 (0.29)	(-2.68, -1.51)			
No	Week 11	CR845	117	100 (85.5)	-3.06 (0.23)	(-3.51, -2.60)	-1.27 (0.30)	(-1.87, -0.68)	<0.001 *
		Placebo	111	102 (91.9)	-1.78 (0.23)	(-2.24, -1.32)			
Yes	Week 11	CR845	72	57 (79.2)	-3.17 (0.31)	(-3.77, -2.57)	-1.12 (0.40)	(-1.90, -0.33)	0.006 *
		Placebo	78	66 (84.6)	-2.06 (0.29)	(-2.63, -1.48)			
No	Week 12	CR845	117	99 (84.6)	-3.16 (0.25)	(-3.65, -2.67)	-1.22 (0.32)	(-1.86, -0.58)	<0.001 *
		Placebo	111	99 (89.2)	-1.94 (0.25)	(-2.43, -1.45)			
Yes	Week 12	CR845	72	58 (80.6)	-3.20 (0.31)	(-3.81, -2.60)	-1.05 (0.40)	(-1.84, -0.26)	0.010 *
		Placebo	78	66 (84.6)	-2.16 (0.29)	(-2.73, -1.59)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor presence of medical condition is also included in the model.
Source Data: aweek, created on: 17FEB2022

Table AT2WICD3_ISPA: Decrease of WI-NRS of at least 3 points by age
ITT

Decrease of WI-NRS of at least 3 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	A: Age										0.055	
	< 65 years	135	112 (83.0)	64 (47.4) [38.8, 56.2]	137	116 (84.7)	34 (24.8) [17.8, 32.9]	1.910 [1.358, 2.687]	2.731 [1.633, 4.567]	22.6 [10.8, 34.4]	<0.001	*
	>= 65 years	54	45 (83.3)	18 (33.3) [21.1, 47.5]	52	49 (94.2)	17 (32.7) [20.3, 47.1]	1.020 [0.593, 1.754]	1.029 [0.458, 2.314]	0.6 [-19.2, 20.4]	0.944	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table AT2WICD3_ISPB: Decrease of WI-NRS of at least 3 points by sex
ITT

		CR845			Placebo						
Decrease of WI-NRS of at least 3 points		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	B: Sex										0.327
	Male	112	90 (80.4)	46 (41.1) [31.9, 50.8]	119	102 (85.7)	27 (22.7) [15.5, 31.3]	1.810 [1.215, 2.698]	2.375 [1.342, 4.202]	18.4 [5.7, 31.1]	0.003 *
	Female	77	67 (87.0)	36 (46.8) [35.3, 58.5]	70	63 (90.0)	24 (34.3) [23.3, 46.6]	1.364 [0.912, 2.039]	1.683 [0.864, 3.277]	12.5 [-4.6, 29.6]	0.126

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table AT2WICD3_ISPC: Decrease of WI-NRS of at least 3 points by race
ITT

Decrease of WI-NRS of at least 3 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	C: Race										0.327	
	Black/African American	82	65 (79.3)	37 (45.1) [34.1, 56.5]	76	67 (88.2)	22 (28.9) [19.1, 40.5]	1.559 [1.019, 2.385]	2.018 [1.044, 3.903]	16.2 [0.1, 32.3]	0.036	*
	White	91	78 (85.7)	40 (44.0) [33.6, 54.8]	93	79 (84.9)	22 (23.7) [15.5, 33.6]	1.858 [1.206, 2.864]	2.531 [1.345, 4.765]	20.3 [5.8, 34.8]	0.004	*
	Other	15	13 (86.7)	5 (33.3) [11.8, 61.6]	18	17 (94.4)	7 (38.9) [17.3, 64.3]	0.857 [0.341, 2.152]	0.786 [0.188, 3.290]	-5.6 [-44.5, 33.4]	0.745	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table AT2WICD3_ISPD: Decrease of WI-NRS of at least 3 points by baseline WI-NRS
ITT

		CR845			Placebo						
Decrease of WI-NRS of at least 3 points		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.116
	>= 4 to < 7	83	67 (80.7)	33 (39.8) [29.2, 51.1]	80	70 (87.5)	14 (17.5) [9.9, 27.6]	2.272 [1.318, 3.916]	3.111 [1.507, 6.425]	22.3 [7.6, 36.9]	0.002 *
	>= 7	106	90 (84.9)	49 (46.2) [36.5, 56.2]	109	95 (87.2)	37 (33.9) [25.1, 43.6]	1.362 [0.976, 1.899]	1.673 [0.965, 2.901]	12.3 [-1.7, 26.2]	0.067

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table AT2WICD3_ISPE: Decrease of WI-NRS of at least 3 points by specific medical condition
ITT

Decrease of WI-NRS of at least 3 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	E: Presence of specific medical conditions										0.066	
	No	164	133 (81.1)	67 (40.9) [33.3, 48.8]	161	141 (87.6)	46 (28.6) [21.7, 36.2]	1.430 [1.053, 1.942]	1.727 [1.087, 2.742]	12.3 [1.4, 23.2]	0.020	*
	Yes	25	24 (96.0)	15 (60.0) [38.7, 78.9]	28	24 (85.7)	5 (17.9) [6.1, 36.9]	3.360 [1.427, 7.912]	6.900 [1.967, 24.209]	42.1 [14.5, 69.8]	0.002	*

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table AT2WICD3_ISPF: Decrease of WI-NRS of at least 3 points by use of concomitant itch medication
ITT

		CR845			Placebo						
Decrease of WI-NRS of at least 3 points		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	F: Use of concomitant itch medication										0.916
	No	117	99 (84.6)	53 (45.3) [36.1, 54.8]	111	99 (89.2)	31 (27.9) [19.8, 37.2]	1.622 [1.133, 2.323]	2.137 [1.231, 3.711]	17.4 [4.2, 30.5]	0.007 *
	Yes	72	58 (80.6)	29 (40.3) [28.9, 52.5]	78	66 (84.6)	20 (25.6) [16.4, 36.8]	1.571 [0.981, 2.516]	1.956 [0.978, 3.911]	14.6 [-1.6, 30.9]	0.057

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table AT2WICD4_ISPA: Decrease of WI-NRS of at least 4 points by age
ITT

		CR845			Placebo							
Decrease of WI-NRS of at least 4 points		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	A: Age										0.161	
	< 65 years	135	112 (83.0)	47 (34.8) [26.8, 43.5]	137	116 (84.7)	22 (16.1) [10.3, 23.3]	2.168 [1.386, 3.390]	2.792 [1.567, 4.973]	18.8 [7.9, 29.6]	<0.001	*
	>= 65 years	54	45 (83.3)	17 (31.5) [19.5, 45.6]	52	49 (94.2)	13 (25.0) [14.0, 38.9]	1.259 [0.682, 2.326]	1.378 [0.589, 3.227]	6.5 [-12.5, 25.5]	0.461	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table AT2WICD4_ISPB: Decrease of WI-NRS of at least 4 points by sex
ITT

		CR845			Placebo						
Decrease of WI-NRS of at least 4 points		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	B: Sex										0.415
	Male	112	90 (80.4)	37 (33.0) [24.4, 42.6]	119	102 (85.7)	19 (16.0) [9.9, 23.8]	2.069 [1.268, 3.375]	2.596 [1.384, 4.870]	17.1 [5.3, 28.9]	0.003 *
	Female	77	67 (87.0)	27 (35.1) [24.5, 46.8]	70	63 (90.0)	16 (22.9) [13.7, 34.4]	1.534 [0.906, 2.598]	1.823 [0.880, 3.775]	12.2 [-3.7, 28.1]	0.105

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table AT2WICD4_ISPC: Decrease of WI-NRS of at least 4 points by race
ITT

		CR845			Placebo						
Decrease of WI-NRS of at least 4 points		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	C: Race										0.186	
	Black/African American	82	65 (79.3)	27 (32.9) [22.9, 44.2]	76	67 (88.2)	15 (19.7) [11.5, 30.5]	1.668 [0.964, 2.888]	1.996 [0.963, 4.138]	13.2 [-1.6, 28.0]	0.062	
	White	91	78 (85.7)	33 (36.3) [26.4, 47.0]	93	79 (84.9)	14 (15.1) [8.5, 24.0]	2.409 [1.384, 4.193]	3.211 [1.577, 6.537]	21.2 [7.9, 34.6]	0.001	*
	Other	15	13 (86.7)	4 (26.7) [7.8, 55.1]	18	17 (94.4)	6 (33.3) [13.3, 59.0]	0.800 [0.276, 2.317]	0.727 [0.161, 3.281]	-6.7 [-44.0, 30.7]	0.722	#

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table AT2WICD4_ISPD: Decrease of WI-NRS of at least 4 points by baseline WI-NRS
ITT

		CR845			Placebo							
Decrease of WI-NRS of at least 4 points		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.511	
	>= 4 to < 7	83	67 (80.7)	19 (22.9) [14.4, 33.4]	80	70 (87.5)	8 (10.0) [4.4, 18.8]	2.289 [1.063, 4.929]	2.672 [1.095, 6.520]	12.9 [0.5, 25.3]	0.027	*
	>= 7	106	90 (84.9)	45 (42.5) [32.9, 52.4]	109	95 (87.2)	27 (24.8) [17.0, 34.0]	1.714 [1.154, 2.544]	2.240 [1.253, 4.005]	17.7 [4.3, 31.0]	0.006	*

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table AT2WICD4_ISPE: Decrease of WI-NRS of at least 4 points by specific medical condition
ITT

Decrease of WI-NRS of at least 4 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	E: Presence of specific medical conditions										0.094	
	No	164	133 (81.1)	52 (31.7) [24.7, 39.4]	161	141 (87.6)	32 (19.9) [14.0, 26.9]	1.595 [1.088, 2.340]	1.872 [1.126, 3.110]	11.8 [1.8, 21.9]	0.015	*
	Yes	25	24 (96.0)	12 (48.0) [27.8, 68.7]	28	24 (85.7)	3 (10.7) [2.3, 28.2]	4.480 [1.426, 14.070]	7.692 [1.838, 32.199]	37.3 [10.8, 63.8]	0.003	*

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table AT2WICD4_ISPF: Decrease of WI-NRS of at least 4 points by use of concomitant itch medication
ITT

		CR845			Placebo						
Decrease of WI-NRS of at least 4 points		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	F: Use of concomitant itch medication										0.548
	No	117	99 (84.6)	42 (35.9) [27.2, 45.3]	111	99 (89.2)	20 (18.0) [11.4, 26.4]	1.992 [1.252, 3.171]	2.548 [1.379, 4.708]	17.9 [5.7, 30.0]	0.002 *
	Yes	72	58 (80.6)	22 (30.6) [20.2, 42.5]	78	66 (84.6)	15 (19.2) [11.2, 29.7]	1.589 [0.896, 2.817]	1.848 [0.869, 3.928]	11.3 [-3.8, 26.4]	0.109

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table AT2WIR_ISPA: Complete WI-NRS responder by age
ITT

Complete WI-NRS responder		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	A: Age										0.158	
	< 65 years	135	135 (100.0)	21 (15.6) [9.9, 22.8]	137	137 (100.0)	8 (5.8) [2.6, 11.2]	2.664 [1.223, 5.805]	2.970 [1.267, 6.966]	9.7 [1.7, 17.7]	0.010	*
	>= 65 years	54	54 (100.0)	5 (9.3) [3.1, 20.3]	52	52 (100.0)	5 (9.6) [3.2, 21.0]	0.963 [0.296, 3.133]	0.959 [0.261, 3.529]	-0.4 [-13.4, 12.7]	1.000	#

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table AT2WIR_ISPB: Complete WI-NRS responder by sex
ITT

		CR845			Placebo						
Complete WI-NRS responder		N	nval	n (%) [95 % CI]	N	nval	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	B: Sex										0.237
	Male	112	112 (100.0)	14 (12.5) [7.0, 20.1]	119	119 (100.0)	5 (4.2) [1.4, 9.5]	2.975 [1.108, 7.990]	3.257 [1.133, 9.366]	8.3 [0.3, 16.3]	0.022 *
	Female	77	77 (100.0)	12 (15.6) [8.3, 25.6]	70	70 (100.0)	8 (11.4) [5.1, 21.3]	1.364 [0.592, 3.140]	1.431 [0.548, 3.736]	4.2 [-8.2, 16.5]	0.464

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table AT2WIR_ISPC: Complete WI-NRS responder by race
ITT

		CR845			Placebo						
Complete WI-NRS responder		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	C: Race										0.819
	Black/African American	82	82 (100.0)	11 (13.4) [6.9, 22.7]	76	76 (100.0)	6 (7.9) [3.0, 16.4]	1.699 [0.661, 4.369]	1.808 [0.634, 5.155]	5.5 [-5.3, 16.3]	0.265
	White	91	91 (100.0)	12 (13.2) [7.0, 21.9]	93	93 (100.0)	6 (6.5) [2.4, 13.5]	2.044 [0.801, 5.214]	2.203 [0.789, 6.146]	6.7 [-2.9, 16.4]	0.125
	Other	15	15 (100.0)	3 (20.0) [4.3, 48.1]	18	18 (100.0)	1 (5.6) [0.1, 27.3]	3.600 [0.416, 31.121]	4.250 [0.393, 45.956]	14.4 [-14.5, 43.4]	0.308 #

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table AT2WIR_ISPD: Complete WI-NRS responder by baseline WI-NRS
ITT

		CR845			Placebo						
Complete WI-NRS responder		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.735
	>= 4 to < 7	83	83 (100.0)	15 (18.1) [10.5, 28.0]	80	80 (100.0)	8 (10.0) [4.4, 18.8]	1.807 [0.811, 4.027]	1.985 [0.791, 4.981]	8.1 [-3.7, 19.9]	0.140
	>= 7	106	106 (100.0)	11 (10.4) [5.3, 17.8]	109	109 (100.0)	5 (4.6) [1.5, 10.4]	2.262 [0.814, 6.291]	2.408 [0.807, 7.186]	5.8 [-2.1, 13.7]	0.107

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table AT2WIR_ISPE: Complete WI-NRS responder by specific medical condition
ITT

		CR845			Placebo						
Complete WI-NRS responder		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	E: Presence of specific medical conditions										0.231
	No	164	164 (100.0)	22 (13.4) [8.6, 19.6]	161	161 (100.0)	13 (8.1) [4.4, 13.4]	1.661 [0.867, 3.183]	1.764 [0.856, 3.635]	5.3 [-2.0, 12.7]	0.121
	Yes	25	25 (100.0)	4 (16.0) [4.5, 36.1]	28	28 (100.0)	0 (0.0) [0.0, 12.3]	10.038 + [0.567, 177.650]	11.930 + [0.609, 233.686]	16.0 [-2.2, 34.2]	0.043 *

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table AT2WIR_ISPF: Complete WI-NRS responder by use of concomitant itch medication
ITT

Complete WI-NRS responder		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	F: Use of concomitant itch medication										0.658	
	No	117	117 (100.0)	19 (16.2) [10.1, 24.2]	111	111 (100.0)	10 (9.0) [4.4, 15.9]	1.803 [0.877, 3.705]	1.958 [0.867, 4.422]	7.2 [-2.2, 16.7]	0.102	
	Yes	72	72 (100.0)	7 (9.7) [4.0, 19.0]	78	78 (100.0)	3 (3.8) [0.8, 10.8]	2.528 [0.679, 9.406]	2.692 [0.669, 10.838]	5.9 [-3.5, 15.3]	0.196	#

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table AT2DTC_ISHA: Change from baseline in 5-D total score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
< 65 years	5-D total score	Baseline	CR845	135	131 (97.0)	16.6 (3.3)	8	16.0	25	
			Placebo	137	137 (100.0)	18.0 (3.4)	10	18.0	25	
		Week 4	CR845	135	119 (88.1)	13.4 (3.2)	6	13.0	24	
			Placebo	137	117 (85.4)	15.8 (4.1)	6	15.0	25	
		Week 8	CR845	135	111 (82.2)	12.3 (3.4)	6	12.0	22	
			Placebo	137	121 (88.3)	14.6 (4.5)	6	14.0	25	
		Week 10	CR845	135	111 (82.2)	11.9 (3.4)	5	12.0	21	
			Placebo	137	118 (86.1)	14.2 (4.3)	5	13.5	25	
		Week 12	CR845	135	113 (83.7)	11.7 (3.5)	5	12.0	22	
			Placebo	137	118 (86.1)	13.9 (4.5)	5	14.0	25	
	Change from baseline in 5-D total score	Week 4	CR845	135	116 (85.9)	-3.4 (3.1)	-14	-3.0	4	-0.32 [-0.57, -0.06]
			Placebo	137	117 (85.4)	-2.2 (4.3)	-12	-1.0	9	
		Week 8	CR845	135	108 (80.0)	-4.3 (3.8)	-14	-4.0	6	-0.23 [-0.49, 0.03]
			Placebo	137	121 (88.3)	-3.3 (4.4)	-18	-3.0	9	
		Week 10	CR845	135	108 (80.0)	-4.7 (4.0)	-15	-5.0	8	-0.21 [-0.47, 0.05]
			Placebo	137	118 (86.1)	-3.8 (4.6)	-18	-4.0	8	
		Week 12	CR845	135	111 (82.2)	-4.9 (4.2)	-15	-5.0	8	-0.21 [-0.47, 0.05]
			Placebo	137	118 (86.1)	-3.9 (4.4)	-17	-3.5	7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DTC_ISHA: Change from baseline in 5-D total score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 65 years	5-D total score	Baseline	CR845	54	54 (100.0)	17.5 (3.8)	10	17.0	25	
			Placebo	52	52 (100.0)	17.6 (3.7)	9	18.0	25	
		Week 4	CR845	54	50 (92.6)	13.8 (4.1)	6	13.0	22	
			Placebo	52	48 (92.3)	15.0 (3.7)	7	15.0	24	
		Week 8	CR845	54	48 (88.9)	13.1 (3.9)	6	13.0	25	
			Placebo	52	49 (94.2)	14.1 (3.9)	6	14.0	25	
		Week 10	CR845	54	46 (85.2)	12.7 (3.7)	6	12.0	21	
			Placebo	52	49 (94.2)	13.6 (4.0)	8	13.0	25	
		Week 12	CR845	54	47 (87.0)	12.7 (4.2)	7	12.0	25	
			Placebo	52	48 (92.3)	13.3 (4.1)	5	13.5	23	
	Change from baseline in 5-D total score	Week 4	CR845	54	50 (92.6)	-3.6 (3.5)	-15	-3.5	4	-0.22 [-0.62, 0.17]
			Placebo	52	48 (92.3)	-2.8 (4.1)	-13	-3.0	9	
		Week 8	CR845	54	48 (88.9)	-4.3 (3.9)	-13	-4.0	5	-0.17 [-0.57, 0.22]
			Placebo	52	49 (94.2)	-3.5 (4.3)	-16	-4.0	8	
		Week 10	CR845	54	46 (85.2)	-4.9 (4.0)	-13	-5.0	6	-0.23 [-0.63, 0.18]
			Placebo	52	49 (94.2)	-4.0 (4.0)	-12	-4.0	4	
		Week 12	CR845	54	47 (87.0)	-5.0 (4.5)	-12	-5.0	6	-0.15 [-0.55, 0.25]
			Placebo	52	48 (92.3)	-4.4 (3.8)	-13	-5.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DTC_ISHB: Change from baseline in 5-D total score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Male	5-D total score	Baseline	CR845	112	110 (98.2)	16.3 (3.3)	8	16.0	25	
			Placebo	119	119 (100.0)	17.6 (3.5)	9	17.0	25	
		Week 4	CR845	112	98 (87.5)	13.3 (3.2)	6	13.0	24	
			Placebo	119	100 (84.0)	15.9 (4.2)	6	15.5	25	
		Week 8	CR845	112	91 (81.3)	12.5 (3.6)	6	13.0	22	
			Placebo	119	106 (89.1)	14.7 (4.3)	6	14.0	25	
		Week 10	CR845	112	91 (81.3)	12.4 (3.5)	6	12.0	21	
			Placebo	119	106 (89.1)	14.0 (4.2)	6	13.0	25	
		Week 12	CR845	112	91 (81.3)	12.0 (3.7)	5	12.0	23	
			Placebo	119	105 (88.2)	13.8 (4.3)	5	14.0	25	
	Change from baseline in 5-D total score	Week 4	CR845	112	97 (86.6)	-3.1 (3.0)	-15	-3.0	4	-0.38 [-0.66, -0.09]
			Placebo	119	100 (84.0)	-1.8 (4.0)	-11	-1.0	8	
		Week 8	CR845	112	90 (80.4)	-3.9 (3.8)	-14	-4.0	6	-0.25 [-0.53, 0.03]
			Placebo	119	106 (89.1)	-2.9 (4.2)	-18	-3.0	9	
		Week 10	CR845	112	90 (80.4)	-4.1 (3.7)	-12	-4.0	8	-0.12 [-0.40, 0.16]
			Placebo	119	106 (89.1)	-3.6 (4.1)	-18	-4.0	8	
		Week 12	CR845	112	90 (80.4)	-4.4 (4.3)	-13	-4.0	8	-0.18 [-0.46, 0.11]
			Placebo	119	105 (88.2)	-3.6 (4.0)	-16	-4.0	7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DTC_ISHB: Change from baseline in 5-D total score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Female	5-D total score	Baseline	CR845	77	75 (97.4)	17.7 (3.5)	10	18.0	25	
			Placebo	70	70 (100.0)	18.3 (3.4)	12	18.0	25	
		Week 4	CR845	77	71 (92.2)	13.7 (3.9)	6	14.0	22	
			Placebo	70	65 (92.9)	15.2 (3.6)	9	15.0	23	
		Week 8	CR845	77	68 (88.3)	12.7 (3.5)	6	12.0	25	
			Placebo	70	64 (91.4)	14.1 (4.3)	6	14.0	25	
		Week 10	CR845	77	66 (85.7)	11.8 (3.4)	5	12.0	21	
			Placebo	70	61 (87.1)	14.0 (4.3)	5	14.0	24	
		Week 12	CR845	77	69 (89.6)	11.9 (3.9)	5	12.0	25	
			Placebo	70	61 (87.1)	13.6 (4.6)	5	14.0	24	
	Change from baseline in 5-D total score	Week 4	CR845	77	69 (89.6)	-3.9 (3.5)	-14	-4.0	4	-0.17 [-0.51, 0.17]
			Placebo	70	65 (92.9)	-3.2 (4.4)	-13	-3.0	9	
		Week 8	CR845	77	66 (85.7)	-4.8 (3.9)	-14	-4.0	3	-0.14 [-0.48, 0.21]
			Placebo	70	64 (91.4)	-4.2 (4.6)	-17	-4.0	5	
		Week 10	CR845	77	64 (83.1)	-5.7 (4.1)	-15	-5.5	4	-0.32 [-0.67, 0.03]
			Placebo	70	61 (87.1)	-4.3 (5.0)	-18	-4.0	5	
		Week 12	CR845	77	68 (88.3)	-5.6 (4.2)	-15	-6.0	6	-0.19 [-0.53, 0.16]
			Placebo	70	61 (87.1)	-4.8 (4.6)	-17	-5.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DTC_ISHC: Change from baseline in 5-D total score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Black/African American	5-D total score	Baseline	CR845	82	81 (98.8)	16.8 (3.4)	8	16.0	25	
			Placebo	76	76 (100.0)	17.6 (3.7)	9	17.0	25	
		Week 4	CR845	82	69 (84.1)	13.0 (3.8)	6	13.0	22	
			Placebo	76	66 (86.8)	15.6 (4.1)	8	15.0	24	
		Week 8	CR845	82	66 (80.5)	12.1 (3.8)	6	12.0	25	
			Placebo	76	68 (89.5)	14.0 (4.2)	6	14.0	25	
		Week 10	CR845	82	64 (78.0)	11.3 (3.1)	6	11.0	21	
			Placebo	76	66 (86.8)	13.8 (4.3)	5	13.0	25	
		Week 12	CR845	82	66 (80.5)	11.2 (3.7)	5	11.0	22	
			Placebo	76	66 (86.8)	13.7 (4.5)	5	14.0	24	
	Change from baseline in 5-D total score	Week 4	CR845	82	68 (82.9)	-3.7 (3.4)	-15	-3.0	4	-0.43 [-0.77, -0.09]
			Placebo	76	66 (86.8)	-2.0 (4.6)	-12	-1.5	9	
		Week 8	CR845	82	65 (79.3)	-4.7 (3.9)	-14	-5.0	6	-0.23 [-0.57, 0.11]
			Placebo	76	68 (89.5)	-3.7 (4.7)	-18	-3.5	9	
		Week 10	CR845	82	63 (76.8)	-5.4 (3.6)	-15	-5.0	1	-0.35 [-0.70, 0.00]
			Placebo	76	66 (86.8)	-4.0 (4.8)	-18	-4.0	8	
		Week 12	CR845	82	65 (79.3)	-5.6 (4.1)	-15	-5.0	6	-0.40 [-0.75, -0.05]
			Placebo	76	66 (86.8)	-3.8 (4.5)	-17	-4.0	7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DTC_ISHC: Change from baseline in 5-D total score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
White	5-D total score	Baseline	CR845	91	88 (96.7)	16.9 (3.5)	9	17.0	25	
			Placebo	93	93 (100.0)	18.0 (3.4)	12	18.0	25	
		Week 4	CR845	91	85 (93.4)	13.9 (3.4)	7	14.0	24	
			Placebo	93	81 (87.1)	15.3 (3.6)	6	15.0	24	
		Week 8	CR845	91	78 (85.7)	12.9 (3.2)	7	13.0	22	
			Placebo	93	83 (89.2)	14.7 (4.3)	6	14.0	25	
		Week 10	CR845	91	79 (86.8)	12.9 (3.5)	6	13.0	21	
			Placebo	93	82 (88.2)	14.3 (4.2)	7	14.0	25	
		Week 12	CR845	91	80 (87.9)	12.3 (3.4)	6	12.0	22	
			Placebo	93	80 (86.0)	14.0 (4.2)	5	14.0	23	
	Change from baseline in 5-D total score	Week 4	CR845	91	83 (91.2)	-3.2 (3.1)	-11	-3.0	4	-0.11 [-0.42, 0.19]
			Placebo	93	81 (87.1)	-2.8 (4.0)	-13	-3.0	9	
		Week 8	CR845	91	76 (83.5)	-3.9 (3.7)	-14	-3.5	5	-0.17 [-0.48, 0.14]
			Placebo	93	83 (89.2)	-3.2 (4.3)	-16	-3.0	8	
		Week 10	CR845	91	77 (84.6)	-4.0 (4.1)	-12	-4.0	8	-0.07 [-0.38, 0.24]
			Placebo	93	82 (88.2)	-3.7 (4.2)	-14	-4.0	5	
		Week 12	CR845	91	79 (86.8)	-4.6 (4.3)	-13	-5.0	8	-0.17 [-0.48, 0.15]
			Placebo	93	80 (86.0)	-3.9 (3.9)	-15	-4.0	4	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DTC_ISHC: Change from baseline in 5-D total score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Other	5-D total score	Baseline	CR845	15	15 (100.0)	17.3 (3.7)	11	16.0	25	
			Placebo	18	18 (100.0)	18.0 (3.0)	14	17.0	24	
		Week 4	CR845	15	14 (93.3)	13.4 (2.6)	10	12.5	17	
			Placebo	18	16 (88.9)	15.8 (4.8)	7	15.0	25	
		Week 8	CR845	15	14 (93.3)	13.1 (4.3)	6	14.0	22	
			Placebo	18	17 (94.4)	14.6 (4.2)	8	15.0	25	
		Week 10	CR845	15	13 (86.7)	11.7 (4.1)	5	11.0	18	
			Placebo	18	17 (94.4)	13.5 (4.7)	8	13.0	25	
		Week 12	CR845	15	13 (86.7)	14.1 (5.5)	7	14.0	25	
			Placebo	18	18 (100.0)	12.7 (4.7)	7	10.5	25	
	Change from baseline in 5-D total score	Week 4	CR845	15	14 (93.3)	-3.8 (3.1)	-8	-3.5	1	-0.39 [-1.11, 0.33]
			Placebo	18	16 (88.9)	-2.4 (4.0)	-9	-1.5	3	
		Week 8	CR845	15	14 (93.3)	-4.6 (4.9)	-13	-4.5	5	-0.25 [-0.96, 0.46]
			Placebo	18	17 (94.4)	-3.5 (4.0)	-9	-4.0	5	
		Week 10	CR845	15	13 (86.7)	-6.1 (4.3)	-14	-7.0	0	-0.42 [-1.15, 0.31]
			Placebo	18	17 (94.4)	-4.3 (4.2)	-12	-4.0	2	
		Week 12	CR845	15	13 (86.7)	-3.6 (5.0)	-12	-4.0	6	0.35 [-0.37, 1.07]
			Placebo	18	18 (100.0)	-5.3 (4.5)	-13	-5.5	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DTC_ISHD: Change from baseline in 5-D total score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 4 to < 7	5-D total score	Baseline	CR845	83	82 (98.8)	14.9 (2.8)	8	15.0	22	
			Placebo	80	80 (100.0)	15.6 (2.9)	9	16.0	23	
		Week 4	CR845	83	73 (88.0)	11.9 (2.6)	6	12.0	18	
			Placebo	80	70 (87.5)	14.5 (3.7)	6	14.0	23	
		Week 8	CR845	83	69 (83.1)	11.9 (2.8)	7	12.0	19	
			Placebo	80	72 (90.0)	13.4 (3.6)	6	13.0	23	
		Week 10	CR845	83	69 (83.1)	11.4 (2.7)	6	11.0	18	
			Placebo	80	71 (88.8)	13.2 (4.0)	7	13.0	25	
		Week 12	CR845	83	68 (81.9)	11.1 (2.8)	5	11.0	17	
			Placebo	80	72 (90.0)	12.6 (4.1)	5	12.0	22	
	Change from baseline in 5-D total score	Week 4	CR845	83	73 (88.0)	-2.9 (3.1)	-15	-3.0	4	-0.51 [-0.84, -0.17]
			Placebo	80	70 (87.5)	-1.2 (3.7)	-11	-1.0	9	
		Week 8	CR845	83	69 (83.1)	-3.2 (3.1)	-13	-3.0	6	-0.27 [-0.60, 0.06]
			Placebo	80	72 (90.0)	-2.3 (3.6)	-12	-2.0	8	
		Week 10	CR845	83	69 (83.1)	-3.6 (3.3)	-12	-4.0	6	-0.33 [-0.66, 0.01]
			Placebo	80	71 (88.8)	-2.5 (3.7)	-14	-2.0	8	
		Week 12	CR845	83	68 (81.9)	-3.8 (3.4)	-13	-3.5	3	-0.22 [-0.55, 0.12]
			Placebo	80	72 (90.0)	-3.0 (3.7)	-15	-3.0	5	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DTC_ISHD: Change from baseline in 5-D total score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 7	5-D total score	Baseline	CR845	106	103 (97.2)	18.4 (3.1)	10	18.0	25	
			Placebo	109	109 (100.0)	19.5 (2.9)	13	19.0	25	
		Week 4	CR845	106	96 (90.6)	14.7 (3.6)	7	15.0	24	
			Placebo	109	95 (87.2)	16.4 (4.0)	8	16.0	25	
		Week 8	CR845	106	90 (84.9)	13.1 (3.9)	6	13.0	25	
			Placebo	109	98 (89.9)	15.3 (4.6)	6	14.5	25	
		Week 10	CR845	106	88 (83.0)	12.7 (3.8)	5	12.0	21	
			Placebo	109	96 (88.1)	14.6 (4.3)	5	14.0	25	
		Week 12	CR845	106	92 (86.8)	12.7 (4.2)	5	12.0	25	
			Placebo	109	94 (86.2)	14.6 (4.4)	6	14.0	25	
	Change from baseline in 5-D total score	Week 4	CR845	106	93 (87.7)	-3.9 (3.3)	-14	-4.0	4	-0.17 [-0.45, 0.12]
			Placebo	109	95 (87.2)	-3.2 (4.4)	-13	-3.0	8	
		Week 8	CR845	106	87 (82.1)	-5.2 (4.2)	-14	-5.0	5	-0.21 [-0.50, 0.08]
			Placebo	109	98 (89.9)	-4.2 (4.8)	-18	-4.0	9	
		Week 10	CR845	106	85 (80.2)	-5.7 (4.2)	-15	-6.0	8	-0.18 [-0.48, 0.11]
			Placebo	109	96 (88.1)	-4.9 (4.7)	-18	-5.0	4	
		Week 12	CR845	106	90 (84.9)	-5.7 (4.7)	-15	-6.0	8	-0.19 [-0.48, 0.10]
			Placebo	109	94 (86.2)	-4.8 (4.5)	-17	-5.0	7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DTC_ISHE: Change from baseline in 5-D total score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	5-D total score	Baseline	CR845	164	160 (97.6)	16.7 (3.5)	8	16.0	25	
			Placebo	161	161 (100.0)	17.7 (3.5)	10	18.0	25	
		Week 4	CR845	164	145 (88.4)	13.3 (3.5)	6	13.0	24	
			Placebo	161	139 (86.3)	15.4 (4.0)	6	15.0	25	
		Week 8	CR845	164	136 (82.9)	12.4 (3.6)	6	12.0	25	
			Placebo	161	143 (88.8)	14.4 (4.3)	6	14.0	25	
		Week 10	CR845	164	135 (82.3)	12.0 (3.5)	5	12.0	21	
			Placebo	161	142 (88.2)	13.8 (4.2)	5	13.0	25	
		Week 12	CR845	164	136 (82.9)	12.1 (3.8)	6	12.0	25	
			Placebo	161	139 (86.3)	13.5 (4.4)	5	13.0	25	
	Change from baseline in 5-D total score	Week 4	CR845	164	142 (86.6)	-3.5 (3.3)	-15	-3.0	4	-0.29 [-0.53, -0.06]
			Placebo	161	139 (86.3)	-2.4 (4.3)	-13	-2.0	9	
		Week 8	CR845	164	133 (81.1)	-4.3 (4.0)	-14	-4.0	6	-0.22 [-0.45, 0.02]
			Placebo	161	143 (88.8)	-3.3 (4.6)	-18	-3.0	9	
		Week 10	CR845	164	132 (80.5)	-4.7 (3.9)	-15	-5.0	8	-0.18 [-0.41, 0.06]
			Placebo	161	142 (88.2)	-4.0 (4.5)	-18	-4.0	8	
		Week 12	CR845	164	134 (81.7)	-4.6 (4.3)	-15	-4.0	8	-0.11 [-0.35, 0.12]
			Placebo	161	139 (86.3)	-4.1 (4.3)	-17	-4.0	7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DTC_ISHE: Change from baseline in 5-D total score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	5-D total score	Baseline	CR845	25	25 (100.0)	18.0 (3.2)	12	18.0	24	
			Placebo	28	28 (100.0)	18.6 (3.3)	9	19.5	24	
		Week 4	CR845	25	24 (96.0)	15.0 (2.9)	10	14.0	21	
			Placebo	28	26 (92.9)	16.5 (4.0)	10	17.0	24	
		Week 8	CR845	25	23 (92.0)	13.7 (3.1)	9	13.0	19	
			Placebo	28	27 (96.4)	15.1 (4.4)	8	15.0	23	
		Week 10	CR845	25	22 (88.0)	12.8 (3.4)	6	11.5	20	
			Placebo	28	25 (89.3)	15.5 (4.3)	8	15.0	22	
		Week 12	CR845	25	24 (96.0)	11.6 (3.4)	5	12.0	18	
			Placebo	28	27 (96.4)	15.1 (4.0)	8	14.0	23	
	Change from baseline in 5-D total score	Week 4	CR845	25	24 (96.0)	-3.0 (3.0)	-9	-3.0	4	-0.25 [-0.81, 0.31]
			Placebo	28	26 (92.9)	-2.1 (3.9)	-9	-2.0	4	
		Week 8	CR845	25	23 (92.0)	-4.3 (3.1)	-12	-4.0	3	-0.20 [-0.76, 0.35]
			Placebo	28	27 (96.4)	-3.6 (3.5)	-10	-4.0	2	
		Week 10	CR845	25	22 (88.0)	-5.0 (4.2)	-14	-5.0	4	-0.45 [-1.03, 0.13]
			Placebo	28	25 (89.3)	-3.2 (4.0)	-14	-2.0	2	
		Week 12	CR845	25	24 (96.0)	-6.4 (3.8)	-15	-6.5	0	-0.72 [-1.29, -0.16]
			Placebo	28	27 (96.4)	-3.6 (3.8)	-13	-3.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DTC_ISHF: Change from baseline in 5-D total score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	5-D total score	Baseline	CR845	117	115 (98.3)	16.5 (3.6)	8	16.0	25	
			Placebo	111	111 (100.0)	17.3 (3.3)	9	17.0	25	
		Week 4	CR845	117	107 (91.5)	13.5 (3.4)	6	14.0	24	
			Placebo	111	94 (84.7)	15.4 (3.5)	7	15.0	24	
		Week 8	CR845	117	101 (86.3)	12.2 (3.3)	6	12.0	22	
			Placebo	111	100 (90.1)	14.3 (3.9)	6	14.0	25	
		Week 10	CR845	117	99 (84.6)	12.0 (3.5)	5	11.0	21	
			Placebo	111	98 (88.3)	13.7 (4.1)	5	13.0	25	
		Week 12	CR845	117	100 (85.5)	11.9 (3.7)	5	12.0	25	
			Placebo	111	100 (90.1)	13.4 (4.3)	5	14.0	24	
	Change from baseline in 5-D total score	Week 4	CR845	117	106 (90.6)	-3.2 (3.0)	-10	-3.0	4	-0.34 [-0.62, -0.06]
			Placebo	111	94 (84.7)	-2.0 (4.2)	-12	-1.0	9	
		Week 8	CR845	117	100 (85.5)	-4.2 (3.9)	-14	-4.0	6	-0.27 [-0.55, 0.01]
			Placebo	111	100 (90.1)	-3.1 (4.6)	-18	-3.0	9	
		Week 10	CR845	117	98 (83.8)	-4.6 (4.1)	-15	-4.0	8	-0.19 [-0.47, 0.09]
			Placebo	111	98 (88.3)	-3.7 (4.8)	-18	-3.0	8	
		Week 12	CR845	117	100 (85.5)	-4.7 (4.3)	-15	-4.0	8	-0.18 [-0.46, 0.10]
			Placebo	111	100 (90.1)	-3.9 (4.4)	-17	-4.0	7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DTC_ISHF: Change from baseline in 5-D total score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	5-D total score	Baseline	CR845	72	70 (97.2)	17.4 (3.2)	10	17.0	24	
			Placebo	78	78 (100.0)	18.6 (3.5)	12	19.0	25	
		Week 4	CR845	72	62 (86.1)	13.6 (3.7)	6	13.0	22	
			Placebo	78	71 (91.0)	15.8 (4.5)	6	15.0	25	
		Week 8	CR845	72	58 (80.6)	13.2 (3.9)	6	13.0	25	
			Placebo	78	70 (89.7)	14.8 (4.8)	6	13.0	25	
		Week 10	CR845	72	58 (80.6)	12.3 (3.4)	6	12.0	21	
			Placebo	78	69 (88.5)	14.6 (4.4)	7	14.0	25	
		Week 12	CR845	72	60 (83.3)	12.1 (3.9)	5	12.0	23	
			Placebo	78	66 (84.6)	14.2 (4.4)	5	14.0	25	
	Change from baseline in 5-D total score	Week 4	CR845	72	60 (83.3)	-3.9 (3.6)	-15	-3.0	1	-0.26 [-0.61, 0.08]
			Placebo	78	71 (91.0)	-2.9 (4.3)	-13	-3.0	9	
		Week 8	CR845	72	56 (77.8)	-4.3 (3.9)	-14	-4.0	5	-0.14 [-0.49, 0.22]
			Placebo	78	70 (89.7)	-3.8 (4.0)	-16	-3.0	6	
		Week 10	CR845	72	56 (77.8)	-5.1 (3.8)	-14	-5.0	6	-0.28 [-0.64, 0.07]
			Placebo	78	69 (88.5)	-4.0 (3.8)	-14	-4.0	4	
		Week 12	CR845	72	58 (80.6)	-5.3 (4.4)	-15	-6.5	7	-0.23 [-0.58, 0.12]
			Placebo	78	66 (84.6)	-4.3 (4.0)	-13	-4.0	4	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DDC_ISHA: Change from baseline in 5-D degree score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
< 65 years	5-D degree score	Baseline	CR845	135	132 (97.8)	3.4 (0.6)	2	3.0	5	
			Placebo	137	137 (100.0)	3.6 (0.8)	1	4.0	5	
		Week 4	CR845	135	119 (88.1)	2.9 (0.8)	1	3.0	5	
			Placebo	137	117 (85.4)	3.3 (0.9)	1	3.0	5	
		Week 8	CR845	135	111 (82.2)	2.7 (0.8)	1	3.0	5	
			Placebo	137	121 (88.3)	3.0 (0.9)	1	3.0	5	
		Week 10	CR845	135	111 (82.2)	2.6 (0.8)	1	2.0	5	
			Placebo	137	118 (86.1)	3.0 (0.9)	1	3.0	5	
		Week 12	CR845	135	113 (83.7)	2.5 (0.7)	1	2.0	5	
			Placebo	137	118 (86.1)	2.8 (1.0)	1	3.0	5	
	Change from baseline in 5-D degree score	Week 4	CR845	135	117 (86.7)	-0.5 (0.8)	-2	-1.0	2	-0.24 [-0.50, 0.02]
			Placebo	137	117 (85.4)	-0.3 (0.9)	-3	0.0	2	
		Week 8	CR845	135	109 (80.7)	-0.7 (0.9)	-3	-1.0	2	-0.07 [-0.33, 0.19]
			Placebo	137	121 (88.3)	-0.6 (1.0)	-4	-1.0	2	
		Week 10	CR845	135	109 (80.7)	-0.8 (0.9)	-3	-1.0	2	-0.23 [-0.50, 0.03]
			Placebo	137	118 (86.1)	-0.6 (1.1)	-4	-1.0	2	
		Week 12	CR845	135	112 (83.0)	-0.9 (0.9)	-3	-1.0	2	-0.17 [-0.43, 0.09]
			Placebo	137	118 (86.1)	-0.7 (1.0)	-3	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DDC_ISHA: Change from baseline in 5-D degree score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 65 years	5-D degree score	Baseline	CR845	54	54 (100.0)	3.5 (0.7)	2	4.0	5	
			Placebo	52	52 (100.0)	3.5 (0.9)	2	3.0	5	
		Week 4	CR845	54	50 (92.6)	2.8 (0.9)	1	3.0	5	
			Placebo	52	48 (92.3)	3.1 (0.7)	2	3.0	5	
		Week 8	CR845	54	48 (88.9)	2.8 (0.8)	1	3.0	5	
			Placebo	52	49 (94.2)	2.9 (0.8)	1	3.0	5	
		Week 10	CR845	54	46 (85.2)	2.7 (0.7)	2	3.0	5	
			Placebo	52	49 (94.2)	2.8 (0.7)	2	3.0	5	
		Week 12	CR845	54	47 (87.0)	2.6 (0.8)	2	2.0	5	
			Placebo	52	48 (92.3)	2.8 (0.8)	1	3.0	5	
	Change from baseline in 5-D degree score	Week 4	CR845	54	50 (92.6)	-0.7 (0.9)	-3	-1.0	2	-0.39 [-0.79, 0.01]
			Placebo	52	48 (92.3)	-0.4 (0.8)	-2	0.0	1	
		Week 8	CR845	54	48 (88.9)	-0.8 (0.9)	-3	-1.0	1	-0.20 [-0.60, 0.20]
			Placebo	52	49 (94.2)	-0.6 (0.9)	-3	0.0	1	
		Week 10	CR845	54	46 (85.2)	-0.9 (0.9)	-2	-1.0	1	-0.29 [-0.70, 0.11]
			Placebo	52	49 (94.2)	-0.6 (0.9)	-2	-1.0	1	
		Week 12	CR845	54	47 (87.0)	-0.9 (1.0)	-2	-1.0	2	-0.17 [-0.57, 0.24]
			Placebo	52	48 (92.3)	-0.8 (0.8)	-3	-1.0	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DDC_ISHB: Change from baseline in 5-D degree score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Male	5-D degree score	Baseline	CR845	112	110 (98.2)	3.3 (0.7)	2	3.0	5	
			Placebo	119	119 (100.0)	3.5 (0.8)	1	4.0	5	
		Week 4	CR845	112	98 (87.5)	2.8 (0.8)	1	3.0	5	
			Placebo	119	100 (84.0)	3.2 (0.9)	1	3.0	5	
		Week 8	CR845	112	91 (81.3)	2.7 (0.8)	1	3.0	5	
			Placebo	119	106 (89.1)	3.0 (0.9)	1	3.0	5	
		Week 10	CR845	112	91 (81.3)	2.6 (0.8)	1	3.0	5	
			Placebo	119	106 (89.1)	3.0 (0.9)	1	3.0	5	
		Week 12	CR845	112	91 (81.3)	2.5 (0.7)	1	2.0	5	
			Placebo	119	105 (88.2)	2.8 (0.9)	1	3.0	5	
	Change from baseline in 5-D degree score	Week 4	CR845	112	97 (86.6)	-0.6 (0.8)	-3	-1.0	2	-0.27 [-0.55, 0.01]
			Placebo	119	100 (84.0)	-0.3 (0.9)	-3	0.0	2	
		Week 8	CR845	112	90 (80.4)	-0.6 (0.9)	-3	-1.0	2	-0.09 [-0.37, 0.19]
			Placebo	119	106 (89.1)	-0.5 (0.9)	-4	0.0	2	
		Week 10	CR845	112	90 (80.4)	-0.7 (0.9)	-2	-1.0	2	-0.22 [-0.50, 0.06]
			Placebo	119	106 (89.1)	-0.5 (1.0)	-4	-0.5	2	
		Week 12	CR845	112	90 (80.4)	-0.8 (0.9)	-2	-1.0	2	-0.14 [-0.42, 0.14]
			Placebo	119	105 (88.2)	-0.7 (0.9)	-3	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DDC_ISHB: Change from baseline in 5-D degree score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Female	5-D degree score	Baseline	CR845	77	76 (98.7)	3.5 (0.7)	2	3.5	5	
			Placebo	70	70 (100.0)	3.6 (0.8)	2	4.0	5	
		Week 4	CR845	77	71 (92.2)	2.9 (0.8)	1	3.0	5	
			Placebo	70	65 (92.9)	3.2 (0.7)	2	3.0	5	
		Week 8	CR845	77	68 (88.3)	2.7 (0.7)	1	3.0	5	
			Placebo	70	64 (91.4)	2.8 (0.9)	1	3.0	5	
		Week 10	CR845	77	66 (85.7)	2.5 (0.7)	1	2.0	5	
			Placebo	70	61 (87.1)	2.9 (0.9)	1	3.0	5	
		Week 12	CR845	77	69 (89.6)	2.5 (0.8)	1	2.0	5	
			Placebo	70	61 (87.1)	2.8 (1.0)	1	3.0	5	
	Change from baseline in 5-D degree score	Week 4	CR845	77	70 (90.9)	-0.6 (0.8)	-2	-1.0	2	-0.31 [-0.65, 0.03]
			Placebo	70	65 (92.9)	-0.4 (0.9)	-2	0.0	2	
		Week 8	CR845	77	67 (87.0)	-0.8 (0.9)	-2	-1.0	1	-0.10 [-0.45, 0.24]
			Placebo	70	64 (91.4)	-0.7 (1.1)	-4	-1.0	1	
		Week 10	CR845	77	65 (84.4)	-1.0 (0.9)	-3	-1.0	1	-0.27 [-0.62, 0.08]
			Placebo	70	61 (87.1)	-0.7 (1.0)	-3	-1.0	1	
		Week 12	CR845	77	69 (89.6)	-1.0 (0.9)	-3	-1.0	2	-0.20 [-0.54, 0.15]
			Placebo	70	61 (87.1)	-0.8 (1.0)	-3	-1.0	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DDC_ISHC: Change from baseline in 5-D degree score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Black/African American	5-D degree score	Baseline	CR845	82	82 (100.0)	3.4 (0.7)	2	3.0	5	
			Placebo	76	76 (100.0)	3.5 (0.9)	1	3.0	5	
		Week 4	CR845	82	69 (84.1)	2.8 (0.9)	1	3.0	5	
			Placebo	76	66 (86.8)	3.2 (0.8)	2	3.0	5	
		Week 8	CR845	82	66 (80.5)	2.6 (0.8)	1	2.0	5	
			Placebo	76	68 (89.5)	2.9 (0.9)	1	3.0	5	
		Week 10	CR845	82	64 (78.0)	2.5 (0.7)	1	2.0	5	
			Placebo	76	66 (86.8)	2.9 (0.9)	1	3.0	5	
		Week 12	CR845	82	66 (80.5)	2.4 (0.8)	1	2.0	5	
			Placebo	76	66 (86.8)	2.8 (0.9)	1	3.0	5	
	Change from baseline in 5-D degree score	Week 4	CR845	82	69 (84.1)	-0.6 (1.0)	-3	-1.0	2	-0.35 [-0.69, -0.01]
			Placebo	76	66 (86.8)	-0.2 (1.0)	-3	0.0	2	
		Week 8	CR845	82	66 (80.5)	-0.8 (1.0)	-3	-1.0	2	-0.15 [-0.49, 0.19]
			Placebo	76	68 (89.5)	-0.7 (1.1)	-4	-1.0	2	
		Week 10	CR845	82	64 (78.0)	-0.9 (0.9)	-3	-1.0	1	-0.35 [-0.70, -0.00]
			Placebo	76	66 (86.8)	-0.6 (1.2)	-4	-1.0	2	
		Week 12	CR845	82	66 (80.5)	-1.0 (0.9)	-3	-1.0	2	-0.34 [-0.68, 0.01]
			Placebo	76	66 (86.8)	-0.7 (1.0)	-3	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DDC_ISHC: Change from baseline in 5-D degree score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
White	5-D degree score	Baseline	CR845	91	88 (96.7)	3.5 (0.7)	2	3.0	5	
			Placebo	93	93 (100.0)	3.6 (0.8)	2	4.0	5	
		Week 4	CR845	91	85 (93.4)	2.9 (0.8)	1	3.0	5	
			Placebo	93	81 (87.1)	3.2 (0.8)	1	3.0	5	
		Week 8	CR845	91	78 (85.7)	2.8 (0.7)	1	3.0	5	
			Placebo	93	83 (89.2)	3.0 (0.9)	1	3.0	5	
		Week 10	CR845	91	79 (86.8)	2.7 (0.8)	1	3.0	5	
			Placebo	93	82 (88.2)	3.0 (0.9)	1	3.0	5	
		Week 12	CR845	91	80 (87.9)	2.6 (0.6)	1	3.0	5	
			Placebo	93	80 (86.0)	2.9 (0.9)	1	3.0	5	
	Change from baseline in 5-D degree score	Week 4	CR845	91	83 (91.2)	-0.6 (0.7)	-2	-1.0	1	-0.18 [-0.49, 0.13]
			Placebo	93	81 (87.1)	-0.5 (0.8)	-2	0.0	1	
		Week 8	CR845	91	76 (83.5)	-0.6 (0.8)	-3	-1.0	2	-0.06 [-0.37, 0.25]
			Placebo	93	83 (89.2)	-0.6 (0.9)	-4	0.0	1	
		Week 10	CR845	91	77 (84.6)	-0.7 (0.9)	-2	-1.0	2	-0.15 [-0.46, 0.17]
			Placebo	93	82 (88.2)	-0.6 (0.9)	-2	-1.0	1	
		Week 12	CR845	91	79 (86.8)	-0.8 (0.8)	-2	-1.0	1	-0.15 [-0.46, 0.16]
			Placebo	93	80 (86.0)	-0.7 (0.8)	-3	-1.0	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DDC_ISHC: Change from baseline in 5-D degree score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Other	5-D degree score	Baseline	CR845	15	15 (100.0)	3.4 (0.6)	3	3.0	5	
			Placebo	18	18 (100.0)	3.6 (0.8)	2	4.0	5	
		Week 4	CR845	15	14 (93.3)	2.9 (0.4)	2	3.0	3	
			Placebo	18	16 (88.9)	3.3 (1.1)	2	3.0	5	
		Week 8	CR845	15	14 (93.3)	2.7 (0.8)	1	3.0	4	
			Placebo	18	17 (94.4)	2.9 (0.8)	2	3.0	5	
		Week 10	CR845	15	13 (86.7)	2.5 (0.8)	1	3.0	4	
			Placebo	18	17 (94.4)	2.9 (1.1)	2	3.0	5	
		Week 12	CR845	15	13 (86.7)	2.9 (1.1)	2	3.0	5	
			Placebo	18	18 (100.0)	2.7 (1.1)	1	2.5	5	
	Change from baseline in 5-D degree score	Week 4	CR845	15	14 (93.3)	-0.6 (0.6)	-2	-0.5	0	-0.36 [-1.08, 0.36]
			Placebo	18	16 (88.9)	-0.3 (1.1)	-2	0.0	1	
		Week 8	CR845	15	14 (93.3)	-0.7 (0.9)	-2	-1.0	1	-0.07 [-0.78, 0.64]
			Placebo	18	17 (94.4)	-0.6 (1.1)	-3	-1.0	1	
		Week 10	CR845	15	13 (86.7)	-0.9 (0.8)	-2	-1.0	0	-0.34 [-1.07, 0.39]
			Placebo	18	17 (94.4)	-0.6 (1.1)	-2	-1.0	1	
		Week 12	CR845	15	13 (86.7)	-0.5 (1.1)	-2	-1.0	2	0.36 [-0.36, 1.07]
			Placebo	18	18 (100.0)	-0.8 (1.0)	-3	-1.0	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DDC_ISHD: Change from baseline in 5-D degree score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 4 to < 7	5-D degree score	Baseline	CR845	83	82 (98.8)	3.1 (0.6)	2	3.0	5	
			Placebo	80	80 (100.0)	3.0 (0.6)	1	3.0	5	
		Week 4	CR845	83	73 (88.0)	2.6 (0.7)	1	3.0	5	
			Placebo	80	70 (87.5)	2.9 (0.7)	1	3.0	5	
		Week 8	CR845	83	69 (83.1)	2.6 (0.8)	1	3.0	5	
			Placebo	80	72 (90.0)	2.7 (0.7)	1	3.0	4	
		Week 10	CR845	83	69 (83.1)	2.6 (0.7)	1	3.0	5	
			Placebo	80	71 (88.8)	2.8 (0.8)	1	3.0	5	
		Week 12	CR845	83	68 (81.9)	2.4 (0.7)	1	2.0	5	
			Placebo	80	72 (90.0)	2.6 (0.9)	1	3.0	4	
	Change from baseline in 5-D degree score	Week 4	CR845	83	73 (88.0)	-0.4 (0.8)	-3	0.0	2	-0.38 [-0.71, -0.05]
			Placebo	80	70 (87.5)	-0.1 (0.7)	-2	0.0	2	
		Week 8	CR845	83	69 (83.1)	-0.4 (0.7)	-2	0.0	2	-0.15 [-0.48, 0.18]
			Placebo	80	72 (90.0)	-0.3 (0.8)	-2	0.0	2	
		Week 10	CR845	83	69 (83.1)	-0.5 (0.8)	-2	-1.0	2	-0.35 [-0.68, -0.01]
			Placebo	80	71 (88.8)	-0.2 (0.9)	-2	0.0	2	
		Week 12	CR845	83	68 (81.9)	-0.7 (0.8)	-2	-1.0	2	-0.25 [-0.58, 0.09]
			Placebo	80	72 (90.0)	-0.5 (0.9)	-2	0.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DDC_ISHD: Change from baseline in 5-D degree score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 7	5-D degree score	Baseline	CR845	106	104 (98.1)	3.7 (0.6)	2	4.0	5	
			Placebo	109	109 (100.0)	4.0 (0.7)	2	4.0	5	
		Week 4	CR845	106	96 (90.6)	3.0 (0.8)	1	3.0	5	
			Placebo	109	95 (87.2)	3.5 (0.8)	2	3.0	5	
		Week 8	CR845	106	90 (84.9)	2.7 (0.8)	1	3.0	5	
			Placebo	109	98 (89.9)	3.2 (1.0)	1	3.0	5	
		Week 10	CR845	106	88 (83.0)	2.6 (0.8)	1	2.5	5	
			Placebo	109	96 (88.1)	3.1 (0.9)	1	3.0	5	
		Week 12	CR845	106	92 (86.8)	2.6 (0.8)	1	3.0	5	
			Placebo	109	94 (86.2)	3.0 (0.9)	1	3.0	5	
	Change from baseline in 5-D degree score	Week 4	CR845	106	94 (88.7)	-0.7 (0.8)	-2	-1.0	2	-0.25 [-0.54, 0.04]
			Placebo	109	95 (87.2)	-0.5 (1.0)	-3	0.0	2	
		Week 8	CR845	106	88 (83.0)	-0.9 (1.0)	-3	-1.0	1	-0.10 [-0.39, 0.19]
			Placebo	109	98 (89.9)	-0.8 (1.1)	-4	-1.0	1	
		Week 10	CR845	106	86 (81.1)	-1.0 (0.9)	-3	-1.0	1	-0.22 [-0.52, 0.07]
			Placebo	109	96 (88.1)	-0.8 (1.0)	-4	-1.0	1	
		Week 12	CR845	106	91 (85.8)	-1.0 (0.9)	-3	-1.0	2	-0.13 [-0.41, 0.16]
			Placebo	109	94 (86.2)	-0.9 (0.9)	-3	-1.0	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DDC_ISHE: Change from baseline in 5-D degree score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	5-D degree score	Baseline	CR845	164	161 (98.2)	3.4 (0.7)	2	3.0	5	
			Placebo	161	161 (100.0)	3.5 (0.8)	1	3.0	5	
		Week 4	CR845	164	145 (88.4)	2.8 (0.8)	1	3.0	5	
			Placebo	161	139 (86.3)	3.2 (0.8)	1	3.0	5	
		Week 8	CR845	164	136 (82.9)	2.7 (0.8)	1	3.0	5	
			Placebo	161	143 (88.8)	2.9 (0.9)	1	3.0	5	
		Week 10	CR845	164	135 (82.3)	2.6 (0.8)	1	2.0	5	
			Placebo	161	142 (88.2)	2.9 (0.9)	1	3.0	5	
		Week 12	CR845	164	136 (82.9)	2.6 (0.8)	1	2.0	5	
			Placebo	161	139 (86.3)	2.8 (1.0)	1	3.0	5	
	Change from baseline in 5-D degree score	Week 4	CR845	164	143 (87.2)	-0.6 (0.8)	-3	-1.0	2	-0.31 [-0.55, -0.08]
			Placebo	161	139 (86.3)	-0.3 (0.9)	-3	0.0	2	
		Week 8	CR845	164	134 (81.7)	-0.7 (0.9)	-3	-1.0	2	-0.10 [-0.33, 0.14]
			Placebo	161	143 (88.8)	-0.6 (1.0)	-4	0.0	2	
		Week 10	CR845	164	133 (81.1)	-0.8 (0.9)	-2	-1.0	2	-0.22 [-0.46, 0.02]
			Placebo	161	142 (88.2)	-0.6 (1.0)	-4	-1.0	2	
		Week 12	CR845	164	135 (82.3)	-0.8 (0.9)	-2	-1.0	2	-0.11 [-0.35, 0.13]
			Placebo	161	139 (86.3)	-0.7 (0.9)	-3	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DDC_ISHE: Change from baseline in 5-D degree score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	5-D degree score	Baseline	CR845	25	25 (100.0)	3.5 (0.6)	2	4.0	4	
			Placebo	28	28 (100.0)	3.8 (0.8)	2	4.0	5	
		Week 4	CR845	25	24 (96.0)	3.0 (0.8)	2	3.0	5	
			Placebo	28	26 (92.9)	3.4 (0.9)	2	3.0	5	
		Week 8	CR845	25	23 (92.0)	2.7 (0.7)	2	3.0	4	
			Placebo	28	27 (96.4)	3.1 (1.0)	2	3.0	5	
		Week 10	CR845	25	22 (88.0)	2.6 (0.7)	1	3.0	4	
			Placebo	28	25 (89.3)	3.2 (0.8)	2	3.0	5	
		Week 12	CR845	25	24 (96.0)	2.3 (0.7)	1	2.0	3	
			Placebo	28	27 (96.4)	3.1 (0.8)	2	3.0	5	
	Change from baseline in 5-D degree score	Week 4	CR845	25	24 (96.0)	-0.5 (0.9)	-2	-1.0	2	-0.17 [-0.72, 0.39]
			Placebo	28	26 (92.9)	-0.4 (1.0)	-2	0.0	2	
		Week 8	CR845	25	23 (92.0)	-0.8 (0.9)	-2	-1.0	1	-0.18 [-0.74, 0.38]
			Placebo	28	27 (96.4)	-0.6 (0.8)	-3	-1.0	1	
		Week 10	CR845	25	22 (88.0)	-0.9 (0.9)	-3	-1.0	1	-0.46 [-1.04, 0.12]
			Placebo	28	25 (89.3)	-0.5 (0.8)	-2	-1.0	1	
		Week 12	CR845	25	24 (96.0)	-1.2 (0.8)	-3	-1.0	0	-0.55 [-1.11, 0.01]
			Placebo	28	27 (96.4)	-0.7 (0.9)	-3	-1.0	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DDC_ISHF: Change from baseline in 5-D degree score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	5-D degree score	Baseline	CR845	117	115 (98.3)	3.3 (0.7)	2	3.0	5	
			Placebo	111	111 (100.0)	3.5 (0.8)	1	3.0	5	
		Week 4	CR845	117	107 (91.5)	2.9 (0.8)	1	3.0	5	
			Placebo	111	94 (84.7)	3.2 (0.8)	2	3.0	5	
		Week 8	CR845	117	101 (86.3)	2.7 (0.7)	1	3.0	5	
			Placebo	111	100 (90.1)	2.9 (0.8)	1	3.0	5	
		Week 10	CR845	117	99 (84.6)	2.6 (0.7)	1	3.0	5	
			Placebo	111	98 (88.3)	2.9 (0.9)	1	3.0	5	
		Week 12	CR845	117	100 (85.5)	2.5 (0.7)	1	2.0	5	
			Placebo	111	100 (90.1)	2.7 (0.9)	1	3.0	5	
	Change from baseline in 5-D degree score	Week 4	CR845	117	106 (90.6)	-0.5 (0.8)	-2	-1.0	2	-0.31 [-0.59, -0.04]
			Placebo	111	94 (84.7)	-0.2 (0.9)	-3	0.0	2	
		Week 8	CR845	117	100 (85.5)	-0.7 (0.9)	-3	-1.0	2	-0.11 [-0.39, 0.17]
			Placebo	111	100 (90.1)	-0.6 (1.0)	-4	0.0	2	
		Week 10	CR845	117	98 (83.8)	-0.8 (0.9)	-2	-1.0	2	-0.22 [-0.50, 0.06]
			Placebo	111	98 (88.3)	-0.5 (1.1)	-4	-1.0	2	
		Week 12	CR845	117	100 (85.5)	-0.8 (0.9)	-2	-1.0	2	-0.08 [-0.35, 0.20]
			Placebo	111	100 (90.1)	-0.7 (0.9)	-3	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DDC_ISHF: Change from baseline in 5-D degree score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	5-D degree score	Baseline	CR845	72	71 (98.6)	3.5 (0.6)	2	4.0	5	
			Placebo	78	78 (100.0)	3.7 (0.8)	2	4.0	5	
		Week 4	CR845	72	62 (86.1)	2.8 (0.8)	1	3.0	5	
			Placebo	78	71 (91.0)	3.2 (0.9)	1	3.0	5	
		Week 8	CR845	72	58 (80.6)	2.7 (0.8)	1	3.0	5	
			Placebo	78	70 (89.7)	3.0 (1.0)	1	3.0	5	
		Week 10	CR845	72	58 (80.6)	2.6 (0.8)	1	2.5	5	
			Placebo	78	69 (88.5)	3.0 (0.8)	1	3.0	5	
		Week 12	CR845	72	60 (83.3)	2.5 (0.8)	1	2.5	5	
			Placebo	78	66 (84.6)	3.0 (1.0)	1	3.0	5	
	Change from baseline in 5-D degree score	Week 4	CR845	72	61 (84.7)	-0.7 (0.8)	-3	-1.0	1	-0.30 [-0.65, 0.04]
			Placebo	78	71 (91.0)	-0.5 (0.8)	-2	0.0	2	
		Week 8	CR845	72	57 (79.2)	-0.8 (0.9)	-3	-1.0	1	-0.12 [-0.47, 0.23]
			Placebo	78	70 (89.7)	-0.7 (1.0)	-4	-1.0	1	
		Week 10	CR845	72	57 (79.2)	-0.9 (0.9)	-3	-1.0	1	-0.32 [-0.68, 0.03]
			Placebo	78	69 (88.5)	-0.7 (0.9)	-3	-1.0	1	
		Week 12	CR845	72	59 (81.9)	-1.0 (0.9)	-3	-1.0	1	-0.33 [-0.69, 0.02]
			Placebo	78	66 (84.6)	-0.7 (0.9)	-3	-1.0	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DLC_ISHA: Change from baseline in 5-D duration score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
< 65 years	5-D duration score	Baseline	CR845	135	131 (97.0)	2.6 (1.3)	1	2.0	5	
			Placebo	137	137 (100.0)	3.2 (1.4)	1	3.0	5	
		Week 4	CR845	135	119 (88.1)	2.1 (1.2)	1	2.0	5	
			Placebo	137	117 (85.4)	2.7 (1.4)	1	2.0	5	
		Week 8	CR845	135	111 (82.2)	1.7 (1.0)	1	1.0	5	
			Placebo	137	121 (88.3)	2.4 (1.4)	1	2.0	5	
		Week 10	CR845	135	111 (82.2)	1.7 (0.9)	1	1.0	5	
			Placebo	137	118 (86.1)	2.3 (1.4)	1	2.0	5	
		Week 12	CR845	135	113 (83.7)	1.8 (1.0)	1	2.0	5	
			Placebo	137	118 (86.1)	2.3 (1.3)	1	2.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	135	116 (85.9)	-0.6 (1.3)	-4	-1.0	4	-0.05 [-0.31, 0.20]
			Placebo	137	117 (85.4)	-0.6 (1.6)	-4	0.0	4	
		Week 8	CR845	135	108 (80.0)	-0.9 (1.4)	-4	-1.0	3	0.00 [-0.26, 0.26]
			Placebo	137	121 (88.3)	-0.9 (1.5)	-4	-1.0	3	
		Week 10	CR845	135	108 (80.0)	-0.9 (1.4)	-4	-1.0	4	0.00 [-0.26, 0.27]
			Placebo	137	118 (86.1)	-0.9 (1.6)	-4	-1.0	3	
		Week 12	CR845	135	111 (82.2)	-0.8 (1.4)	-4	-1.0	3	0.05 [-0.21, 0.31]
			Placebo	137	118 (86.1)	-0.9 (1.5)	-4	-1.0	4	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DLC_ISHA: Change from baseline in 5-D duration score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 65 years	5-D duration score	Baseline	CR845	54	54 (100.0)	2.9 (1.3)	1	3.0	5	
			Placebo	52	52 (100.0)	3.1 (1.4)	1	3.0	5	
		Week 4	CR845	54	50 (92.6)	2.2 (1.2)	1	2.0	5	
			Placebo	52	48 (92.3)	2.6 (1.5)	1	2.0	5	
		Week 8	CR845	54	48 (88.9)	1.9 (1.1)	1	2.0	5	
			Placebo	52	49 (94.2)	2.4 (1.3)	1	2.0	5	
		Week 10	CR845	54	46 (85.2)	1.8 (0.8)	1	2.0	4	
			Placebo	52	49 (94.2)	2.2 (1.2)	1	2.0	5	
		Week 12	CR845	54	47 (87.0)	1.7 (1.0)	1	1.0	5	
			Placebo	52	48 (92.3)	2.0 (1.1)	1	2.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	54	50 (92.6)	-0.7 (1.3)	-4	-1.0	2	-0.18 [-0.58, 0.21]
			Placebo	52	48 (92.3)	-0.5 (1.8)	-4	-0.5	4	
		Week 8	CR845	54	48 (88.9)	-1.1 (1.5)	-4	-1.0	3	-0.25 [-0.65, 0.15]
			Placebo	52	49 (94.2)	-0.7 (1.8)	-4	-1.0	4	
		Week 10	CR845	54	46 (85.2)	-1.1 (1.3)	-4	-1.0	2	-0.19 [-0.59, 0.21]
			Placebo	52	49 (94.2)	-0.8 (1.7)	-4	-1.0	4	
		Week 12	CR845	54	47 (87.0)	-1.3 (1.5)	-4	-1.0	3	-0.17 [-0.58, 0.23]
			Placebo	52	48 (92.3)	-1.0 (1.5)	-4	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DLC_ISHB: Change from baseline in 5-D duration score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Male	5-D duration score	Baseline	CR845	112	110 (98.2)	2.6 (1.3)	1	2.0	5	
			Placebo	119	119 (100.0)	3.1 (1.4)	1	3.0	5	
		Week 4	CR845	112	98 (87.5)	2.0 (1.2)	1	2.0	5	
			Placebo	119	100 (84.0)	2.9 (1.5)	1	3.0	5	
		Week 8	CR845	112	91 (81.3)	1.8 (1.0)	1	1.0	5	
			Placebo	119	106 (89.1)	2.5 (1.4)	1	2.0	5	
		Week 10	CR845	112	91 (81.3)	1.8 (0.9)	1	2.0	5	
			Placebo	119	106 (89.1)	2.3 (1.3)	1	2.0	5	
		Week 12	CR845	112	91 (81.3)	1.8 (1.1)	1	1.0	5	
			Placebo	119	105 (88.2)	2.2 (1.3)	1	2.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	112	97 (86.6)	-0.6 (1.3)	-4	-1.0	4	-0.20 [-0.48, 0.08]
			Placebo	119	100 (84.0)	-0.3 (1.5)	-4	0.0	4	
		Week 8	CR845	112	90 (80.4)	-0.8 (1.3)	-4	-1.0	3	-0.07 [-0.35, 0.21]
			Placebo	119	106 (89.1)	-0.7 (1.5)	-4	-1.0	4	
		Week 10	CR845	112	90 (80.4)	-0.7 (1.4)	-4	-1.0	4	0.07 [-0.21, 0.35]
			Placebo	119	106 (89.1)	-0.8 (1.4)	-4	-1.0	3	
		Week 12	CR845	112	90 (80.4)	-0.8 (1.5)	-4	-1.0	3	0.06 [-0.23, 0.34]
			Placebo	119	105 (88.2)	-0.8 (1.4)	-4	-1.0	4	

ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DLC_ISHB: Change from baseline in 5-D duration score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Female	5-D duration score	Baseline	CR845	77	75 (97.4)	3.0 (1.4)	1	3.0	5	
			Placebo	70	70 (100.0)	3.3 (1.4)	1	3.0	5	
		Week 4	CR845	77	71 (92.2)	2.2 (1.2)	1	2.0	5	
			Placebo	70	65 (92.9)	2.4 (1.4)	1	2.0	5	
		Week 8	CR845	77	68 (88.3)	1.8 (1.1)	1	1.0	5	
			Placebo	70	64 (91.4)	2.3 (1.3)	1	2.0	5	
		Week 10	CR845	77	66 (85.7)	1.6 (0.8)	1	1.0	4	
			Placebo	70	61 (87.1)	2.3 (1.4)	1	2.0	5	
		Week 12	CR845	77	69 (89.6)	1.7 (0.9)	1	1.0	5	
			Placebo	70	61 (87.1)	2.1 (1.2)	1	2.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	77	69 (89.6)	-0.8 (1.2)	-4	-1.0	1	0.06 [-0.27, 0.40]
			Placebo	70	65 (92.9)	-0.9 (1.7)	-4	-1.0	4	
		Week 8	CR845	77	66 (85.7)	-1.2 (1.6)	-4	-1.0	3	-0.06 [-0.41, 0.28]
			Placebo	70	64 (91.4)	-1.0 (1.7)	-4	-1.0	4	
		Week 10	CR845	77	64 (83.1)	-1.3 (1.4)	-4	-1.0	2	-0.19 [-0.54, 0.17]
			Placebo	70	61 (87.1)	-1.0 (1.9)	-4	-1.0	4	
		Week 12	CR845	77	68 (88.3)	-1.3 (1.4)	-4	-1.0	2	-0.08 [-0.43, 0.26]
			Placebo	70	61 (87.1)	-1.1 (1.6)	-4	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DLC_ISHC: Change from baseline in 5-D duration score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Black/African American	5-D duration score	Baseline	CR845	82	81 (98.8)	2.8 (1.3)	1	2.0	5	
			Placebo	76	76 (100.0)	3.1 (1.4)	1	3.0	5	
		Week 4	CR845	82	69 (84.1)	2.0 (1.2)	1	2.0	5	
			Placebo	76	66 (86.8)	2.6 (1.5)	1	2.0	5	
		Week 8	CR845	82	66 (80.5)	1.8 (1.0)	1	1.0	5	
			Placebo	76	68 (89.5)	2.3 (1.4)	1	2.0	5	
		Week 10	CR845	82	64 (78.0)	1.5 (0.8)	1	1.0	4	
			Placebo	76	66 (86.8)	2.3 (1.4)	1	2.0	5	
		Week 12	CR845	82	66 (80.5)	1.7 (0.9)	1	1.0	5	
			Placebo	76	66 (86.8)	2.2 (1.3)	1	2.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	82	68 (82.9)	-0.8 (1.2)	-4	-1.0	2	-0.16 [-0.50, 0.18]
			Placebo	76	66 (86.8)	-0.6 (1.6)	-4	0.0	3	
		Week 8	CR845	82	65 (79.3)	-1.0 (1.3)	-4	-1.0	3	-0.06 [-0.40, 0.28]
			Placebo	76	68 (89.5)	-0.9 (1.6)	-4	-1.0	3	
		Week 10	CR845	82	63 (76.8)	-1.2 (1.3)	-4	-1.0	2	-0.25 [-0.60, 0.09]
			Placebo	76	66 (86.8)	-0.8 (1.5)	-4	-1.0	3	
		Week 12	CR845	82	65 (79.3)	-1.2 (1.3)	-4	-1.0	2	-0.19 [-0.53, 0.16]
			Placebo	76	66 (86.8)	-0.9 (1.4)	-4	-1.0	4	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DLC_ISHC: Change from baseline in 5-D duration score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
White	5-D duration score	Baseline	CR845	91	88 (96.7)	2.8 (1.3)	1	2.0	5	
			Placebo	93	93 (100.0)	3.2 (1.4)	1	3.0	5	
		Week 4	CR845	91	85 (93.4)	2.2 (1.1)	1	2.0	5	
			Placebo	93	81 (87.1)	2.7 (1.3)	1	3.0	5	
		Week 8	CR845	91	78 (85.7)	1.8 (1.0)	1	2.0	5	
			Placebo	93	83 (89.2)	2.5 (1.4)	1	2.0	5	
		Week 10	CR845	91	79 (86.8)	1.9 (1.0)	1	2.0	5	
			Placebo	93	82 (88.2)	2.3 (1.4)	1	2.0	5	
		Week 12	CR845	91	80 (87.9)	1.8 (1.0)	1	1.5	5	
			Placebo	93	80 (86.0)	2.3 (1.3)	1	2.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	91	83 (91.2)	-0.7 (1.2)	-4	-1.0	3	-0.14 [-0.44, 0.17]
			Placebo	93	81 (87.1)	-0.5 (1.7)	-4	0.0	4	
		Week 8	CR845	91	76 (83.5)	-0.9 (1.5)	-4	-1.0	3	-0.17 [-0.48, 0.15]
			Placebo	93	83 (89.2)	-0.7 (1.7)	-4	-1.0	4	
		Week 10	CR845	91	77 (84.6)	-0.9 (1.5)	-4	-1.0	4	-0.01 [-0.32, 0.30]
			Placebo	93	82 (88.2)	-0.8 (1.8)	-4	-1.0	4	
		Week 12	CR845	91	79 (86.8)	-1.0 (1.5)	-4	-1.0	3	-0.07 [-0.39, 0.24]
			Placebo	93	80 (86.0)	-0.9 (1.6)	-4	-1.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DLC_ISHC: Change from baseline in 5-D duration score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Other	5-D duration score	Baseline	CR845	15	15 (100.0)	2.4 (1.5)	1	2.0	5	
			Placebo	18	18 (100.0)	3.2 (1.3)	1	3.0	5	
		Week 4	CR845	15	14 (93.3)	2.1 (1.2)	1	2.0	5	
			Placebo	18	16 (88.9)	2.6 (1.5)	1	2.0	5	
		Week 8	CR845	15	14 (93.3)	1.8 (1.4)	1	1.0	5	
			Placebo	18	17 (94.4)	2.1 (1.1)	1	2.0	5	
		Week 10	CR845	15	13 (86.7)	1.8 (0.8)	1	2.0	3	
			Placebo	18	17 (94.4)	1.9 (1.1)	1	2.0	5	
		Week 12	CR845	15	13 (86.7)	2.4 (1.7)	1	2.0	5	
			Placebo	18	18 (100.0)	1.8 (1.1)	1	1.5	5	
	Change from baseline in 5-D duration score	Week 4	CR845	15	14 (93.3)	-0.2 (1.4)	-3	0.0	2	0.34 [-0.38, 1.06]
			Placebo	18	16 (88.9)	-0.7 (1.4)	-3	-0.5	2	
		Week 8	CR845	15	14 (93.3)	-0.7 (2.0)	-4	0.0	3	0.23 [-0.48, 0.94]
			Placebo	18	17 (94.4)	-1.1 (1.6)	-4	-1.0	3	
		Week 10	CR845	15	13 (86.7)	-0.8 (1.2)	-3	0.0	1	0.44 [-0.29, 1.18]
			Placebo	18	17 (94.4)	-1.4 (1.4)	-4	-1.0	1	
		Week 12	CR845	15	13 (86.7)	-0.1 (1.8)	-4	0.0	3	0.86 [0.11, 1.61]
			Placebo	18	18 (100.0)	-1.4 (1.2)	-4	-1.5	0	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DLC_ISHD: Change from baseline in 5-D duration score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 4 to < 7	5-D duration score	Baseline	CR845	83	82 (98.8)	2.1 (1.1)	1	2.0	5	
			Placebo	80	80 (100.0)	2.5 (1.2)	1	2.0	5	
		Week 4	CR845	83	73 (88.0)	1.7 (0.9)	1	1.0	5	
			Placebo	80	70 (87.5)	2.4 (1.3)	1	2.0	5	
		Week 8	CR845	83	69 (83.1)	1.6 (0.7)	1	1.0	4	
			Placebo	80	72 (90.0)	2.1 (1.3)	1	2.0	5	
		Week 10	CR845	83	69 (83.1)	1.6 (0.8)	1	1.0	5	
			Placebo	80	71 (88.8)	2.0 (1.3)	1	2.0	5	
		Week 12	CR845	83	68 (81.9)	1.6 (0.9)	1	1.0	5	
			Placebo	80	72 (90.0)	1.9 (1.2)	1	2.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	83	73 (88.0)	-0.4 (1.2)	-4	0.0	4	-0.21 [-0.54, 0.12]
			Placebo	80	70 (87.5)	-0.1 (1.5)	-4	0.0	4	
		Week 8	CR845	83	69 (83.1)	-0.5 (1.1)	-4	0.0	2	-0.10 [-0.43, 0.23]
			Placebo	80	72 (90.0)	-0.4 (1.5)	-4	0.0	4	
		Week 10	CR845	83	69 (83.1)	-0.5 (1.3)	-4	0.0	4	0.00 [-0.33, 0.33]
			Placebo	80	71 (88.8)	-0.5 (1.5)	-4	0.0	4	
		Week 12	CR845	83	68 (81.9)	-0.5 (1.1)	-3	0.0	2	0.06 [-0.27, 0.39]
			Placebo	80	72 (90.0)	-0.5 (1.3)	-4	-1.0	4	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DLC_ISHD: Change from baseline in 5-D duration score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 7	5-D duration score	Baseline	CR845	106	103 (97.2)	3.3 (1.3)	1	3.0	5	
			Placebo	109	109 (100.0)	3.7 (1.3)	1	4.0	5	
		Week 4	CR845	106	96 (90.6)	2.4 (1.3)	1	2.0	5	
			Placebo	109	95 (87.2)	2.9 (1.5)	1	3.0	5	
		Week 8	CR845	106	90 (84.9)	1.9 (1.2)	1	2.0	5	
			Placebo	109	98 (89.9)	2.6 (1.4)	1	2.0	5	
		Week 10	CR845	106	88 (83.0)	1.9 (1.0)	1	2.0	5	
			Placebo	109	96 (88.1)	2.5 (1.4)	1	2.0	5	
		Week 12	CR845	106	92 (86.8)	1.9 (1.1)	1	2.0	5	
			Placebo	109	94 (86.2)	2.4 (1.3)	1	2.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	106	93 (87.7)	-0.9 (1.2)	-4	-1.0	3	-0.03 [-0.31, 0.26]
			Placebo	109	95 (87.2)	-0.9 (1.6)	-4	-1.0	4	
		Week 8	CR845	106	87 (82.1)	-1.3 (1.6)	-4	-1.0	3	-0.08 [-0.37, 0.20]
			Placebo	109	98 (89.9)	-1.2 (1.6)	-4	-1.0	3	
		Week 10	CR845	106	85 (80.2)	-1.4 (1.3)	-4	-1.0	2	-0.12 [-0.41, 0.17]
			Placebo	109	96 (88.1)	-1.2 (1.6)	-4	-1.0	3	
		Week 12	CR845	106	90 (84.9)	-1.4 (1.6)	-4	-1.0	3	-0.06 [-0.35, 0.23]
			Placebo	109	94 (86.2)	-1.3 (1.5)	-4	-1.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DLC_ISHE: Change from baseline in 5-D duration score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	5-D duration score	Baseline	CR845	164	160 (97.6)	2.7 (1.3)	1	2.0	5	
			Placebo	161	161 (100.0)	3.2 (1.4)	1	3.0	5	
		Week 4	CR845	164	145 (88.4)	2.1 (1.2)	1	2.0	5	
			Placebo	161	139 (86.3)	2.7 (1.4)	1	2.0	5	
		Week 8	CR845	164	136 (82.9)	1.7 (1.0)	1	1.0	5	
			Placebo	161	143 (88.8)	2.3 (1.4)	1	2.0	5	
		Week 10	CR845	164	135 (82.3)	1.7 (0.9)	1	1.0	5	
			Placebo	161	142 (88.2)	2.2 (1.3)	1	2.0	5	
		Week 12	CR845	164	136 (82.9)	1.8 (1.1)	1	1.0	5	
			Placebo	161	139 (86.3)	2.1 (1.3)	1	2.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	164	142 (86.6)	-0.7 (1.3)	-4	-1.0	4	-0.09 [-0.33, 0.14]
			Placebo	161	139 (86.3)	-0.5 (1.6)	-4	0.0	4	
		Week 8	CR845	164	133 (81.1)	-1.0 (1.4)	-4	-1.0	3	-0.08 [-0.32, 0.15]
			Placebo	161	143 (88.8)	-0.8 (1.7)	-4	-1.0	4	
		Week 10	CR845	164	132 (80.5)	-1.0 (1.3)	-4	-1.0	2	-0.02 [-0.25, 0.22]
			Placebo	161	142 (88.2)	-1.0 (1.7)	-4	-1.0	4	
		Week 12	CR845	164	134 (81.7)	-0.9 (1.5)	-4	-1.0	3	0.03 [-0.21, 0.27]
			Placebo	161	139 (86.3)	-1.0 (1.5)	-4	-1.0	4	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DLC_ISHE: Change from baseline in 5-D duration score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	5-D duration score	Baseline	CR845	25	25 (100.0)	3.0 (1.5)	1	3.0	5	
			Placebo	28	28 (100.0)	3.3 (1.2)	1	3.0	5	
		Week 4	CR845	25	24 (96.0)	2.3 (1.2)	1	2.0	5	
			Placebo	28	26 (92.9)	2.8 (1.5)	1	2.5	5	
		Week 8	CR845	25	23 (92.0)	2.2 (1.3)	1	2.0	5	
			Placebo	28	27 (96.4)	2.6 (1.3)	1	3.0	5	
		Week 10	CR845	25	22 (88.0)	2.0 (1.1)	1	2.0	5	
			Placebo	28	25 (89.3)	2.8 (1.3)	1	3.0	5	
		Week 12	CR845	25	24 (96.0)	1.8 (0.8)	1	2.0	3	
			Placebo	28	27 (96.4)	2.5 (1.3)	1	3.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	25	24 (96.0)	-0.7 (1.2)	-3	0.0	1	-0.09 [-0.64, 0.47]
			Placebo	28	26 (92.9)	-0.5 (1.6)	-4	0.0	3	
		Week 8	CR845	25	23 (92.0)	-0.8 (1.5)	-4	0.0	3	-0.03 [-0.59, 0.53]
			Placebo	28	27 (96.4)	-0.7 (1.3)	-3	-1.0	2	
		Week 10	CR845	25	22 (88.0)	-1.0 (1.9)	-4	-1.0	4	-0.24 [-0.82, 0.33]
			Placebo	28	25 (89.3)	-0.6 (1.5)	-4	-1.0	2	
		Week 12	CR845	25	24 (96.0)	-1.2 (1.5)	-4	-1.0	1	-0.29 [-0.84, 0.27]
			Placebo	28	27 (96.4)	-0.8 (1.2)	-3	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DLC_ISHF: Change from baseline in 5-D duration score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	5-D duration score	Baseline	CR845	117	115 (98.3)	2.7 (1.3)	1	3.0	5	
			Placebo	111	111 (100.0)	2.9 (1.3)	1	3.0	5	
		Week 4	CR845	117	107 (91.5)	2.1 (1.1)	1	2.0	5	
			Placebo	111	94 (84.7)	2.5 (1.3)	1	2.0	5	
		Week 8	CR845	117	101 (86.3)	1.7 (0.9)	1	1.0	5	
			Placebo	111	100 (90.1)	2.3 (1.3)	1	2.0	5	
		Week 10	CR845	117	99 (84.6)	1.8 (0.9)	1	2.0	5	
			Placebo	111	98 (88.3)	2.2 (1.3)	1	2.0	5	
		Week 12	CR845	117	100 (85.5)	1.8 (1.0)	1	1.0	5	
			Placebo	111	100 (90.1)	2.1 (1.2)	1	2.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	117	106 (90.6)	-0.6 (1.2)	-3	-1.0	4	-0.15 [-0.43, 0.12]
			Placebo	111	94 (84.7)	-0.4 (1.7)	-4	0.0	4	
		Week 8	CR845	117	100 (85.5)	-1.0 (1.3)	-4	-1.0	3	-0.26 [-0.54, 0.02]
			Placebo	111	100 (90.1)	-0.6 (1.7)	-4	-0.5	4	
		Week 10	CR845	117	98 (83.8)	-0.9 (1.3)	-4	-1.0	4	-0.12 [-0.40, 0.16]
			Placebo	111	98 (88.3)	-0.7 (1.7)	-4	-1.0	4	
		Week 12	CR845	117	100 (85.5)	-1.0 (1.4)	-4	-1.0	3	-0.12 [-0.39, 0.16]
			Placebo	111	100 (90.1)	-0.8 (1.6)	-4	-1.0	4	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DLC_ISHF: Change from baseline in 5-D duration score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	5-D duration score	Baseline	CR845	72	70 (97.2)	2.8 (1.4)	1	2.0	5	
			Placebo	78	78 (100.0)	3.6 (1.5)	1	4.0	5	
		Week 4	CR845	72	62 (86.1)	2.0 (1.3)	1	2.0	5	
			Placebo	78	71 (91.0)	2.9 (1.6)	1	2.0	5	
		Week 8	CR845	72	58 (80.6)	1.9 (1.2)	1	2.0	5	
			Placebo	78	70 (89.7)	2.4 (1.5)	1	2.0	5	
		Week 10	CR845	72	58 (80.6)	1.7 (0.9)	1	1.0	4	
			Placebo	78	69 (88.5)	2.5 (1.5)	1	2.0	5	
		Week 12	CR845	72	60 (83.3)	1.8 (1.0)	1	1.0	5	
			Placebo	78	66 (84.6)	2.4 (1.4)	1	2.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	72	60 (83.3)	-0.8 (1.4)	-4	-0.5	3	-0.03 [-0.37, 0.31]
			Placebo	78	71 (91.0)	-0.7 (1.5)	-4	0.0	4	
		Week 8	CR845	72	56 (77.8)	-0.9 (1.7)	-4	-1.0	3	0.20 [-0.16, 0.55]
			Placebo	78	70 (89.7)	-1.2 (1.4)	-4	-1.0	2	
		Week 10	CR845	72	56 (77.8)	-1.1 (1.5)	-4	-1.0	2	0.04 [-0.32, 0.39]
			Placebo	78	69 (88.5)	-1.2 (1.4)	-4	-1.0	2	
		Week 12	CR845	72	58 (80.6)	-1.0 (1.6)	-4	-1.0	3	0.14 [-0.22, 0.49]
			Placebo	78	66 (84.6)	-1.2 (1.3)	-4	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DWC_ISHA: Change from baseline in 5-D direction score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
< 65 years	5-D direction score	Baseline	CR845	135	132 (97.8)	3.9 (0.6)	2	4.0	5	
			Placebo	137	137 (100.0)	4.0 (0.6)	2	4.0	5	
		Week 4	CR845	135	119 (88.1)	2.7 (0.8)	1	3.0	5	
			Placebo	137	117 (85.4)	3.2 (0.9)	1	3.0	5	
		Week 8	CR845	135	111 (82.2)	2.5 (0.7)	1	2.0	5	
			Placebo	137	121 (88.3)	3.1 (1.0)	1	3.0	5	
		Week 10	CR845	135	111 (82.2)	2.4 (0.7)	1	2.0	5	
			Placebo	137	118 (86.1)	3.0 (1.0)	1	3.0	5	
		Week 12	CR845	135	113 (83.7)	2.4 (0.8)	1	2.0	5	
			Placebo	137	118 (86.1)	3.0 (1.0)	1	3.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	135	117 (86.7)	-1.2 (1.0)	-4	-1.0	1	-0.52 [-0.78, -0.26]
			Placebo	137	117 (85.4)	-0.7 (1.1)	-3	-1.0	3	
		Week 8	CR845	135	109 (80.7)	-1.4 (0.9)	-3	-2.0	2	-0.60 [-0.86, -0.33]
			Placebo	137	121 (88.3)	-0.9 (1.1)	-4	-1.0	2	
		Week 10	CR845	135	109 (80.7)	-1.4 (1.0)	-4	-2.0	1	-0.46 [-0.72, -0.20]
			Placebo	137	118 (86.1)	-1.0 (1.0)	-4	-1.0	2	
		Week 12	CR845	135	112 (83.0)	-1.4 (1.0)	-4	-2.0	2	-0.45 [-0.71, -0.19]
			Placebo	137	118 (86.1)	-1.0 (1.1)	-3	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DWC_ISHA: Change from baseline in 5-D direction score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 65 years	5-D direction score	Baseline	CR845	54	54 (100.0)	3.8 (0.7)	2	4.0	5	
			Placebo	52	52 (100.0)	3.9 (0.7)	2	4.0	5	
		Week 4	CR845	54	50 (92.6)	2.7 (0.7)	1	3.0	4	
			Placebo	52	48 (92.3)	2.9 (0.8)	1	3.0	5	
		Week 8	CR845	54	48 (88.9)	2.8 (0.9)	1	3.0	5	
			Placebo	52	49 (94.2)	2.7 (0.8)	1	3.0	5	
		Week 10	CR845	54	46 (85.2)	2.5 (0.7)	1	2.0	4	
			Placebo	52	49 (94.2)	2.7 (0.9)	2	2.0	5	
		Week 12	CR845	54	47 (87.0)	2.6 (0.8)	2	2.0	5	
			Placebo	52	48 (92.3)	2.7 (0.9)	1	3.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	54	50 (92.6)	-1.1 (0.8)	-3	-1.0	1	-0.18 [-0.58, 0.22]
			Placebo	52	48 (92.3)	-0.9 (1.0)	-4	-1.0	1	
		Week 8	CR845	54	48 (88.9)	-1.0 (1.0)	-3	-1.0	2	0.12 [-0.28, 0.52]
			Placebo	52	49 (94.2)	-1.2 (1.0)	-4	-1.0	1	
		Week 10	CR845	54	46 (85.2)	-1.3 (0.8)	-3	-1.0	0	-0.23 [-0.63, 0.18]
			Placebo	52	49 (94.2)	-1.1 (1.0)	-3	-1.0	1	
		Week 12	CR845	54	47 (87.0)	-1.2 (0.9)	-3	-1.0	1	-0.05 [-0.45, 0.36]
			Placebo	52	48 (92.3)	-1.2 (1.1)	-3	-1.0	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DWC_ISHB: Change from baseline in 5-D direction score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Male	5-D direction score	Baseline	CR845	112	110 (98.2)	3.8 (0.6)	2	4.0	5	
			Placebo	119	119 (100.0)	3.9 (0.6)	2	4.0	5	
		Week 4	CR845	112	98 (87.5)	2.7 (0.7)	1	3.0	5	
			Placebo	119	100 (84.0)	3.2 (1.0)	1	3.0	5	
		Week 8	CR845	112	91 (81.3)	2.6 (0.8)	1	2.0	5	
			Placebo	119	106 (89.1)	3.1 (0.9)	1	3.0	5	
		Week 10	CR845	112	91 (81.3)	2.5 (0.7)	1	2.0	4	
			Placebo	119	106 (89.1)	2.9 (0.9)	1	3.0	5	
		Week 12	CR845	112	91 (81.3)	2.5 (0.8)	1	2.0	5	
			Placebo	119	105 (88.2)	3.0 (1.0)	1	3.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	112	97 (86.6)	-1.1 (0.9)	-3	-1.0	1	-0.44 [-0.72, -0.15]
			Placebo	119	100 (84.0)	-0.7 (1.0)	-4	-1.0	2	
		Week 8	CR845	112	90 (80.4)	-1.2 (0.9)	-3	-1.0	2	-0.37 [-0.65, -0.08]
			Placebo	119	106 (89.1)	-0.9 (1.0)	-4	-1.0	2	
		Week 10	CR845	112	90 (80.4)	-1.3 (0.8)	-3	-1.0	0	-0.31 [-0.60, -0.03]
			Placebo	119	106 (89.1)	-1.0 (0.9)	-4	-1.0	2	
		Week 12	CR845	112	90 (80.4)	-1.3 (1.0)	-4	-1.0	2	-0.33 [-0.62, -0.05]
			Placebo	119	105 (88.2)	-1.0 (1.1)	-3	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DWC_ISHB: Change from baseline in 5-D direction score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Female	5-D direction score	Baseline	CR845	77	76 (98.7)	3.9 (0.7)	2	4.0	5	
			Placebo	70	70 (100.0)	3.9 (0.6)	2	4.0	5	
		Week 4	CR845	77	71 (92.2)	2.7 (0.8)	1	3.0	5	
			Placebo	70	65 (92.9)	3.0 (0.8)	2	3.0	5	
		Week 8	CR845	77	68 (88.3)	2.5 (0.7)	1	2.0	5	
			Placebo	70	64 (91.4)	2.9 (1.0)	1	3.0	5	
		Week 10	CR845	77	66 (85.7)	2.4 (0.7)	1	2.0	5	
			Placebo	70	61 (87.1)	2.9 (1.0)	1	3.0	5	
		Week 12	CR845	77	69 (89.6)	2.5 (0.8)	1	2.0	5	
			Placebo	70	61 (87.1)	2.8 (1.0)	1	3.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	77	70 (90.9)	-1.3 (1.0)	-4	-1.0	1	-0.40 [-0.75, -0.06]
			Placebo	70	65 (92.9)	-0.9 (1.0)	-3	-1.0	3	
		Week 8	CR845	77	67 (87.0)	-1.4 (1.0)	-3	-2.0	2	-0.37 [-0.72, -0.02]
			Placebo	70	64 (91.4)	-1.0 (1.1)	-4	-1.0	2	
		Week 10	CR845	77	65 (84.4)	-1.6 (1.0)	-4	-2.0	1	-0.49 [-0.84, -0.14]
			Placebo	70	61 (87.1)	-1.0 (1.2)	-3	-1.0	2	
		Week 12	CR845	77	69 (89.6)	-1.5 (1.1)	-4	-2.0	1	-0.32 [-0.67, 0.03]
			Placebo	70	61 (87.1)	-1.1 (1.1)	-3	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DWC_ISHC: Change from baseline in 5-D direction score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Black/African American	5-D direction score	Baseline	CR845	82	82 (100.0)	3.9 (0.7)	2	4.0	5	
			Placebo	76	76 (100.0)	3.9 (0.6)	2	4.0	5	
		Week 4	CR845	82	69 (84.1)	2.6 (0.8)	1	3.0	5	
			Placebo	76	66 (86.8)	3.2 (0.8)	2	3.0	5	
		Week 8	CR845	82	66 (80.5)	2.5 (0.8)	1	2.0	5	
			Placebo	76	68 (89.5)	2.9 (0.9)	1	3.0	5	
		Week 10	CR845	82	64 (78.0)	2.3 (0.5)	1	2.0	4	
			Placebo	76	66 (86.8)	2.8 (0.9)	1	3.0	5	
		Week 12	CR845	82	66 (80.5)	2.4 (0.7)	1	2.0	4	
			Placebo	76	66 (86.8)	2.9 (1.0)	1	3.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	82	69 (84.1)	-1.3 (1.0)	-4	-1.0	1	-0.63 [-0.98, -0.29]
			Placebo	76	66 (86.8)	-0.7 (1.0)	-2	-1.0	3	
		Week 8	CR845	82	66 (80.5)	-1.5 (1.0)	-3	-2.0	2	-0.42 [-0.76, -0.08]
			Placebo	76	68 (89.5)	-1.0 (1.1)	-4	-1.0	2	
		Week 10	CR845	82	64 (78.0)	-1.6 (0.9)	-4	-2.0	1	-0.51 [-0.86, -0.16]
			Placebo	76	66 (86.8)	-1.0 (1.1)	-4	-1.0	2	
		Week 12	CR845	82	66 (80.5)	-1.5 (1.1)	-4	-2.0	2	-0.46 [-0.81, -0.12]
			Placebo	76	66 (86.8)	-1.0 (1.1)	-3	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DWC_ISHC: Change from baseline in 5-D direction score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
White	5-D direction score	Baseline	CR845	91	88 (96.7)	3.8 (0.6)	2	4.0	5	
			Placebo	93	93 (100.0)	4.0 (0.5)	2	4.0	5	
		Week 4	CR845	91	85 (93.4)	2.8 (0.8)	1	3.0	4	
			Placebo	93	81 (87.1)	3.1 (1.0)	1	3.0	5	
		Week 8	CR845	91	78 (85.7)	2.6 (0.7)	1	3.0	4	
			Placebo	93	83 (89.2)	3.1 (0.9)	1	3.0	5	
		Week 10	CR845	91	79 (86.8)	2.6 (0.8)	1	2.0	5	
			Placebo	93	82 (88.2)	3.0 (1.0)	1	3.0	5	
		Week 12	CR845	91	80 (87.9)	2.5 (0.8)	1	2.0	5	
			Placebo	93	80 (86.0)	3.0 (1.0)	1	3.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	91	83 (91.2)	-1.1 (0.9)	-3	-1.0	1	-0.20 [-0.51, 0.11]
			Placebo	93	81 (87.1)	-0.9 (1.0)	-4	-1.0	1	
		Week 8	CR845	91	76 (83.5)	-1.2 (0.8)	-3	-1.0	1	-0.26 [-0.57, 0.05]
			Placebo	93	83 (89.2)	-0.9 (1.0)	-4	-1.0	1	
		Week 10	CR845	91	77 (84.6)	-1.3 (0.9)	-3	-1.0	1	-0.30 [-0.61, 0.01]
			Placebo	93	82 (88.2)	-1.0 (1.0)	-3	-1.0	1	
		Week 12	CR845	91	79 (86.8)	-1.3 (0.9)	-3	-1.0	1	-0.29 [-0.60, 0.02]
			Placebo	93	80 (86.0)	-1.0 (1.0)	-3	-1.0	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DWC_ISHC: Change from baseline in 5-D direction score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Other	5-D direction score	Baseline	CR845	15	15 (100.0)	4.1 (0.6)	3	4.0	5	
			Placebo	18	18 (100.0)	3.9 (0.7)	2	4.0	5	
		Week 4	CR845	15	14 (93.3)	2.7 (0.6)	2	3.0	4	
			Placebo	18	16 (88.9)	3.1 (1.0)	2	3.0	5	
		Week 8	CR845	15	14 (93.3)	2.6 (0.9)	1	2.5	4	
			Placebo	18	17 (94.4)	3.1 (1.1)	2	3.0	5	
		Week 10	CR845	15	13 (86.7)	2.6 (1.0)	1	2.0	4	
			Placebo	18	17 (94.4)	2.8 (1.0)	2	2.0	5	
		Week 12	CR845	15	13 (86.7)	2.8 (1.1)	2	2.0	5	
			Placebo	18	18 (100.0)	2.8 (1.2)	1	2.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	15	14 (93.3)	-1.4 (0.7)	-3	-1.0	0	-0.57 [-1.30, 0.16]
			Placebo	18	16 (88.9)	-0.8 (1.1)	-3	-0.5	1	
		Week 8	CR845	15	14 (93.3)	-1.5 (0.9)	-3	-1.5	0	-0.63 [-1.35, 0.10]
			Placebo	18	17 (94.4)	-0.8 (1.2)	-2	-1.0	2	
		Week 10	CR845	15	13 (86.7)	-1.5 (0.9)	-3	-2.0	0	-0.32 [-1.05, 0.40]
			Placebo	18	17 (94.4)	-1.2 (0.9)	-2	-1.0	0	
		Week 12	CR845	15	13 (86.7)	-1.2 (1.2)	-3	-1.0	0	-0.05 [-0.77, 0.66]
			Placebo	18	18 (100.0)	-1.2 (1.3)	-3	-1.5	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DWC_ISHD: Change from baseline in 5-D direction score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 4 to < 7	5-D direction score	Baseline	CR845	83	82 (98.8)	3.8 (0.6)	2	4.0	5	
			Placebo	80	80 (100.0)	3.8 (0.7)	2	4.0	5	
		Week 4	CR845	83	73 (88.0)	2.5 (0.7)	1	2.0	5	
			Placebo	80	70 (87.5)	3.1 (0.9)	1	3.0	5	
		Week 8	CR845	83	69 (83.1)	2.5 (0.7)	1	2.0	5	
			Placebo	80	72 (90.0)	2.9 (0.9)	1	3.0	5	
		Week 10	CR845	83	69 (83.1)	2.4 (0.6)	2	2.0	4	
			Placebo	80	71 (88.8)	2.8 (0.9)	1	3.0	5	
		Week 12	CR845	83	68 (81.9)	2.4 (0.7)	1	2.0	4	
			Placebo	80	72 (90.0)	2.8 (1.0)	1	3.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	83	73 (88.0)	-1.2 (0.9)	-4	-1.0	1	-0.50 [-0.83, -0.17]
			Placebo	80	70 (87.5)	-0.7 (1.0)	-3	-1.0	3	
		Week 8	CR845	83	69 (83.1)	-1.2 (0.9)	-3	-1.0	1	-0.34 [-0.68, -0.01]
			Placebo	80	72 (90.0)	-0.9 (1.0)	-3	-1.0	2	
		Week 10	CR845	83	69 (83.1)	-1.3 (0.8)	-3	-1.0	0	-0.35 [-0.69, -0.02]
			Placebo	80	71 (88.8)	-1.0 (1.0)	-3	-1.0	2	
		Week 12	CR845	83	68 (81.9)	-1.3 (1.0)	-4	-1.0	2	-0.29 [-0.62, 0.04]
			Placebo	80	72 (90.0)	-1.0 (1.1)	-3	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DWC_ISHD: Change from baseline in 5-D direction score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 7	5-D direction score	Baseline	CR845	106	104 (98.1)	4.0 (0.6)	2	4.0	5	
			Placebo	109	109 (100.0)	4.0 (0.5)	2	4.0	5	
		Week 4	CR845	106	96 (90.6)	2.8 (0.8)	1	3.0	5	
			Placebo	109	95 (87.2)	3.2 (0.9)	1	3.0	5	
		Week 8	CR845	106	90 (84.9)	2.6 (0.8)	1	2.0	5	
			Placebo	109	98 (89.9)	3.1 (1.0)	1	3.0	5	
		Week 10	CR845	106	88 (83.0)	2.5 (0.8)	1	2.0	5	
			Placebo	109	96 (88.1)	3.0 (1.0)	1	3.0	5	
		Week 12	CR845	106	92 (86.8)	2.5 (0.8)	1	2.0	5	
			Placebo	109	94 (86.2)	3.0 (1.0)	1	3.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	106	94 (88.7)	-1.2 (0.9)	-3	-1.0	1	-0.37 [-0.66, -0.09]
			Placebo	109	95 (87.2)	-0.8 (1.1)	-4	-1.0	2	
		Week 8	CR845	106	88 (83.0)	-1.4 (1.0)	-3	-1.5	2	-0.40 [-0.69, -0.11]
			Placebo	109	98 (89.9)	-1.0 (1.1)	-4	-1.0	2	
		Week 10	CR845	106	86 (81.1)	-1.5 (1.0)	-4	-1.5	1	-0.43 [-0.73, -0.14]
			Placebo	109	96 (88.1)	-1.1 (1.0)	-4	-1.0	1	
		Week 12	CR845	106	91 (85.8)	-1.4 (1.0)	-4	-2.0	1	-0.37 [-0.66, -0.08]
			Placebo	109	94 (86.2)	-1.0 (1.1)	-3	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DWC_ISHE: Change from baseline in 5-D direction score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	5-D direction score	Baseline	CR845	164	161 (98.2)	3.8 (0.6)	2	4.0	5	
			Placebo	161	161 (100.0)	3.9 (0.6)	2	4.0	5	
		Week 4	CR845	164	145 (88.4)	2.7 (0.8)	1	3.0	5	
			Placebo	161	139 (86.3)	3.1 (0.9)	1	3.0	5	
		Week 8	CR845	164	136 (82.9)	2.6 (0.8)	1	2.0	5	
			Placebo	161	143 (88.8)	3.0 (1.0)	1	3.0	5	
		Week 10	CR845	164	135 (82.3)	2.5 (0.7)	1	2.0	4	
			Placebo	161	142 (88.2)	2.9 (0.9)	1	3.0	5	
		Week 12	CR845	164	136 (82.9)	2.5 (0.8)	1	2.0	5	
			Placebo	161	139 (86.3)	2.8 (0.9)	1	3.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	164	143 (87.2)	-1.2 (0.9)	-4	-1.0	1	-0.39 [-0.62, -0.15]
			Placebo	161	139 (86.3)	-0.8 (1.1)	-4	-1.0	3	
		Week 8	CR845	164	134 (81.7)	-1.2 (1.0)	-3	-1.0	2	-0.32 [-0.56, -0.08]
			Placebo	161	143 (88.8)	-0.9 (1.0)	-4	-1.0	2	
		Week 10	CR845	164	133 (81.1)	-1.3 (0.9)	-3	-1.0	1	-0.31 [-0.55, -0.07]
			Placebo	161	142 (88.2)	-1.0 (1.0)	-4	-1.0	2	
		Week 12	CR845	164	135 (82.3)	-1.3 (1.0)	-3	-1.0	2	-0.20 [-0.44, 0.03]
			Placebo	161	139 (86.3)	-1.1 (1.1)	-3	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DWC_ISHE: Change from baseline in 5-D direction score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	5-D direction score	Baseline	CR845	25	25 (100.0)	4.2 (0.7)	3	4.0	5	
			Placebo	28	28 (100.0)	4.0 (0.6)	2	4.0	5	
		Week 4	CR845	25	24 (96.0)	2.8 (0.8)	2	3.0	5	
			Placebo	28	26 (92.9)	3.4 (1.0)	2	3.0	5	
		Week 8	CR845	25	23 (92.0)	2.4 (0.5)	2	2.0	3	
			Placebo	28	27 (96.4)	3.0 (1.0)	2	3.0	5	
		Week 10	CR845	25	22 (88.0)	2.4 (0.8)	1	2.0	5	
			Placebo	28	25 (89.3)	3.2 (1.0)	2	4.0	5	
		Week 12	CR845	25	24 (96.0)	2.2 (0.6)	1	2.0	4	
			Placebo	28	27 (96.4)	3.2 (1.1)	1	3.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	25	24 (96.0)	-1.3 (1.1)	-3	-1.0	1	-0.65 [-1.21, -0.08]
			Placebo	28	26 (92.9)	-0.7 (1.0)	-2	-1.0	1	
		Week 8	CR845	25	23 (92.0)	-1.7 (0.8)	-3	-2.0	-1	-0.74 [-1.31, -0.16]
			Placebo	28	27 (96.4)	-1.0 (1.1)	-3	-1.0	1	
		Week 10	CR845	25	22 (88.0)	-1.8 (1.2)	-4	-2.0	1	-0.82 [-1.41, -0.22]
			Placebo	28	25 (89.3)	-0.8 (1.2)	-3	0.0	1	
		Week 12	CR845	25	24 (96.0)	-2.0 (1.0)	-4	-2.0	0	-1.06 [-1.65, -0.47]
			Placebo	28	27 (96.4)	-0.9 (1.2)	-3	-1.0	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DWC_ISHF: Change from baseline in 5-D direction score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	5-D direction score	Baseline	CR845	117	115 (98.3)	3.8 (0.7)	2	4.0	5	
			Placebo	111	111 (100.0)	3.9 (0.6)	2	4.0	5	
		Week 4	CR845	117	107 (91.5)	2.7 (0.7)	1	3.0	5	
			Placebo	111	94 (84.7)	3.2 (0.9)	1	3.0	5	
		Week 8	CR845	117	101 (86.3)	2.5 (0.7)	1	2.0	5	
			Placebo	111	100 (90.1)	2.9 (0.8)	1	3.0	5	
		Week 10	CR845	117	99 (84.6)	2.5 (0.7)	1	2.0	5	
			Placebo	111	98 (88.3)	2.8 (0.9)	1	3.0	5	
		Week 12	CR845	117	100 (85.5)	2.5 (0.7)	1	2.0	5	
			Placebo	111	100 (90.1)	2.9 (1.0)	1	3.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	117	106 (90.6)	-1.1 (0.9)	-4	-1.0	1	-0.47 [-0.75, -0.19]
			Placebo	111	94 (84.7)	-0.7 (1.0)	-4	-1.0	2	
		Week 8	CR845	117	100 (85.5)	-1.3 (0.9)	-3	-1.0	1	-0.36 [-0.64, -0.08]
			Placebo	111	100 (90.1)	-1.0 (1.0)	-4	-1.0	2	
		Week 10	CR845	117	98 (83.8)	-1.3 (0.9)	-3	-1.0	1	-0.26 [-0.54, 0.02]
			Placebo	111	98 (88.3)	-1.1 (1.1)	-4	-1.0	2	
		Week 12	CR845	117	100 (85.5)	-1.4 (1.0)	-4	-1.0	2	-0.34 [-0.62, -0.06]
			Placebo	111	100 (90.1)	-1.0 (1.1)	-3	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DWC_ISHF: Change from baseline in 5-D direction score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	5-D direction score	Baseline	CR845	72	71 (98.6)	3.9 (0.6)	2	4.0	5	
			Placebo	78	78 (100.0)	4.0 (0.6)	2	4.0	5	
		Week 4	CR845	72	62 (86.1)	2.6 (0.8)	1	3.0	5	
			Placebo	78	71 (91.0)	3.1 (1.0)	1	3.0	5	
		Week 8	CR845	72	58 (80.6)	2.6 (0.8)	1	3.0	5	
			Placebo	78	70 (89.7)	3.1 (1.1)	1	3.0	5	
		Week 10	CR845	72	58 (80.6)	2.4 (0.7)	1	2.0	4	
			Placebo	78	69 (88.5)	3.1 (1.0)	1	3.0	5	
		Week 12	CR845	72	60 (83.3)	2.5 (0.9)	1	2.0	5	
			Placebo	78	66 (84.6)	2.9 (1.0)	1	3.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	72	61 (84.7)	-1.3 (1.0)	-3	-1.0	0	-0.41 [-0.75, -0.06]
			Placebo	78	71 (91.0)	-0.9 (1.1)	-3	-1.0	3	
		Week 8	CR845	72	57 (79.2)	-1.3 (1.0)	-3	-1.0	2	-0.39 [-0.75, -0.04]
			Placebo	78	70 (89.7)	-0.9 (1.1)	-4	-1.0	2	
		Week 10	CR845	72	57 (79.2)	-1.5 (1.0)	-4	-2.0	1	-0.61 [-0.97, -0.25]
			Placebo	78	69 (88.5)	-0.9 (1.0)	-2	-1.0	2	
		Week 12	CR845	72	59 (81.9)	-1.4 (1.1)	-4	-2.0	1	-0.33 [-0.69, 0.02]
			Placebo	78	66 (84.6)	-1.0 (1.1)	-3	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DNC_ISHA: Change from baseline in 5-D disability score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
< 65 years	5-D disability score	Baseline	CR845	135	132 (97.8)	3.4 (1.1)	1	4.0	5	
			Placebo	137	137 (100.0)	3.8 (1.1)	1	4.0	5	
		Week 4	CR845	135	119 (88.1)	2.9 (1.0)	1	3.0	5	
			Placebo	137	117 (85.4)	3.4 (1.2)	1	3.0	5	
		Week 8	CR845	135	111 (82.2)	2.7 (1.1)	1	3.0	5	
			Placebo	137	121 (88.3)	3.1 (1.2)	1	3.0	5	
		Week 10	CR845	135	111 (82.2)	2.4 (1.1)	1	2.0	5	
			Placebo	137	118 (86.1)	2.9 (1.2)	1	3.0	5	
		Week 12	CR845	135	113 (83.7)	2.4 (1.2)	1	2.0	5	
			Placebo	137	118 (86.1)	2.8 (1.3)	1	3.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	135	117 (86.7)	-0.6 (1.1)	-4	-1.0	2	-0.15 [-0.40, 0.11]
			Placebo	137	117 (85.4)	-0.4 (1.4)	-3	0.0	3	
		Week 8	CR845	135	109 (80.7)	-0.8 (1.2)	-4	-1.0	4	-0.08 [-0.34, 0.18]
			Placebo	137	121 (88.3)	-0.7 (1.3)	-4	-1.0	3	
		Week 10	CR845	135	109 (80.7)	-1.0 (1.3)	-4	-1.0	2	-0.10 [-0.36, 0.17]
			Placebo	137	118 (86.1)	-0.9 (1.4)	-4	-1.0	2	
		Week 12	CR845	135	112 (83.0)	-1.1 (1.5)	-4	-1.0	3	-0.03 [-0.29, 0.23]
			Placebo	137	118 (86.1)	-1.0 (1.4)	-4	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DNC_ISHA: Change from baseline in 5-D disability score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 65 years	5-D disability score	Baseline	CR845	54	54 (100.0)	3.8 (1.1)	1	4.0	5	
			Placebo	52	52 (100.0)	3.8 (1.1)	1	4.0	5	
		Week 4	CR845	54	50 (92.6)	3.0 (1.3)	1	3.0	5	
			Placebo	52	48 (92.3)	3.0 (1.2)	1	3.0	5	
		Week 8	CR845	54	48 (88.9)	2.9 (1.2)	1	3.0	5	
			Placebo	52	49 (94.2)	2.9 (1.2)	1	3.0	5	
		Week 10	CR845	54	46 (85.2)	2.9 (1.2)	1	3.0	5	
			Placebo	52	49 (94.2)	2.8 (1.2)	1	3.0	5	
		Week 12	CR845	54	47 (87.0)	2.8 (1.2)	1	3.0	5	
			Placebo	52	48 (92.3)	2.7 (1.1)	1	3.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	54	50 (92.6)	-0.7 (1.1)	-4	-1.0	1	0.09 [-0.31, 0.48]
			Placebo	52	48 (92.3)	-0.8 (1.5)	-4	-1.0	4	
		Week 8	CR845	54	48 (88.9)	-0.8 (1.2)	-3	-1.0	1	0.05 [-0.35, 0.45]
			Placebo	52	49 (94.2)	-0.9 (1.4)	-4	-1.0	2	
		Week 10	CR845	54	46 (85.2)	-0.9 (1.4)	-4	-1.0	3	0.06 [-0.34, 0.46]
			Placebo	52	49 (94.2)	-1.0 (1.3)	-4	-1.0	1	
		Week 12	CR845	54	47 (87.0)	-1.1 (1.3)	-4	-1.0	2	0.03 [-0.37, 0.43]
			Placebo	52	48 (92.3)	-1.1 (1.2)	-3	-1.0	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DNC_ISHB: Change from baseline in 5-D disability score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Male	5-D disability score	Baseline	CR845	112	110 (98.2)	3.4 (1.1)	1	4.0	5	
			Placebo	119	119 (100.0)	3.7 (1.1)	1	4.0	5	
		Week 4	CR845	112	98 (87.5)	2.9 (1.1)	1	3.0	5	
			Placebo	119	100 (84.0)	3.3 (1.2)	1	3.0	5	
		Week 8	CR845	112	91 (81.3)	2.7 (1.2)	1	3.0	5	
			Placebo	119	106 (89.1)	3.0 (1.3)	1	3.0	5	
		Week 10	CR845	112	91 (81.3)	2.7 (1.1)	1	2.0	5	
			Placebo	119	106 (89.1)	2.7 (1.2)	1	3.0	5	
		Week 12	CR845	112	91 (81.3)	2.5 (1.2)	1	2.0	5	
			Placebo	119	105 (88.2)	2.7 (1.2)	1	3.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	112	97 (86.6)	-0.5 (1.1)	-3	0.0	2	-0.15 [-0.43, 0.13]
			Placebo	119	100 (84.0)	-0.4 (1.4)	-3	0.0	4	
		Week 8	CR845	112	90 (80.4)	-0.7 (1.3)	-4	-1.0	4	-0.08 [-0.36, 0.20]
			Placebo	119	106 (89.1)	-0.6 (1.4)	-4	-1.0	3	
		Week 10	CR845	112	90 (80.4)	-0.8 (1.3)	-4	-1.0	3	0.10 [-0.18, 0.38]
			Placebo	119	106 (89.1)	-0.9 (1.4)	-4	-1.0	2	
		Week 12	CR845	112	90 (80.4)	-0.9 (1.4)	-4	-1.0	3	0.02 [-0.26, 0.30]
			Placebo	119	105 (88.2)	-1.0 (1.4)	-4	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DNC_ISHB: Change from baseline in 5-D disability score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Female	5-D disability score	Baseline	CR845	77	76 (98.7)	3.7 (1.1)	1	4.0	5	
			Placebo	70	70 (100.0)	4.0 (0.9)	2	4.0	5	
		Week 4	CR845	77	71 (92.2)	3.0 (1.1)	1	3.0	5	
			Placebo	70	65 (92.9)	3.2 (1.1)	1	3.0	5	
		Week 8	CR845	77	68 (88.3)	2.8 (1.1)	1	3.0	5	
			Placebo	70	64 (91.4)	3.1 (1.1)	1	3.0	5	
		Week 10	CR845	77	66 (85.7)	2.4 (1.1)	1	2.0	5	
			Placebo	70	61 (87.1)	3.0 (1.2)	1	3.0	5	
		Week 12	CR845	77	69 (89.6)	2.5 (1.2)	1	2.0	5	
			Placebo	70	61 (87.1)	2.8 (1.3)	1	3.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	77	70 (90.9)	-0.7 (1.2)	-4	-1.0	1	0.04 [-0.29, 0.38]
			Placebo	70	65 (92.9)	-0.8 (1.4)	-4	-1.0	3	
		Week 8	CR845	77	67 (87.0)	-0.9 (1.1)	-4	-1.0	1	0.04 [-0.31, 0.38]
			Placebo	70	64 (91.4)	-0.9 (1.3)	-4	-1.0	1	
		Week 10	CR845	77	65 (84.4)	-1.3 (1.4)	-4	-1.0	1	-0.25 [-0.60, 0.10]
			Placebo	70	61 (87.1)	-1.0 (1.4)	-4	-1.0	1	
		Week 12	CR845	77	69 (89.6)	-1.2 (1.5)	-4	-1.0	2	-0.04 [-0.38, 0.31]
			Placebo	70	61 (87.1)	-1.2 (1.3)	-4	-1.0	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DNC_ISHC: Change from baseline in 5-D disability score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Black/African American	5-D disability score	Baseline	CR845	82	82 (100.0)	3.5 (1.1)	1	4.0	5	
			Placebo	76	76 (100.0)	3.8 (1.0)	1	4.0	5	
		Week 4	CR845	82	69 (84.1)	2.8 (1.2)	1	3.0	5	
			Placebo	76	66 (86.8)	3.2 (1.1)	1	3.0	5	
		Week 8	CR845	82	66 (80.5)	2.5 (1.2)	1	2.0	5	
			Placebo	76	68 (89.5)	2.9 (1.2)	1	3.0	5	
		Week 10	CR845	82	64 (78.0)	2.3 (1.2)	1	2.0	5	
			Placebo	76	66 (86.8)	2.7 (1.3)	1	2.5	5	
		Week 12	CR845	82	66 (80.5)	2.3 (1.2)	1	2.0	5	
			Placebo	76	66 (86.8)	2.7 (1.3)	1	3.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	82	69 (84.1)	-0.7 (1.2)	-4	-1.0	2	-0.14 [-0.48, 0.20]
			Placebo	76	66 (86.8)	-0.5 (1.4)	-3	0.0	3	
		Week 8	CR845	82	66 (80.5)	-0.9 (1.3)	-4	-1.0	4	-0.06 [-0.40, 0.28]
			Placebo	76	68 (89.5)	-0.9 (1.4)	-4	-1.0	3	
		Week 10	CR845	82	64 (78.0)	-1.2 (1.3)	-4	-1.0	2	-0.01 [-0.36, 0.33]
			Placebo	76	66 (86.8)	-1.1 (1.5)	-4	-1.0	2	
		Week 12	CR845	82	66 (80.5)	-1.2 (1.4)	-4	-1.0	2	-0.08 [-0.42, 0.26]
			Placebo	76	66 (86.8)	-1.1 (1.3)	-4	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DNC_ISHC: Change from baseline in 5-D disability score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
White	5-D disability score	Baseline	CR845	91	88 (96.7)	3.5 (1.1)	1	4.0	5	
			Placebo	93	93 (100.0)	3.8 (1.1)	1	4.0	5	
		Week 4	CR845	91	85 (93.4)	3.0 (1.0)	1	3.0	5	
			Placebo	93	81 (87.1)	3.2 (1.2)	1	3.0	5	
		Week 8	CR845	91	78 (85.7)	2.9 (1.1)	1	3.0	5	
			Placebo	93	83 (89.2)	3.0 (1.3)	1	3.0	5	
		Week 10	CR845	91	79 (86.8)	2.8 (1.1)	1	3.0	5	
			Placebo	93	82 (88.2)	2.9 (1.2)	1	3.0	5	
		Week 12	CR845	91	80 (87.9)	2.6 (1.1)	1	2.0	5	
			Placebo	93	80 (86.0)	2.9 (1.2)	1	3.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	91	83 (91.2)	-0.6 (1.0)	-2	0.0	2	0.02 [-0.28, 0.33]
			Placebo	93	81 (87.1)	-0.6 (1.3)	-4	-1.0	2	
		Week 8	CR845	91	76 (83.5)	-0.7 (1.2)	-3	-1.0	2	0.02 [-0.29, 0.33]
			Placebo	93	83 (89.2)	-0.7 (1.3)	-4	-1.0	2	
		Week 10	CR845	91	77 (84.6)	-0.8 (1.3)	-3	-1.0	3	0.05 [-0.26, 0.36]
			Placebo	93	82 (88.2)	-0.8 (1.4)	-4	-1.0	2	
		Week 12	CR845	91	79 (86.8)	-1.0 (1.4)	-4	-1.0	3	-0.05 [-0.36, 0.26]
			Placebo	93	80 (86.0)	-0.9 (1.4)	-4	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DNC_ISHC: Change from baseline in 5-D disability score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Other	5-D disability score	Baseline	CR845	15	15 (100.0)	4.0 (0.8)	2	4.0	5	
			Placebo	18	18 (100.0)	4.1 (0.8)	3	4.0	5	
		Week 4	CR845	15	14 (93.3)	3.2 (0.9)	2	3.0	5	
			Placebo	18	16 (88.9)	3.6 (1.4)	1	4.0	5	
		Week 8	CR845	15	14 (93.3)	3.2 (1.3)	1	3.0	5	
			Placebo	18	17 (94.4)	3.4 (1.1)	2	3.0	5	
		Week 10	CR845	15	13 (86.7)	2.2 (1.2)	1	2.0	4	
			Placebo	18	17 (94.4)	3.2 (1.2)	1	3.0	5	
		Week 12	CR845	15	13 (86.7)	3.1 (1.4)	1	3.0	5	
			Placebo	18	18 (100.0)	2.6 (1.3)	1	2.5	5	
	Change from baseline in 5-D disability score	Week 4	CR845	15	14 (93.3)	-0.8 (1.3)	-3	-1.0	2	-0.12 [-0.84, 0.60]
			Placebo	18	16 (88.9)	-0.6 (1.4)	-3	-1.0	2	
		Week 8	CR845	15	14 (93.3)	-0.9 (1.2)	-3	-1.0	1	-0.23 [-0.94, 0.48]
			Placebo	18	17 (94.4)	-0.7 (0.7)	-2	-1.0	0	
		Week 10	CR845	15	13 (86.7)	-1.9 (1.4)	-4	-2.0	0	-0.81 [-1.56, -0.05]
			Placebo	18	17 (94.4)	-0.9 (1.2)	-3	-1.0	1	
		Week 12	CR845	15	13 (86.7)	-1.1 (1.4)	-3	-1.0	1	0.30 [-0.42, 1.02]
			Placebo	18	18 (100.0)	-1.5 (1.4)	-4	-1.5	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DNC_ISHD: Change from baseline in 5-D disability score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 4 to < 7	5-D disability score	Baseline	CR845	83	82 (98.8)	3.1 (1.1)	1	3.0	5	
			Placebo	80	80 (100.0)	3.3 (1.0)	1	3.0	5	
		Week 4	CR845	83	73 (88.0)	2.5 (0.9)	1	2.0	4	
			Placebo	80	70 (87.5)	3.0 (1.2)	1	3.0	5	
		Week 8	CR845	83	69 (83.1)	2.5 (1.1)	1	2.0	5	
			Placebo	80	72 (90.0)	2.8 (1.2)	1	3.0	5	
		Week 10	CR845	83	69 (83.1)	2.3 (1.1)	1	2.0	5	
			Placebo	80	71 (88.8)	2.7 (1.2)	1	3.0	5	
		Week 12	CR845	83	68 (81.9)	2.2 (1.1)	1	2.0	5	
			Placebo	80	72 (90.0)	2.4 (1.2)	1	2.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	83	73 (88.0)	-0.6 (1.2)	-4	-1.0	2	-0.27 [-0.59, 0.06]
			Placebo	80	70 (87.5)	-0.3 (1.4)	-3	0.0	3	
		Week 8	CR845	83	69 (83.1)	-0.6 (1.2)	-3	-1.0	4	-0.07 [-0.40, 0.27]
			Placebo	80	72 (90.0)	-0.5 (1.2)	-3	-1.0	3	
		Week 10	CR845	83	69 (83.1)	-0.8 (1.3)	-4	-1.0	3	-0.12 [-0.45, 0.21]
			Placebo	80	71 (88.8)	-0.6 (1.2)	-4	-1.0	1	
		Week 12	CR845	83	68 (81.9)	-0.9 (1.4)	-4	-1.0	2	-0.04 [-0.37, 0.29]
			Placebo	80	72 (90.0)	-0.9 (1.3)	-4	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DNC_ISHD: Change from baseline in 5-D disability score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 7	5-D disability score	Baseline	CR845	106	104 (98.1)	3.9 (1.0)	1	4.0	5	
			Placebo	109	109 (100.0)	4.1 (1.0)	1	4.0	5	
		Week 4	CR845	106	96 (90.6)	3.3 (1.1)	1	3.0	5	
			Placebo	109	95 (87.2)	3.5 (1.1)	1	3.0	5	
		Week 8	CR845	106	90 (84.9)	2.9 (1.2)	1	3.0	5	
			Placebo	109	98 (89.9)	3.2 (1.2)	1	3.0	5	
		Week 10	CR845	106	88 (83.0)	2.7 (1.2)	1	3.0	5	
			Placebo	109	96 (88.1)	3.0 (1.3)	1	3.0	5	
		Week 12	CR845	106	92 (86.8)	2.8 (1.2)	1	3.0	5	
			Placebo	109	94 (86.2)	3.0 (1.2)	1	3.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	106	94 (88.7)	-0.6 (1.0)	-4	-0.5	1	0.07 [-0.21, 0.36]
			Placebo	109	95 (87.2)	-0.7 (1.4)	-4	-1.0	4	
		Week 8	CR845	106	88 (83.0)	-1.0 (1.2)	-4	-1.0	2	-0.04 [-0.32, 0.25]
			Placebo	109	98 (89.9)	-0.9 (1.4)	-4	-1.0	2	
		Week 10	CR845	106	86 (81.1)	-1.2 (1.4)	-4	-1.0	2	-0.01 [-0.30, 0.28]
			Placebo	109	96 (88.1)	-1.2 (1.5)	-4	-1.0	2	
		Week 12	CR845	106	91 (85.8)	-1.2 (1.5)	-4	-1.0	3	0.00 [-0.28, 0.29]
			Placebo	109	94 (86.2)	-1.2 (1.4)	-4	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DNC_ISHE: Change from baseline in 5-D disability score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	5-D disability score	Baseline	CR845	164	161 (98.2)	3.5 (1.1)	1	4.0	5	
			Placebo	161	161 (100.0)	3.8 (1.1)	1	4.0	5	
		Week 4	CR845	164	145 (88.4)	2.8 (1.1)	1	3.0	5	
			Placebo	161	139 (86.3)	3.2 (1.2)	1	3.0	5	
		Week 8	CR845	164	136 (82.9)	2.7 (1.2)	1	3.0	5	
			Placebo	161	143 (88.8)	3.0 (1.3)	1	3.0	5	
		Week 10	CR845	164	135 (82.3)	2.5 (1.2)	1	2.0	5	
			Placebo	161	142 (88.2)	2.8 (1.2)	1	3.0	5	
		Week 12	CR845	164	136 (82.9)	2.5 (1.2)	1	2.0	5	
			Placebo	161	139 (86.3)	2.7 (1.3)	1	3.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	164	143 (87.2)	-0.7 (1.1)	-4	-1.0	2	-0.08 [-0.31, 0.16]
			Placebo	161	139 (86.3)	-0.6 (1.4)	-4	0.0	3	
		Week 8	CR845	164	134 (81.7)	-0.8 (1.3)	-4	-1.0	4	-0.02 [-0.26, 0.21]
			Placebo	161	143 (88.8)	-0.8 (1.4)	-4	-1.0	3	
		Week 10	CR845	164	133 (81.1)	-1.0 (1.4)	-4	-1.0	3	-0.03 [-0.27, 0.21]
			Placebo	161	142 (88.2)	-1.0 (1.4)	-4	-1.0	2	
		Week 12	CR845	164	135 (82.3)	-1.0 (1.5)	-4	-1.0	3	0.03 [-0.20, 0.27]
			Placebo	161	139 (86.3)	-1.1 (1.4)	-4	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DNC_ISHE: Change from baseline in 5-D disability score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	5-D disability score	Baseline	CR845	25	25 (100.0)	3.9 (1.0)	1	4.0	5	
			Placebo	28	28 (100.0)	3.9 (1.1)	1	4.0	5	
		Week 4	CR845	25	24 (96.0)	3.5 (1.1)	1	3.5	5	
			Placebo	28	26 (92.9)	3.5 (1.3)	1	4.0	5	
		Week 8	CR845	25	23 (92.0)	3.0 (1.1)	1	3.0	5	
			Placebo	28	27 (96.4)	3.1 (1.0)	2	3.0	5	
		Week 10	CR845	25	22 (88.0)	2.8 (1.0)	1	3.0	5	
			Placebo	28	25 (89.3)	3.0 (1.2)	1	3.0	5	
		Week 12	CR845	25	24 (96.0)	2.6 (1.1)	1	2.5	5	
			Placebo	28	27 (96.4)	2.9 (1.0)	1	3.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	25	24 (96.0)	-0.4 (1.1)	-2	0.0	2	-0.05 [-0.61, 0.50]
			Placebo	28	26 (92.9)	-0.3 (1.4)	-3	0.0	4	
		Week 8	CR845	25	23 (92.0)	-0.9 (1.0)	-3	-1.0	1	-0.20 [-0.76, 0.36]
			Placebo	28	27 (96.4)	-0.7 (1.1)	-3	-1.0	1	
		Week 10	CR845	25	22 (88.0)	-1.0 (1.4)	-4	-1.0	2	-0.17 [-0.74, 0.41]
			Placebo	28	25 (89.3)	-0.8 (1.1)	-3	-1.0	1	
		Week 12	CR845	25	24 (96.0)	-1.3 (1.2)	-4	-1.0	1	-0.37 [-0.93, 0.18]
			Placebo	28	27 (96.4)	-0.9 (1.0)	-3	-1.0	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DNC_ISHF: Change from baseline in 5-D disability score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	5-D disability score	Baseline	CR845	117	115 (98.3)	3.4 (1.1)	1	4.0	5	
			Placebo	111	111 (100.0)	3.7 (1.0)	1	4.0	5	
		Week 4	CR845	117	107 (91.5)	2.9 (1.1)	1	3.0	5	
			Placebo	111	94 (84.7)	3.2 (1.1)	1	3.0	5	
		Week 8	CR845	117	101 (86.3)	2.7 (1.1)	1	3.0	5	
			Placebo	111	100 (90.1)	3.0 (1.1)	1	3.0	5	
		Week 10	CR845	117	99 (84.6)	2.5 (1.1)	1	2.0	5	
			Placebo	111	98 (88.3)	2.8 (1.2)	1	3.0	5	
		Week 12	CR845	117	100 (85.5)	2.5 (1.2)	1	2.0	5	
			Placebo	111	100 (90.1)	2.7 (1.2)	1	3.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	117	106 (90.6)	-0.6 (1.0)	-4	-1.0	2	-0.02 [-0.30, 0.26]
			Placebo	111	94 (84.7)	-0.5 (1.2)	-3	-1.0	2	
		Week 8	CR845	117	100 (85.5)	-0.8 (1.3)	-4	-1.0	4	-0.01 [-0.28, 0.27]
			Placebo	111	100 (90.1)	-0.8 (1.4)	-4	-1.0	3	
		Week 10	CR845	117	98 (83.8)	-1.0 (1.4)	-4	-1.0	2	-0.05 [-0.33, 0.23]
			Placebo	111	98 (88.3)	-0.9 (1.5)	-4	-1.0	2	
		Week 12	CR845	117	100 (85.5)	-1.0 (1.5)	-4	-1.0	3	0.09 [-0.19, 0.37]
			Placebo	111	100 (90.1)	-1.1 (1.4)	-4	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DNC_ISHF: Change from baseline in 5-D disability score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	5-D disability score	Baseline	CR845	72	71 (98.6)	3.7 (1.1)	1	4.0	5	
			Placebo	78	78 (100.0)	3.9 (1.1)	1	4.0	5	
		Week 4	CR845	72	62 (86.1)	3.0 (1.2)	1	3.0	5	
			Placebo	78	71 (91.0)	3.3 (1.3)	1	3.0	5	
		Week 8	CR845	72	58 (80.6)	2.9 (1.2)	1	3.0	5	
			Placebo	78	70 (89.7)	3.1 (1.3)	1	3.0	5	
		Week 10	CR845	72	58 (80.6)	2.7 (1.1)	1	3.0	5	
			Placebo	78	69 (88.5)	2.9 (1.3)	1	3.0	5	
		Week 12	CR845	72	60 (83.3)	2.5 (1.1)	1	2.0	5	
			Placebo	78	66 (84.6)	2.8 (1.3)	1	3.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	72	61 (84.7)	-0.7 (1.2)	-4	-1.0	2	-0.15 [-0.49, 0.19]
			Placebo	78	71 (91.0)	-0.5 (1.6)	-4	0.0	4	
		Week 8	CR845	72	57 (79.2)	-0.9 (1.1)	-4	-1.0	1	-0.11 [-0.46, 0.24]
			Placebo	78	70 (89.7)	-0.7 (1.3)	-4	-1.0	2	
		Week 10	CR845	72	57 (79.2)	-1.0 (1.4)	-4	-1.0	3	-0.04 [-0.39, 0.31]
			Placebo	78	69 (88.5)	-0.9 (1.3)	-4	-1.0	2	
		Week 12	CR845	72	59 (81.9)	-1.2 (1.4)	-4	-1.0	2	-0.20 [-0.55, 0.16]
			Placebo	78	66 (84.6)	-1.0 (1.3)	-4	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DVC_ISHA: Change from baseline in 5-D distribution score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
< 65 years	5-D distribution score	Baseline	CR845	135	132 (97.8)	3.3 (1.1)	1	3.0	5	
			Placebo	137	137 (100.0)	3.4 (1.1)	1	3.0	5	
		Week 4	CR845	135	119 (88.1)	2.9 (1.1)	1	3.0	5	
			Placebo	137	117 (85.4)	3.3 (1.2)	1	3.0	5	
		Week 8	CR845	135	111 (82.2)	2.8 (1.2)	1	3.0	5	
			Placebo	137	121 (88.3)	3.1 (1.3)	1	3.0	5	
		Week 10	CR845	135	111 (82.2)	2.7 (1.2)	1	3.0	5	
			Placebo	137	118 (86.1)	3.0 (1.2)	1	3.0	5	
		Week 12	CR845	135	113 (83.7)	2.6 (1.2)	1	3.0	5	
			Placebo	137	118 (86.1)	3.1 (1.3)	1	3.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	135	117 (86.7)	-0.4 (1.0)	-3	0.0	3	-0.22 [-0.47, 0.04]
			Placebo	137	117 (85.4)	-0.2 (1.0)	-3	0.0	2	
		Week 8	CR845	135	109 (80.7)	-0.5 (1.2)	-3	0.0	4	-0.17 [-0.43, 0.09]
			Placebo	137	121 (88.3)	-0.3 (1.3)	-4	0.0	3	
		Week 10	CR845	135	109 (80.7)	-0.5 (1.2)	-4	0.0	3	-0.08 [-0.34, 0.18]
			Placebo	137	118 (86.1)	-0.4 (1.2)	-4	0.0	3	
		Week 12	CR845	135	112 (83.0)	-0.6 (1.2)	-4	0.0	2	-0.28 [-0.54, -0.02]
			Placebo	137	118 (86.1)	-0.3 (1.2)	-4	0.0	3	

ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DVC_ISHA: Change from baseline in 5-D distribution score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 65 years	5-D distribution score	Baseline	CR845	54	54 (100.0)	3.4 (1.1)	1	3.0	5	
			Placebo	52	52 (100.0)	3.4 (1.2)	1	3.0	5	
		Week 4	CR845	54	50 (92.6)	3.1 (1.2)	1	3.0	5	
			Placebo	52	48 (92.3)	3.3 (1.2)	1	3.0	5	
		Week 8	CR845	54	48 (88.9)	2.8 (1.1)	1	3.0	5	
			Placebo	52	49 (94.2)	3.2 (1.0)	1	3.0	5	
		Week 10	CR845	54	46 (85.2)	2.8 (1.1)	1	3.0	5	
			Placebo	52	49 (94.2)	3.0 (1.2)	1	3.0	5	
		Week 12	CR845	54	47 (87.0)	2.9 (1.2)	1	3.0	5	
			Placebo	52	48 (92.3)	3.1 (1.2)	1	3.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	54	50 (92.6)	-0.3 (1.2)	-3	0.0	2	-0.15 [-0.54, 0.25]
			Placebo	52	48 (92.3)	-0.2 (1.2)	-3	0.0	3	
		Week 8	CR845	54	48 (88.9)	-0.6 (1.0)	-3	0.0	2	-0.29 [-0.69, 0.11]
			Placebo	52	49 (94.2)	-0.2 (1.2)	-2	0.0	4	
		Week 10	CR845	54	46 (85.2)	-0.6 (1.3)	-3	0.0	2	-0.20 [-0.60, 0.21]
			Placebo	52	49 (94.2)	-0.3 (1.1)	-3	0.0	2	
		Week 12	CR845	54	47 (87.0)	-0.5 (1.2)	-3	0.0	2	-0.19 [-0.59, 0.21]
			Placebo	52	48 (92.3)	-0.3 (1.1)	-3	0.0	2	

ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DVC_ISHB: Change from baseline in 5-D distribution score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Male	5-D distribution score	Baseline	CR845	112	110 (98.2)	3.2 (1.2)	1	3.0	5	
			Placebo	119	119 (100.0)	3.3 (1.2)	1	3.0	5	
		Week 4	CR845	112	98 (87.5)	2.9 (1.2)	1	3.0	5	
			Placebo	119	100 (84.0)	3.3 (1.3)	1	3.0	5	
		Week 8	CR845	112	91 (81.3)	2.7 (1.2)	1	2.0	5	
			Placebo	119	106 (89.1)	3.2 (1.2)	1	3.0	5	
		Week 10	CR845	112	91 (81.3)	2.7 (1.2)	1	3.0	5	
			Placebo	119	106 (89.1)	3.0 (1.2)	1	3.0	5	
		Week 12	CR845	112	91 (81.3)	2.6 (1.2)	1	3.0	5	
			Placebo	119	105 (88.2)	3.1 (1.2)	1	3.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	112	97 (86.6)	-0.3 (1.0)	-3	0.0	3	-0.21 [-0.49, 0.07]
			Placebo	119	100 (84.0)	-0.1 (1.1)	-3	0.0	2	
		Week 8	CR845	112	90 (80.4)	-0.5 (1.1)	-3	0.0	2	-0.31 [-0.59, -0.02]
			Placebo	119	106 (89.1)	-0.1 (1.3)	-3	0.0	4	
		Week 10	CR845	112	90 (80.4)	-0.5 (1.2)	-3	0.0	3	-0.16 [-0.44, 0.12]
			Placebo	119	106 (89.1)	-0.3 (1.2)	-3	0.0	3	
		Week 12	CR845	112	90 (80.4)	-0.6 (1.2)	-3	0.0	2	-0.31 [-0.59, -0.03]
			Placebo	119	105 (88.2)	-0.2 (1.2)	-3	0.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DVC_ISHB: Change from baseline in 5-D distribution score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Female	5-D distribution score	Baseline	CR845	77	76 (98.7)	3.5 (1.1)	1	3.0	5	
			Placebo	70	70 (100.0)	3.5 (1.0)	2	3.0	5	
		Week 4	CR845	77	71 (92.2)	3.0 (1.1)	1	3.0	5	
			Placebo	70	65 (92.9)	3.3 (1.2)	1	3.0	5	
		Week 8	CR845	77	68 (88.3)	3.0 (1.1)	1	3.0	5	
			Placebo	70	64 (91.4)	3.1 (1.3)	1	3.0	5	
		Week 10	CR845	77	66 (85.7)	2.8 (1.1)	1	3.0	5	
			Placebo	70	61 (87.1)	3.0 (1.2)	1	3.0	5	
		Week 12	CR845	77	69 (89.6)	2.8 (1.2)	1	3.0	5	
			Placebo	70	61 (87.1)	3.0 (1.3)	1	3.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	77	70 (90.9)	-0.5 (1.1)	-3	0.0	3	-0.15 [-0.49, 0.18]
			Placebo	70	65 (92.9)	-0.3 (1.0)	-3	0.0	3	
		Week 8	CR845	77	67 (87.0)	-0.5 (1.1)	-3	-1.0	4	-0.03 [-0.38, 0.31]
			Placebo	70	64 (91.4)	-0.5 (1.2)	-4	0.0	2	
		Week 10	CR845	77	65 (84.4)	-0.6 (1.2)	-4	0.0	2	-0.02 [-0.37, 0.33]
			Placebo	70	61 (87.1)	-0.6 (1.2)	-4	0.0	2	
		Week 12	CR845	77	69 (89.6)	-0.7 (1.1)	-4	0.0	2	-0.13 [-0.47, 0.22]
			Placebo	70	61 (87.1)	-0.5 (1.1)	-4	0.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DVC_ISHC: Change from baseline in 5-D distribution score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Black/African American	5-D distribution score	Baseline	CR845	82	82 (100.0)	3.3 (1.1)	1	3.0	5	
			Placebo	76	76 (100.0)	3.3 (1.1)	1	3.0	5	
		Week 4	CR845	82	69 (84.1)	2.9 (1.1)	1	3.0	5	
			Placebo	76	66 (86.8)	3.4 (1.3)	1	3.0	5	
		Week 8	CR845	82	66 (80.5)	2.8 (1.2)	1	3.0	5	
			Placebo	76	68 (89.5)	3.1 (1.2)	1	3.0	5	
		Week 10	CR845	82	64 (78.0)	2.6 (1.1)	1	3.0	5	
			Placebo	76	66 (86.8)	3.0 (1.4)	1	3.0	5	
		Week 12	CR845	82	66 (80.5)	2.6 (1.2)	1	2.0	5	
			Placebo	76	66 (86.8)	3.2 (1.3)	1	3.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	82	69 (84.1)	-0.4 (1.0)	-3	0.0	3	-0.38 [-0.72, -0.04]
			Placebo	76	66 (86.8)	0.0 (1.0)	-3	0.0	2	
		Week 8	CR845	82	66 (80.5)	-0.5 (1.1)	-3	0.0	4	-0.20 [-0.54, 0.14]
			Placebo	76	68 (89.5)	-0.3 (1.2)	-4	0.0	2	
		Week 10	CR845	82	64 (78.0)	-0.6 (1.1)	-4	0.0	1	-0.19 [-0.53, 0.16]
			Placebo	76	66 (86.8)	-0.4 (1.4)	-4	0.0	3	
		Week 12	CR845	82	66 (80.5)	-0.7 (1.1)	-4	-0.5	1	-0.44 [-0.79, -0.10]
			Placebo	76	66 (86.8)	-0.2 (1.3)	-4	0.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DVC_ISHC: Change from baseline in 5-D distribution score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
White	5-D distribution score	Baseline	CR845	91	88 (96.7)	3.3 (1.2)	1	3.0	5	
			Placebo	93	93 (100.0)	3.5 (1.1)	1	3.0	5	
		Week 4	CR845	91	85 (93.4)	3.1 (1.1)	1	3.0	5	
			Placebo	93	81 (87.1)	3.1 (1.2)	1	3.0	5	
		Week 8	CR845	91	78 (85.7)	2.8 (1.2)	1	3.0	5	
			Placebo	93	83 (89.2)	3.2 (1.2)	1	3.0	5	
		Week 10	CR845	91	79 (86.8)	2.9 (1.2)	1	3.0	5	
			Placebo	93	82 (88.2)	3.1 (1.1)	1	3.0	5	
		Week 12	CR845	91	80 (87.9)	2.8 (1.1)	1	3.0	5	
			Placebo	93	80 (86.0)	3.1 (1.2)	1	3.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	91	83 (91.2)	-0.3 (1.1)	-3	0.0	3	0.10 [-0.21, 0.41]
			Placebo	93	81 (87.1)	-0.4 (1.0)	-3	0.0	3	
		Week 8	CR845	91	76 (83.5)	-0.5 (1.1)	-3	0.0	2	-0.12 [-0.43, 0.19]
			Placebo	93	83 (89.2)	-0.3 (1.3)	-4	0.0	4	
		Week 10	CR845	91	77 (84.6)	-0.4 (1.3)	-3	0.0	3	0.06 [-0.25, 0.37]
			Placebo	93	82 (88.2)	-0.5 (1.2)	-3	0.0	2	
		Week 12	CR845	91	79 (86.8)	-0.5 (1.2)	-4	0.0	2	-0.08 [-0.39, 0.23]
			Placebo	93	80 (86.0)	-0.4 (1.1)	-3	0.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DVC_ISHC: Change from baseline in 5-D distribution score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Other	5-D distribution score	Baseline	CR845	15	15 (100.0)	3.4 (1.3)	1	3.0	5	
			Placebo	18	18 (100.0)	3.2 (1.0)	1	3.0	5	
		Week 4	CR845	15	14 (93.3)	2.4 (1.2)	1	2.0	5	
			Placebo	18	16 (88.9)	3.3 (1.2)	1	3.0	5	
		Week 8	CR845	15	14 (93.3)	2.9 (1.1)	1	3.0	5	
			Placebo	18	17 (94.4)	3.1 (1.2)	1	3.0	5	
		Week 10	CR845	15	13 (86.7)	2.5 (1.2)	1	3.0	5	
			Placebo	18	17 (94.4)	2.8 (1.0)	1	3.0	5	
		Week 12	CR845	15	13 (86.7)	2.8 (1.5)	1	3.0	5	
			Placebo	18	18 (100.0)	2.8 (0.8)	2	3.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	15	14 (93.3)	-0.9 (1.1)	-3	0.0	0	-0.83 [-1.58, -0.08]
			Placebo	18	16 (88.9)	0.0 (1.0)	-1	0.0	2	
		Week 8	CR845	15	14 (93.3)	-0.7 (1.2)	-3	-0.5	1	-0.45 [-1.17, 0.27]
			Placebo	18	17 (94.4)	-0.2 (1.2)	-2	0.0	2	
		Week 10	CR845	15	13 (86.7)	-1.0 (1.4)	-4	-1.0	1	-0.65 [-1.39, 0.10]
			Placebo	18	17 (94.4)	-0.3 (0.8)	-1	0.0	1	
		Week 12	CR845	15	13 (86.7)	-0.8 (1.3)	-4	0.0	1	-0.32 [-1.04, 0.40]
			Placebo	18	18 (100.0)	-0.4 (1.1)	-3	-0.5	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DVC_ISHD: Change from baseline in 5-D distribution score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 4 to < 7	5-D distribution score	Baseline	CR845	83	82 (98.8)	2.9 (1.0)	1	3.0	5	
			Placebo	80	80 (100.0)	3.1 (1.1)	1	3.0	5	
		Week 4	CR845	83	73 (88.0)	2.6 (1.0)	1	3.0	5	
			Placebo	80	70 (87.5)	3.1 (1.2)	1	3.0	5	
		Week 8	CR845	83	69 (83.1)	2.6 (1.0)	1	2.0	5	
			Placebo	80	72 (90.0)	2.9 (1.1)	1	3.0	5	
		Week 10	CR845	83	69 (83.1)	2.5 (1.1)	1	2.0	5	
			Placebo	80	71 (88.8)	3.0 (1.2)	1	3.0	5	
		Week 12	CR845	83	68 (81.9)	2.5 (1.0)	1	3.0	5	
			Placebo	80	72 (90.0)	2.9 (1.2)	1	3.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	83	73 (88.0)	-0.3 (0.9)	-3	0.0	2	-0.35 [-0.68, -0.02]
			Placebo	80	70 (87.5)	0.0 (0.9)	-2	0.0	3	
		Week 8	CR845	83	69 (83.1)	-0.4 (1.0)	-3	0.0	2	-0.23 [-0.57, 0.10]
			Placebo	80	72 (90.0)	-0.1 (1.2)	-3	0.0	3	
		Week 10	CR845	83	69 (83.1)	-0.5 (1.0)	-3	0.0	2	-0.33 [-0.67, -0.00]
			Placebo	80	71 (88.8)	-0.1 (1.1)	-2	0.0	3	
		Week 12	CR845	83	68 (81.9)	-0.4 (1.0)	-3	0.0	2	-0.27 [-0.61, 0.06]
			Placebo	80	72 (90.0)	-0.2 (1.1)	-3	0.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DVC_ISHD: Change from baseline in 5-D distribution score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 7	5-D distribution score	Baseline	CR845	106	104 (98.1)	3.6 (1.1)	1	3.5	5	
			Placebo	109	109 (100.0)	3.6 (1.1)	1	4.0	5	
		Week 4	CR845	106	96 (90.6)	3.2 (1.2)	1	3.0	5	
			Placebo	109	95 (87.2)	3.4 (1.2)	1	3.0	5	
		Week 8	CR845	106	90 (84.9)	2.9 (1.2)	1	3.0	5	
			Placebo	109	98 (89.9)	3.3 (1.3)	1	3.0	5	
		Week 10	CR845	106	88 (83.0)	3.0 (1.2)	1	3.0	5	
			Placebo	109	96 (88.1)	3.1 (1.2)	1	3.0	5	
		Week 12	CR845	106	92 (86.8)	2.8 (1.3)	1	3.0	5	
			Placebo	109	94 (86.2)	3.2 (1.2)	1	3.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	106	94 (88.7)	-0.4 (1.1)	-3	0.0	3	-0.10 [-0.39, 0.18]
			Placebo	109	95 (87.2)	-0.3 (1.2)	-3	0.0	2	
		Week 8	CR845	106	88 (83.0)	-0.6 (1.2)	-3	-1.0	4	-0.19 [-0.48, 0.10]
			Placebo	109	98 (89.9)	-0.4 (1.3)	-4	0.0	4	
		Week 10	CR845	106	86 (81.1)	-0.6 (1.3)	-4	0.0	3	0.02 [-0.27, 0.31]
			Placebo	109	96 (88.1)	-0.6 (1.2)	-4	0.0	2	
		Week 12	CR845	106	91 (85.8)	-0.7 (1.3)	-4	-1.0	2	-0.24 [-0.53, 0.05]
			Placebo	109	94 (86.2)	-0.4 (1.3)	-4	0.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DVC_ISHE: Change from baseline in 5-D distribution score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	5-D distribution score	Baseline	CR845	164	161 (98.2)	3.3 (1.1)	1	3.0	5	
			Placebo	161	161 (100.0)	3.3 (1.1)	1	3.0	5	
		Week 4	CR845	164	145 (88.4)	2.9 (1.2)	1	3.0	5	
			Placebo	161	139 (86.3)	3.2 (1.2)	1	3.0	5	
		Week 8	CR845	164	136 (82.9)	2.7 (1.1)	1	3.0	5	
			Placebo	161	143 (88.8)	3.1 (1.2)	1	3.0	5	
		Week 10	CR845	164	135 (82.3)	2.7 (1.2)	1	3.0	5	
			Placebo	161	142 (88.2)	3.0 (1.2)	1	3.0	5	
		Week 12	CR845	164	136 (82.9)	2.7 (1.2)	1	3.0	5	
			Placebo	161	139 (86.3)	3.0 (1.3)	1	3.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	164	143 (87.2)	-0.4 (1.0)	-3	0.0	3	-0.25 [-0.49, -0.02]
			Placebo	161	139 (86.3)	-0.1 (1.1)	-3	0.0	3	
		Week 8	CR845	164	134 (81.7)	-0.6 (1.1)	-3	0.0	2	-0.31 [-0.55, -0.07]
			Placebo	161	143 (88.8)	-0.2 (1.3)	-4	0.0	4	
		Week 10	CR845	164	133 (81.1)	-0.6 (1.2)	-4	0.0	3	-0.15 [-0.39, 0.08]
			Placebo	161	142 (88.2)	-0.4 (1.2)	-4	0.0	3	
		Week 12	CR845	164	135 (82.3)	-0.6 (1.2)	-4	0.0	2	-0.24 [-0.48, -0.01]
			Placebo	161	139 (86.3)	-0.3 (1.2)	-4	0.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DVC_ISHE: Change from baseline in 5-D distribution score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	5-D distribution score	Baseline	CR845	25	25 (100.0)	3.4 (1.2)	1	3.0	5	
			Placebo	28	28 (100.0)	3.7 (1.2)	2	3.5	5	
		Week 4	CR845	25	24 (96.0)	3.3 (1.0)	1	3.0	5	
			Placebo	28	26 (92.9)	3.4 (1.2)	1	3.0	5	
		Week 8	CR845	25	23 (92.0)	3.3 (1.2)	1	3.0	5	
			Placebo	28	27 (96.4)	3.2 (1.2)	1	3.0	5	
		Week 10	CR845	25	22 (88.0)	3.0 (1.0)	1	3.0	5	
			Placebo	28	25 (89.3)	3.3 (1.2)	1	3.0	5	
		Week 12	CR845	25	24 (96.0)	2.8 (1.1)	1	3.0	5	
			Placebo	28	27 (96.4)	3.4 (1.0)	2	3.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	25	24 (96.0)	-0.1 (1.1)	-2	0.0	3	0.13 [-0.42, 0.69]
			Placebo	28	26 (92.9)	-0.2 (1.1)	-3	0.0	2	
		Week 8	CR845	25	23 (92.0)	-0.1 (1.3)	-2	0.0	4	0.36 [-0.20, 0.92]
			Placebo	28	27 (96.4)	-0.5 (1.2)	-3	0.0	2	
		Week 10	CR845	25	22 (88.0)	-0.3 (1.2)	-2	0.0	2	0.10 [-0.47, 0.68]
			Placebo	28	25 (89.3)	-0.4 (1.3)	-4	0.0	2	
		Week 12	CR845	25	24 (96.0)	-0.7 (1.1)	-4	-0.5	1	-0.29 [-0.85, 0.26]
			Placebo	28	27 (96.4)	-0.3 (1.2)	-3	0.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DVC_ISHF: Change from baseline in 5-D distribution score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	5-D distribution score	Baseline	CR845	117	115 (98.3)	3.2 (1.1)	1	3.0	5	
			Placebo	111	111 (100.0)	3.3 (1.2)	1	3.0	5	
		Week 4	CR845	117	107 (91.5)	2.9 (1.1)	1	3.0	5	
			Placebo	111	94 (84.7)	3.3 (1.2)	1	3.0	5	
		Week 8	CR845	117	101 (86.3)	2.7 (1.1)	1	3.0	5	
			Placebo	111	100 (90.1)	3.1 (1.2)	1	3.0	5	
		Week 10	CR845	117	99 (84.6)	2.7 (1.2)	1	3.0	5	
			Placebo	111	98 (88.3)	2.9 (1.2)	1	3.0	5	
		Week 12	CR845	117	100 (85.5)	2.7 (1.2)	1	3.0	5	
			Placebo	111	100 (90.1)	3.1 (1.2)	1	3.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	117	106 (90.6)	-0.3 (1.1)	-3	0.0	3	-0.23 [-0.51, 0.05]
			Placebo	111	94 (84.7)	-0.1 (1.1)	-3	0.0	3	
		Week 8	CR845	117	100 (85.5)	-0.5 (1.1)	-3	0.0	2	-0.23 [-0.51, 0.05]
			Placebo	111	100 (90.1)	-0.2 (1.3)	-4	0.0	4	
		Week 10	CR845	117	98 (83.8)	-0.5 (1.2)	-4	0.0	3	-0.08 [-0.36, 0.21]
			Placebo	111	98 (88.3)	-0.4 (1.2)	-4	0.0	3	
		Week 12	CR845	117	100 (85.5)	-0.6 (1.2)	-4	0.0	2	-0.27 [-0.55, 0.01]
			Placebo	111	100 (90.1)	-0.3 (1.2)	-4	0.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DVC_ISHF: Change from baseline in 5-D distribution score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	5-D distribution score	Baseline	CR845	72	71 (98.6)	3.4 (1.2)	1	3.0	5	
			Placebo	78	78 (100.0)	3.5 (1.1)	1	3.0	5	
		Week 4	CR845	72	62 (86.1)	3.0 (1.2)	1	3.0	5	
			Placebo	78	71 (91.0)	3.3 (1.2)	1	3.0	5	
		Week 8	CR845	72	58 (80.6)	2.9 (1.2)	1	3.0	5	
			Placebo	78	70 (89.7)	3.2 (1.2)	1	3.0	5	
		Week 10	CR845	72	58 (80.6)	2.9 (1.2)	1	3.0	5	
			Placebo	78	69 (88.5)	3.2 (1.3)	1	3.0	5	
		Week 12	CR845	72	60 (83.3)	2.8 (1.2)	1	3.0	5	
			Placebo	78	66 (84.6)	3.1 (1.2)	1	3.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	72	61 (84.7)	-0.4 (1.0)	-3	0.0	3	-0.14 [-0.48, 0.20]
			Placebo	78	71 (91.0)	-0.3 (1.0)	-3	0.0	2	
		Week 8	CR845	72	57 (79.2)	-0.5 (1.2)	-3	0.0	4	-0.16 [-0.51, 0.19]
			Placebo	78	70 (89.7)	-0.3 (1.2)	-3	0.0	3	
		Week 10	CR845	72	57 (79.2)	-0.5 (1.2)	-3	0.0	2	-0.18 [-0.53, 0.17]
			Placebo	78	69 (88.5)	-0.3 (1.2)	-4	0.0	2	
		Week 12	CR845	72	59 (81.9)	-0.7 (1.1)	-3	0.0	2	-0.23 [-0.58, 0.13]
			Placebo	78	66 (84.6)	-0.4 (1.1)	-3	0.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table AT2DTC_ISCA: Change from baseline in 5-D total score - MMRM results by age
ITT

Change from baseline in 5-D total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
A: Age									0.105
< 65 years	Week 4	CR845	135	116 (85.9)	-3.5 (0.4)	(-4.2, -2.8)	-2.1 (0.4)	(-2.9, -1.2)	<0.001 *
		Placebo	137	117 (85.4)	-1.4 (0.4)	(-2.1, -0.7)			
>= 65 years	Week 4	CR845	54	50 (92.6)	-3.2 (0.6)	(-4.4, -2.1)	-0.8 (0.7)	(-2.1, 0.6)	0.250
		Placebo	52	48 (92.3)	-2.4 (0.5)	(-3.5, -1.4)			
< 65 years	Week 8	CR845	135	108 (80.0)	-4.5 (0.4)	(-5.3, -3.7)	-1.8 (0.5)	(-2.8, -0.9)	<0.001 *
		Placebo	137	121 (88.3)	-2.7 (0.4)	(-3.5, -1.9)			
>= 65 years	Week 8	CR845	54	48 (88.9)	-3.9 (0.6)	(-5.1, -2.7)	-0.6 (0.7)	(-2.0, 0.9)	0.419
		Placebo	52	49 (94.2)	-3.3 (0.6)	(-4.4, -2.1)			
< 65 years	Week 10	CR845	135	108 (80.0)	-4.9 (0.4)	(-5.7, -4.1)	-1.7 (0.5)	(-2.7, -0.8)	<0.001 *
		Placebo	137	118 (86.1)	-3.2 (0.4)	(-4.0, -2.4)			
>= 65 years	Week 10	CR845	54	46 (85.2)	-4.2 (0.6)	(-5.4, -3.0)	-0.5 (0.7)	(-1.9, 0.9)	0.496
		Placebo	52	49 (94.2)	-3.7 (0.6)	(-4.9, -2.6)			
< 65 years	Week 12	CR845	135	111 (82.2)	-5.0 (0.4)	(-5.8, -4.2)	-1.7 (0.5)	(-2.7, -0.7)	<0.001 *
		Placebo	137	118 (86.1)	-3.3 (0.4)	(-4.1, -2.5)			
>= 65 years	Week 12	CR845	54	47 (87.0)	-4.6 (0.6)	(-5.8, -3.4)	-0.5 (0.8)	(-2.0, 1.0)	0.501
		Placebo	52	48 (92.3)	-4.1 (0.6)	(-5.3, -2.9)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DTC_ISCB: Change from baseline in 5-D total score - MMRM results by sex
ITT

Change from baseline in 5-D total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
B: Sex									0.556
Male	Week 4	CR845	112	97 (86.6)	-3.2 (0.4)	(-4.0, -2.4)	-1.9 (0.5)	(-2.8, -1.0)	<0.001 *
		Placebo	119	100 (84.0)	-1.3 (0.4)	(-2.0, -0.5)			
Female	Week 4	CR845	77	69 (89.6)	-3.8 (0.5)	(-4.8, -2.9)	-1.3 (0.6)	(-2.4, -0.1)	0.036 *
		Placebo	70	65 (92.9)	-2.6 (0.5)	(-3.5, -1.7)			
Male	Week 8	CR845	112	90 (80.4)	-4.1 (0.5)	(-5.0, -3.2)	-1.6 (0.5)	(-2.6, -0.6)	0.003 *
		Placebo	119	106 (89.1)	-2.5 (0.4)	(-3.3, -1.6)			
Female	Week 8	CR845	77	66 (85.7)	-4.8 (0.5)	(-5.8, -3.8)	-1.1 (0.6)	(-2.4, 0.1)	0.078
		Placebo	70	64 (91.4)	-3.7 (0.5)	(-4.7, -2.7)			
Male	Week 10	CR845	112	90 (80.4)	-4.2 (0.4)	(-5.1, -3.3)	-1.0 (0.5)	(-2.0, -0.0)	0.045 *
		Placebo	119	106 (89.1)	-3.2 (0.4)	(-4.0, -2.4)			
Female	Week 10	CR845	77	64 (83.1)	-5.5 (0.5)	(-6.5, -4.5)	-1.7 (0.7)	(-3.0, -0.4)	0.012 *
		Placebo	70	61 (87.1)	-3.8 (0.5)	(-4.9, -2.8)			
Male	Week 12	CR845	112	90 (80.4)	-4.5 (0.5)	(-5.4, -3.6)	-1.2 (0.5)	(-2.3, -0.2)	0.020 *
		Placebo	119	105 (88.2)	-3.2 (0.4)	(-4.1, -2.4)			
Female	Week 12	CR845	77	68 (88.3)	-5.6 (0.5)	(-6.6, -4.5)	-1.3 (0.7)	(-2.7, 0.0)	0.055
		Placebo	70	61 (87.1)	-4.2 (0.5)	(-5.3, -3.1)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DTC_ISCC: Change from baseline in 5-D total score - MMRM results by race
ITT

Change from baseline in 5-D total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
C: Race									0.276
Black/African American	Week 4	CR845	82	68 (82.9)	-3.6 (0.5)	(-4.6, -2.7)	-2.3 (0.6)	(-3.5, -1.1)	<0.001 *
		Placebo	76	66 (86.8)	-1.3 (0.5)	(-2.3, -0.3)			
White	Week 4	CR845	91	83 (91.2)	-3.3 (0.4)	(-4.1, -2.5)	-1.1 (0.5)	(-2.0, -0.1)	0.029 *
		Placebo	93	81 (87.1)	-2.3 (0.4)	(-3.0, -1.5)			
Other	Week 4	CR845	15	14 (93.3)	-4.7 (1.4)	(-7.6, -1.8)	-2.7 (1.3)	(-5.5, 0.1)	0.056
		Placebo	18	16 (88.9)	-2.0 (1.3)	(-4.7, 0.6)			
Black/African American	Week 8	CR845	82	65 (79.3)	-4.7 (0.5)	(-5.7, -3.7)	-1.6 (0.6)	(-2.9, -0.4)	0.012 *
		Placebo	76	68 (89.5)	-3.0 (0.5)	(-4.1, -2.0)			
White	Week 8	CR845	91	76 (83.5)	-4.2 (0.5)	(-5.1, -3.3)	-1.4 (0.6)	(-2.5, -0.3)	0.015 *
		Placebo	93	83 (89.2)	-2.8 (0.4)	(-3.7, -2.0)			
Other	Week 8	CR845	15	14 (93.3)	-4.6 (1.5)	(-7.6, -1.6)	-1.4 (1.5)	(-4.5, 1.6)	0.333
		Placebo	18	17 (94.4)	-3.2 (1.4)	(-5.9, -0.4)			
Black/African American	Week 10	CR845	82	63 (76.8)	-5.3 (0.5)	(-6.3, -4.4)	-2.0 (0.6)	(-3.2, -0.8)	0.002 *
		Placebo	76	66 (86.8)	-3.4 (0.5)	(-4.4, -2.4)			
White	Week 10	CR845	91	77 (84.6)	-4.3 (0.5)	(-5.2, -3.3)	-0.9 (0.6)	(-2.0, 0.2)	0.108
		Placebo	93	82 (88.2)	-3.3 (0.4)	(-4.2, -2.4)			
Other	Week 10	CR845	15	13 (86.7)	-5.5 (1.5)	(-8.6, -2.4)	-1.5 (1.5)	(-4.6, 1.7)	0.352
		Placebo	18	17 (94.4)	-4.0 (1.4)	(-6.9, -1.2)			
Black/African American	Week 12	CR845	82	65 (79.3)	-5.5 (0.5)	(-6.6, -4.5)	-2.4 (0.7)	(-3.7, -1.1)	<0.001 *
		Placebo	76	66 (86.8)	-3.1 (0.5)	(-4.2, -2.1)			
White	Week 12	CR845	91	79 (86.8)	-4.8 (0.5)	(-5.7, -3.9)	-1.2 (0.6)	(-2.3, -0.1)	0.037 *
		Placebo	93	80 (86.0)	-3.6 (0.5)	(-4.5, -2.7)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DTC_ISCC: Change from baseline in 5-D total score - MMRM results by race
ITT

Change from baseline in 5-D total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Other	Week 12	CR845	15	13 (86.7)	-3.6 (1.6)	(-6.9, -0.2)	1.2 (1.7)	(-2.4, 4.7)	0.510
		Placebo	18	18 (100.0)	-4.7 (1.5)	(-7.7, -1.7)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DTC_ISCD: Change from baseline in 5-D total score - MMRM results by baseline WI-NRS
ITT

Change from baseline in 5-D total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
D: Baseline worst itching NRS score (WI-NRS)									0.500
>= 4 to < 7	Week 4	CR845	83	73 (88.0)	-3.4 (0.4)	(-4.2, -2.5)	-2.2 (0.5)	(-3.2, -1.2)	<0.001 *
		Placebo	80	70 (87.5)	-1.1 (0.4)	(-2.0, -0.3)			
>= 7	Week 4	CR845	106	93 (87.7)	-3.7 (0.4)	(-4.5, -2.9)	-1.3 (0.5)	(-2.3, -0.3)	0.010 *
		Placebo	109	95 (87.2)	-2.4 (0.4)	(-3.2, -1.6)			
>= 4 to < 7	Week 8	CR845	83	69 (83.1)	-3.7 (0.5)	(-4.6, -2.8)	-1.4 (0.5)	(-2.4, -0.4)	0.008 *
		Placebo	80	72 (90.0)	-2.3 (0.4)	(-3.1, -1.4)			
>= 7	Week 8	CR845	106	87 (82.1)	-5.1 (0.5)	(-6.0, -4.2)	-1.6 (0.6)	(-2.7, -0.4)	0.009 *
		Placebo	109	98 (89.9)	-3.5 (0.5)	(-4.4, -2.6)			
>= 4 to < 7	Week 10	CR845	83	69 (83.1)	-4.1 (0.5)	(-5.0, -3.1)	-1.6 (0.5)	(-2.6, -0.5)	0.004 *
		Placebo	80	71 (88.8)	-2.5 (0.5)	(-3.4, -1.6)			
>= 7	Week 10	CR845	106	85 (80.2)	-5.5 (0.5)	(-6.4, -4.6)	-1.2 (0.6)	(-2.4, -0.1)	0.037 *
		Placebo	109	96 (88.1)	-4.3 (0.5)	(-5.2, -3.4)			
>= 4 to < 7	Week 12	CR845	83	68 (81.9)	-4.3 (0.5)	(-5.2, -3.3)	-1.2 (0.6)	(-2.3, -0.1)	0.038 *
		Placebo	80	72 (90.0)	-3.1 (0.5)	(-4.0, -2.2)			
>= 7	Week 12	CR845	106	90 (84.9)	-5.6 (0.5)	(-6.6, -4.7)	-1.5 (0.6)	(-2.8, -0.3)	0.013 *
		Placebo	109	94 (86.2)	-4.1 (0.5)	(-5.0, -3.2)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DTC_ISCE: Change from baseline in 5-D total score - MMRM results by specific medical condition
ITT

Change from baseline in 5-D total score					Repeated measures analysis					
					Change from Baseline		Treatment Difference			
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value	
E: Presence of specific medical conditions									0.809	
No	Week 4	CR845	164	142 (86.6)	-3.8 (0.3)	(-4.3, -3.2)	-1.7 (0.4)	(-2.5, -1.0)	<0.001	*
		Placebo	161	139 (86.3)	-2.0 (0.3)	(-2.6, -1.5)				
Yes	Week 4	CR845	25	24 (96.0)	-3.2 (0.6)	(-4.5, -1.8)	-1.2 (0.9)	(-3.1, 0.6)	0.173	
		Placebo	28	26 (92.9)	-1.9 (0.6)	(-3.2, -0.7)				
No	Week 8	CR845	164	133 (81.1)	-4.6 (0.3)	(-5.2, -4.0)	-1.5 (0.4)	(-2.4, -0.6)	<0.001	*
		Placebo	161	143 (88.8)	-3.1 (0.3)	(-3.7, -2.5)				
Yes	Week 8	CR845	25	23 (92.0)	-4.6 (0.7)	(-5.9, -3.2)	-1.1 (0.9)	(-2.8, 0.7)	0.245	
		Placebo	28	27 (96.4)	-3.5 (0.6)	(-4.7, -2.3)				
No	Week 10	CR845	164	132 (80.5)	-5.0 (0.3)	(-5.6, -4.4)	-1.3 (0.4)	(-2.1, -0.4)	0.004	*
		Placebo	161	142 (88.2)	-3.7 (0.3)	(-4.3, -3.1)				
Yes	Week 10	CR845	25	22 (88.0)	-4.8 (0.8)	(-6.4, -3.2)	-1.4 (1.1)	(-3.6, 0.8)	0.209	
		Placebo	28	25 (89.3)	-3.4 (0.8)	(-4.9, -1.9)				
No	Week 12	CR845	164	134 (81.7)	-4.9 (0.3)	(-5.6, -4.3)	-1.0 (0.5)	(-1.9, -0.1)	0.029	*
		Placebo	161	139 (86.3)	-3.9 (0.3)	(-4.5, -3.3)				
Yes	Week 12	CR845	25	24 (96.0)	-6.5 (0.7)	(-7.9, -5.1)	-3.0 (1.0)	(-4.9, -1.1)	0.003	*
		Placebo	28	27 (96.4)	-3.5 (0.7)	(-4.8, -2.2)				

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor previous use of anti-itch medication is also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DTC_ISCF: Change from baseline in 5-D total score - MMRM results by use of concomitant itch medication
ITT

Change from baseline in 5-D total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
F: Use of concomitant itch medication									0.888
No	Week 4	CR845	117	106 (90.6)	-2.9 (0.4)	(-3.7, -2.2)	-1.7 (0.4)	(-2.5, -0.8)	<0.001 *
		Placebo	111	94 (84.7)	-1.3 (0.4)	(-2.0, -0.5)			
Yes	Week 4	CR845	72	60 (83.3)	-4.2 (0.5)	(-5.2, -3.1)	-1.6 (0.6)	(-2.9, -0.3)	0.014 *
		Placebo	78	71 (91.0)	-2.6 (0.5)	(-3.5, -1.6)			
No	Week 8	CR845	117	100 (85.5)	-4.1 (0.4)	(-5.0, -3.3)	-1.7 (0.5)	(-2.6, -0.7)	<0.001 *
		Placebo	111	100 (90.1)	-2.5 (0.4)	(-3.3, -1.7)			
Yes	Week 8	CR845	72	56 (77.8)	-4.6 (0.5)	(-5.7, -3.5)	-1.0 (0.7)	(-2.3, 0.4)	0.150
		Placebo	78	70 (89.7)	-3.6 (0.5)	(-4.6, -2.6)			
No	Week 10	CR845	117	98 (83.8)	-4.4 (0.4)	(-5.3, -3.6)	-1.3 (0.5)	(-2.3, -0.3)	0.011 *
		Placebo	111	98 (88.3)	-3.1 (0.4)	(-4.0, -2.3)			
Yes	Week 10	CR845	72	56 (77.8)	-5.1 (0.5)	(-6.1, -4.1)	-1.2 (0.6)	(-2.5, 0.0)	0.059
		Placebo	78	69 (88.5)	-3.9 (0.5)	(-4.9, -2.9)			
No	Week 12	CR845	117	100 (85.5)	-4.5 (0.4)	(-5.4, -3.7)	-1.2 (0.5)	(-2.2, -0.1)	0.028 *
		Placebo	111	100 (90.1)	-3.4 (0.4)	(-4.2, -2.5)			
Yes	Week 12	CR845	72	58 (80.6)	-5.5 (0.5)	(-6.6, -4.4)	-1.5 (0.7)	(-2.9, -0.2)	0.029 *
		Placebo	78	66 (84.6)	-4.0 (0.5)	(-5.0, -2.9)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor presence of medical condition is also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DDC_ISCA: Change from baseline in 5-D degree score - MMRM results by age
ITT

Change from baseline in 5-D degree score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
A: Age									0.589
< 65 years	Week 4	CR845	135	117 (86.7)	-0.6 (0.1)	(-0.8, -0.4)	-0.4 (0.1)	(-0.5, -0.2)	<0.001 *
		Placebo	137	117 (85.4)	-0.2 (0.1)	(-0.4, -0.1)			
>= 65 years	Week 4	CR845	54	50 (92.6)	-0.6 (0.1)	(-0.9, -0.4)	-0.3 (0.1)	(-0.6, -0.0)	0.033 *
		Placebo	52	48 (92.3)	-0.3 (0.1)	(-0.5, -0.1)			
< 65 years	Week 8	CR845	135	109 (80.7)	-0.8 (0.1)	(-0.9, -0.6)	-0.2 (0.1)	(-0.4, 0.0)	0.057
		Placebo	137	121 (88.3)	-0.6 (0.1)	(-0.7, -0.4)			
>= 65 years	Week 8	CR845	54	48 (88.9)	-0.7 (0.1)	(-0.9, -0.4)	-0.1 (0.2)	(-0.5, 0.2)	0.343
		Placebo	52	49 (94.2)	-0.5 (0.1)	(-0.8, -0.3)			
< 65 years	Week 10	CR845	135	109 (80.7)	-0.9 (0.1)	(-1.0, -0.7)	-0.3 (0.1)	(-0.6, -0.1)	0.003 *
		Placebo	137	118 (86.1)	-0.5 (0.1)	(-0.7, -0.3)			
>= 65 years	Week 10	CR845	54	46 (85.2)	-0.8 (0.1)	(-1.0, -0.5)	-0.2 (0.1)	(-0.4, 0.1)	0.300
		Placebo	52	49 (94.2)	-0.6 (0.1)	(-0.8, -0.4)			
< 65 years	Week 12	CR845	135	112 (83.0)	-0.9 (0.1)	(-1.1, -0.8)	-0.3 (0.1)	(-0.5, -0.1)	0.010 *
		Placebo	137	118 (86.1)	-0.7 (0.1)	(-0.8, -0.5)			
>= 65 years	Week 12	CR845	54	47 (87.0)	-0.8 (0.1)	(-1.1, -0.6)	-0.1 (0.1)	(-0.4, 0.2)	0.344
		Placebo	52	48 (92.3)	-0.7 (0.1)	(-0.9, -0.4)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DDC_ISCB: Change from baseline in 5-D degree score - MMRM results by sex
ITT

Change from baseline in 5-D degree score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
B: Sex									0.826
Male	Week 4	CR845	112	97 (86.6)	-0.6 (0.1)	(-0.8, -0.4)	-0.4 (0.1)	(-0.6, -0.1)	0.001 *
		Placebo	119	100 (84.0)	-0.3 (0.1)	(-0.4, -0.1)			
Female	Week 4	CR845	77	70 (90.9)	-0.6 (0.1)	(-0.8, -0.4)	-0.3 (0.1)	(-0.6, -0.1)	0.005 *
		Placebo	70	65 (92.9)	-0.3 (0.1)	(-0.5, -0.1)			
Male	Week 8	CR845	112	90 (80.4)	-0.7 (0.1)	(-0.9, -0.5)	-0.2 (0.1)	(-0.5, -0.0)	0.050 *
		Placebo	119	106 (89.1)	-0.5 (0.1)	(-0.6, -0.3)			
Female	Week 8	CR845	77	67 (87.0)	-0.8 (0.1)	(-1.0, -0.6)	-0.1 (0.1)	(-0.4, 0.1)	0.330
		Placebo	70	64 (91.4)	-0.7 (0.1)	(-0.9, -0.5)			
Male	Week 10	CR845	112	90 (80.4)	-0.8 (0.1)	(-1.0, -0.6)	-0.3 (0.1)	(-0.6, -0.1)	0.007 *
		Placebo	119	106 (89.1)	-0.5 (0.1)	(-0.7, -0.3)			
Female	Week 10	CR845	77	65 (84.4)	-0.9 (0.1)	(-1.1, -0.7)	-0.2 (0.1)	(-0.5, 0.0)	0.083
		Placebo	70	61 (87.1)	-0.7 (0.1)	(-0.9, -0.5)			
Male	Week 12	CR845	112	90 (80.4)	-0.9 (0.1)	(-1.1, -0.7)	-0.2 (0.1)	(-0.4, -0.0)	0.043 *
		Placebo	119	105 (88.2)	-0.6 (0.1)	(-0.8, -0.5)			
Female	Week 12	CR845	77	69 (89.6)	-1.0 (0.1)	(-1.2, -0.8)	-0.3 (0.1)	(-0.6, 0.0)	0.061
		Placebo	70	61 (87.1)	-0.7 (0.1)	(-0.9, -0.5)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DDC_ISCC: Change from baseline in 5-D degree score - MMRM results by race
ITT

Change from baseline in 5-D degree score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
C: Race									0.344
Black/African American	Week 4	CR845	82	69 (84.1)	-0.6 (0.1)	(-0.8, -0.4)	-0.4 (0.1)	(-0.7, -0.2)	0.001 *
		Placebo	76	66 (86.8)	-0.1 (0.1)	(-0.4, 0.1)			
White	Week 4	CR845	91	83 (91.2)	-0.7 (0.1)	(-0.8, -0.5)	-0.2 (0.1)	(-0.4, -0.0)	0.021 *
		Placebo	93	81 (87.1)	-0.4 (0.1)	(-0.6, -0.2)			
Other	Week 4	CR845	15	14 (93.3)	-0.9 (0.3)	(-1.5, -0.2)	-0.6 (0.3)	(-1.2, 0.0)	0.066
		Placebo	18	16 (88.9)	-0.3 (0.3)	(-0.9, 0.3)			
Black/African American	Week 8	CR845	82	66 (80.5)	-0.8 (0.1)	(-1.0, -0.6)	-0.3 (0.1)	(-0.6, 0.0)	0.059
		Placebo	76	68 (89.5)	-0.5 (0.1)	(-0.8, -0.3)			
White	Week 8	CR845	91	76 (83.5)	-0.7 (0.1)	(-0.9, -0.5)	-0.2 (0.1)	(-0.4, 0.1)	0.201
		Placebo	93	83 (89.2)	-0.6 (0.1)	(-0.7, -0.4)			
Other	Week 8	CR845	15	14 (93.3)	-0.9 (0.3)	(-1.5, -0.3)	-0.3 (0.3)	(-0.9, 0.3)	0.388
		Placebo	18	17 (94.4)	-0.7 (0.3)	(-1.2, -0.1)			
Black/African American	Week 10	CR845	82	64 (78.0)	-0.9 (0.1)	(-1.1, -0.7)	-0.4 (0.1)	(-0.7, -0.1)	0.006 *
		Placebo	76	66 (86.8)	-0.5 (0.1)	(-0.7, -0.3)			
White	Week 10	CR845	91	77 (84.6)	-0.8 (0.1)	(-1.0, -0.6)	-0.2 (0.1)	(-0.5, 0.0)	0.050
		Placebo	93	82 (88.2)	-0.5 (0.1)	(-0.7, -0.4)			
Other	Week 10	CR845	15	13 (86.7)	-1.0 (0.3)	(-1.7, -0.3)	-0.3 (0.3)	(-1.0, 0.4)	0.379
		Placebo	18	17 (94.4)	-0.7 (0.3)	(-1.3, -0.1)			
Black/African American	Week 12	CR845	82	66 (80.5)	-1.0 (0.1)	(-1.2, -0.8)	-0.4 (0.1)	(-0.7, -0.2)	0.002 *
		Placebo	76	66 (86.8)	-0.6 (0.1)	(-0.8, -0.3)			
White	Week 12	CR845	91	79 (86.8)	-0.9 (0.1)	(-1.1, -0.7)	-0.2 (0.1)	(-0.4, 0.0)	0.062
		Placebo	93	80 (86.0)	-0.7 (0.1)	(-0.9, -0.5)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DDC_ISCC: Change from baseline in 5-D degree score - MMRM results by race
ITT

Change from baseline in 5-D degree score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Other	Week 12	CR845	15	13 (86.7)	-0.7 (0.4)	(-1.4, 0.1)	0.2 (0.4)	(-0.6, 0.9)	0.696
		Placebo	18	18 (100.0)	-0.8 (0.3)	(-1.5, -0.2)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DDC_ISCD: Change from baseline in 5-D degree score - MMRM results by baseline WI-NRS
ITT

Change from baseline in 5-D degree score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
D: Baseline worst itching NRS score (WI-NRS)									0.286
>= 4 to < 7	Week 4	CR845	83	73 (88.0)	-0.4 (0.1)	(-0.6, -0.2)	-0.3 (0.1)	(-0.5, -0.1)	0.011 *
		Placebo	80	70 (87.5)	-0.1 (0.1)	(-0.3, 0.0)			
>= 7	Week 4	CR845	106	94 (88.7)	-0.8 (0.1)	(-1.0, -0.6)	-0.4 (0.1)	(-0.6, -0.2)	<0.001 *
		Placebo	109	95 (87.2)	-0.4 (0.1)	(-0.5, -0.2)			
>= 4 to < 7	Week 8	CR845	83	69 (83.1)	-0.5 (0.1)	(-0.7, -0.3)	-0.1 (0.1)	(-0.3, 0.1)	0.368
		Placebo	80	72 (90.0)	-0.4 (0.1)	(-0.6, -0.2)			
>= 7	Week 8	CR845	106	88 (83.0)	-1.0 (0.1)	(-1.2, -0.8)	-0.3 (0.1)	(-0.6, -0.0)	0.021 *
		Placebo	109	98 (89.9)	-0.7 (0.1)	(-0.9, -0.5)			
>= 4 to < 7	Week 10	CR845	83	69 (83.1)	-0.6 (0.1)	(-0.8, -0.4)	-0.3 (0.1)	(-0.5, -0.0)	0.039 *
		Placebo	80	71 (88.8)	-0.3 (0.1)	(-0.5, -0.1)			
>= 7	Week 10	CR845	106	86 (81.1)	-1.1 (0.1)	(-1.3, -0.9)	-0.3 (0.1)	(-0.6, -0.1)	0.006 *
		Placebo	109	96 (88.1)	-0.7 (0.1)	(-0.9, -0.5)			
>= 4 to < 7	Week 12	CR845	83	68 (81.9)	-0.7 (0.1)	(-0.9, -0.5)	-0.2 (0.1)	(-0.4, 0.1)	0.139
		Placebo	80	72 (90.0)	-0.5 (0.1)	(-0.7, -0.3)			
>= 7	Week 12	CR845	106	91 (85.8)	-1.1 (0.1)	(-1.3, -0.9)	-0.3 (0.1)	(-0.6, -0.1)	0.009 *
		Placebo	109	94 (86.2)	-0.8 (0.1)	(-1.0, -0.6)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DDC_ISCE: Change from baseline in 5-D degree score - MMRM results by specific medical condition
ITT

Change from baseline in 5-D degree score					Repeated measures analysis					
					Change from Baseline		Treatment Difference			
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value	
E: Presence of specific medical conditions									0.342	
No	Week 4	CR845	164	143 (87.2)	-0.6 (0.1)	(-0.8, -0.5)	-0.4 (0.1)	(-0.5, -0.2)	<0.001	*
		Placebo	161	139 (86.3)	-0.3 (0.1)	(-0.4, -0.2)				
Yes	Week 4	CR845	25	24 (96.0)	-0.6 (0.2)	(-1.0, -0.3)	-0.3 (0.2)	(-0.8, 0.1)	0.130	
		Placebo	28	26 (92.9)	-0.3 (0.2)	(-0.6, 0.0)				
No	Week 8	CR845	164	134 (81.7)	-0.7 (0.1)	(-0.9, -0.6)	-0.2 (0.1)	(-0.4, 0.0)	0.089	
		Placebo	161	143 (88.8)	-0.6 (0.1)	(-0.7, -0.4)				
Yes	Week 8	CR845	25	23 (92.0)	-0.9 (0.2)	(-1.3, -0.6)	-0.4 (0.2)	(-0.8, 0.1)	0.100	
		Placebo	28	27 (96.4)	-0.6 (0.2)	(-0.9, -0.2)				
No	Week 10	CR845	164	133 (81.1)	-0.8 (0.1)	(-1.0, -0.7)	-0.3 (0.1)	(-0.5, -0.1)	0.006	*
		Placebo	161	142 (88.2)	-0.6 (0.1)	(-0.7, -0.4)				
Yes	Week 10	CR845	25	22 (88.0)	-0.9 (0.2)	(-1.2, -0.6)	-0.4 (0.2)	(-0.8, 0.0)	0.068	
		Placebo	28	25 (89.3)	-0.5 (0.1)	(-0.8, -0.2)				
No	Week 12	CR845	164	135 (82.3)	-0.9 (0.1)	(-1.0, -0.7)	-0.2 (0.1)	(-0.4, 0.0)	0.070	
		Placebo	161	139 (86.3)	-0.7 (0.1)	(-0.8, -0.6)				
Yes	Week 12	CR845	25	24 (96.0)	-1.3 (0.1)	(-1.5, -1.0)	-0.6 (0.2)	(-1.0, -0.2)	0.002	*
		Placebo	28	27 (96.4)	-0.6 (0.1)	(-0.9, -0.4)				

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor previous use of anti-itch medication is also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DDC_ISCF: Change from baseline in 5-D degree score - MMRM results by use of concomitant itch medication
ITT

Change from baseline in 5-D degree score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
F: Use of concomitant itch medication									0.523
No	Week 4	CR845	117	106 (90.6)	-0.5 (0.1)	(-0.6, -0.3)	-0.4 (0.1)	(-0.6, -0.2)	<0.001 *
		Placebo	111	94 (84.7)	-0.1 (0.1)	(-0.3, 0.1)			
Yes	Week 4	CR845	72	61 (84.7)	-0.8 (0.1)	(-1.0, -0.6)	-0.3 (0.1)	(-0.6, -0.1)	0.011 *
		Placebo	78	71 (91.0)	-0.5 (0.1)	(-0.7, -0.3)			
No	Week 8	CR845	117	100 (85.5)	-0.6 (0.1)	(-0.8, -0.5)	-0.2 (0.1)	(-0.4, 0.0)	0.085
		Placebo	111	100 (90.1)	-0.4 (0.1)	(-0.6, -0.3)			
Yes	Week 8	CR845	72	57 (79.2)	-0.9 (0.1)	(-1.1, -0.6)	-0.2 (0.2)	(-0.5, 0.1)	0.193
		Placebo	78	70 (89.7)	-0.7 (0.1)	(-0.9, -0.4)			
No	Week 10	CR845	117	98 (83.8)	-0.7 (0.1)	(-0.9, -0.5)	-0.3 (0.1)	(-0.5, -0.1)	0.015 *
		Placebo	111	98 (88.3)	-0.4 (0.1)	(-0.6, -0.3)			
Yes	Week 10	CR845	72	57 (79.2)	-1.0 (0.1)	(-1.2, -0.7)	-0.3 (0.1)	(-0.6, -0.0)	0.042 *
		Placebo	78	69 (88.5)	-0.7 (0.1)	(-0.9, -0.5)			
No	Week 12	CR845	117	100 (85.5)	-0.8 (0.1)	(-1.0, -0.6)	-0.2 (0.1)	(-0.4, 0.1)	0.141
		Placebo	111	100 (90.1)	-0.6 (0.1)	(-0.8, -0.4)			
Yes	Week 12	CR845	72	59 (81.9)	-1.1 (0.1)	(-1.3, -0.8)	-0.4 (0.1)	(-0.7, -0.1)	0.011 *
		Placebo	78	66 (84.6)	-0.7 (0.1)	(-0.9, -0.5)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor presence of medical condition is also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DLC_ISCA: Change from baseline in 5-D duration score - MMRM results by age
ITT

Change from baseline in 5-D duration score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
A: Age									0.588
< 65 years	Week 4	CR845	135	116 (85.9)	-0.7 (0.1)	(-1.0, -0.5)	-0.5 (0.2)	(-0.8, -0.2)	0.002 *
		Placebo	137	117 (85.4)	-0.3 (0.1)	(-0.5, -0.0)			
>= 65 years	Week 4	CR845	54	50 (92.6)	-0.7 (0.2)	(-1.1, -0.3)	-0.3 (0.3)	(-0.9, 0.2)	0.204
		Placebo	52	48 (92.3)	-0.3 (0.2)	(-0.7, 0.1)			
< 65 years	Week 8	CR845	135	108 (80.0)	-1.0 (0.1)	(-1.3, -0.8)	-0.4 (0.2)	(-0.7, -0.1)	0.008 *
		Placebo	137	121 (88.3)	-0.6 (0.1)	(-0.9, -0.4)			
>= 65 years	Week 8	CR845	54	48 (88.9)	-1.0 (0.2)	(-1.4, -0.6)	-0.4 (0.2)	(-0.9, 0.0)	0.067
		Placebo	52	49 (94.2)	-0.5 (0.2)	(-0.9, -0.2)			
< 65 years	Week 10	CR845	135	108 (80.0)	-1.1 (0.1)	(-1.3, -0.8)	-0.4 (0.2)	(-0.7, -0.1)	0.009 *
		Placebo	137	118 (86.1)	-0.7 (0.1)	(-0.9, -0.4)			
>= 65 years	Week 10	CR845	54	46 (85.2)	-1.0 (0.2)	(-1.3, -0.6)	-0.2 (0.2)	(-0.7, 0.2)	0.264
		Placebo	52	49 (94.2)	-0.7 (0.2)	(-1.1, -0.4)			
< 65 years	Week 12	CR845	135	111 (82.2)	-1.0 (0.1)	(-1.2, -0.7)	-0.3 (0.1)	(-0.6, -0.0)	0.031 *
		Placebo	137	118 (86.1)	-0.6 (0.1)	(-0.9, -0.4)			
>= 65 years	Week 12	CR845	54	47 (87.0)	-1.2 (0.2)	(-1.6, -0.9)	-0.2 (0.2)	(-0.7, 0.2)	0.258
		Placebo	52	48 (92.3)	-1.0 (0.2)	(-1.3, -0.6)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DLC_ISCB: Change from baseline in 5-D duration score - MMRM results by sex
ITT

Change from baseline in 5-D duration score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
B: Sex									0.516
Male	Week 4	CR845	112	97 (86.6)	-0.6 (0.1)	(-0.9, -0.4)	-0.6 (0.2)	(-1.0, -0.3)	<0.001 *
		Placebo	119	100 (84.0)	-0.0 (0.1)	(-0.3, 0.2)			
Female	Week 4	CR845	77	69 (89.6)	-0.8 (0.2)	(-1.2, -0.5)	-0.2 (0.2)	(-0.6, 0.2)	0.446
		Placebo	70	65 (92.9)	-0.7 (0.2)	(-1.0, -0.4)			
Male	Week 8	CR845	112	90 (80.4)	-0.9 (0.1)	(-1.2, -0.6)	-0.5 (0.2)	(-0.8, -0.1)	0.006 *
		Placebo	119	106 (89.1)	-0.4 (0.1)	(-0.7, -0.2)			
Female	Week 8	CR845	77	66 (85.7)	-1.2 (0.2)	(-1.5, -0.9)	-0.3 (0.2)	(-0.7, 0.1)	0.108
		Placebo	70	64 (91.4)	-0.9 (0.2)	(-1.2, -0.6)			
Male	Week 10	CR845	112	90 (80.4)	-0.8 (0.1)	(-1.1, -0.6)	-0.2 (0.2)	(-0.5, 0.1)	0.140
		Placebo	119	106 (89.1)	-0.6 (0.1)	(-0.8, -0.3)			
Female	Week 10	CR845	77	64 (83.1)	-1.3 (0.2)	(-1.6, -1.0)	-0.5 (0.2)	(-0.9, -0.1)	0.012 *
		Placebo	70	61 (87.1)	-0.8 (0.2)	(-1.1, -0.5)			
Male	Week 12	CR845	112	90 (80.4)	-0.8 (0.1)	(-1.1, -0.6)	-0.3 (0.2)	(-0.6, 0.1)	0.112
		Placebo	119	105 (88.2)	-0.6 (0.1)	(-0.8, -0.3)			
Female	Week 12	CR845	77	68 (88.3)	-1.3 (0.1)	(-1.6, -1.0)	-0.3 (0.2)	(-0.7, 0.0)	0.066
		Placebo	70	61 (87.1)	-1.0 (0.1)	(-1.3, -0.7)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DLC_ISCC: Change from baseline in 5-D duration score - MMRM results by race
ITT

Change from baseline in 5-D duration score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
C: Race									0.125
Black/African American	Week 4	CR845	82	68 (82.9)	-0.8 (0.2)	(-1.1, -0.5)	-0.5 (0.2)	(-0.9, -0.1)	0.022 *
		Placebo	76	66 (86.8)	-0.3 (0.2)	(-0.7, -0.0)			
White	Week 4	CR845	91	83 (91.2)	-0.8 (0.1)	(-1.1, -0.5)	-0.5 (0.2)	(-0.9, -0.1)	0.006 *
		Placebo	93	81 (87.1)	-0.3 (0.1)	(-0.6, 0.0)			
Other	Week 4	CR845	15	14 (93.3)	-0.7 (0.4)	(-1.6, 0.2)	-0.3 (0.5)	(-1.3, 0.7)	0.555
		Placebo	18	16 (88.9)	-0.4 (0.4)	(-1.3, 0.4)			
Black/African American	Week 8	CR845	82	65 (79.3)	-1.0 (0.2)	(-1.3, -0.7)	-0.3 (0.2)	(-0.7, 0.0)	0.075
		Placebo	76	68 (89.5)	-0.7 (0.2)	(-1.0, -0.4)			
White	Week 8	CR845	91	76 (83.5)	-1.1 (0.2)	(-1.4, -0.8)	-0.6 (0.2)	(-0.9, -0.2)	0.003 *
		Placebo	93	83 (89.2)	-0.5 (0.1)	(-0.8, -0.2)			
Other	Week 8	CR845	15	14 (93.3)	-1.1 (0.4)	(-1.9, -0.2)	-0.2 (0.5)	(-1.2, 0.7)	0.646
		Placebo	18	17 (94.4)	-0.8 (0.4)	(-1.6, -0.0)			
Black/African American	Week 10	CR845	82	63 (76.8)	-1.2 (0.1)	(-1.5, -0.9)	-0.6 (0.2)	(-1.0, -0.2)	0.001 *
		Placebo	76	66 (86.8)	-0.6 (0.1)	(-0.9, -0.3)			
White	Week 10	CR845	91	77 (84.6)	-1.0 (0.2)	(-1.3, -0.7)	-0.3 (0.2)	(-0.7, 0.1)	0.105
		Placebo	93	82 (88.2)	-0.7 (0.1)	(-1.0, -0.4)			
Other	Week 10	CR845	15	13 (86.7)	-0.9 (0.4)	(-1.7, -0.2)	0.1 (0.4)	(-0.7, 0.9)	0.782
		Placebo	18	17 (94.4)	-1.0 (0.4)	(-1.8, -0.3)			
Black/African American	Week 12	CR845	82	65 (79.3)	-1.2 (0.1)	(-1.4, -0.9)	-0.5 (0.2)	(-0.9, -0.2)	0.005 *
		Placebo	76	66 (86.8)	-0.6 (0.1)	(-0.9, -0.4)			
White	Week 12	CR845	91	79 (86.8)	-1.1 (0.1)	(-1.4, -0.8)	-0.4 (0.2)	(-0.7, -0.0)	0.037 *
		Placebo	93	80 (86.0)	-0.7 (0.1)	(-1.0, -0.5)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DLC_ISCC: Change from baseline in 5-D duration score - MMRM results by race
ITT

Change from baseline in 5-D duration score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Other	Week 12	CR845	15	13 (86.7)	-0.5 (0.4)	(-1.3, 0.4)	0.6 (0.5)	(-0.4, 1.6)	0.211
		Placebo	18	18 (100.0)	-1.1 (0.4)	(-1.9, -0.3)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DLC_ISCD: Change from baseline in 5-D duration score - MMRM results by baseline WI-NRS
ITT

Change from baseline in 5-D duration score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
D: Baseline worst itching NRS score (WI-NRS)									0.869
>= 4 to < 7	Week 4	CR845	83	73 (88.0)	-0.5 (0.2)	(-0.8, -0.2)	-0.6 (0.2)	(-0.9, -0.2)	0.003 *
		Placebo	80	70 (87.5)	0.0 (0.2)	(-0.3, 0.3)			
>= 7	Week 4	CR845	106	93 (87.7)	-1.0 (0.1)	(-1.2, -0.7)	-0.4 (0.2)	(-0.7, -0.0)	0.045 *
		Placebo	109	95 (87.2)	-0.6 (0.1)	(-0.9, -0.3)			
>= 4 to < 7	Week 8	CR845	83	69 (83.1)	-0.7 (0.1)	(-1.0, -0.4)	-0.4 (0.2)	(-0.7, -0.1)	0.018 *
		Placebo	80	72 (90.0)	-0.3 (0.1)	(-0.5, 0.0)			
>= 7	Week 8	CR845	106	87 (82.1)	-1.4 (0.1)	(-1.7, -1.1)	-0.5 (0.2)	(-0.8, -0.1)	0.015 *
		Placebo	109	98 (89.9)	-0.9 (0.1)	(-1.2, -0.6)			
>= 4 to < 7	Week 10	CR845	83	69 (83.1)	-0.6 (0.2)	(-0.9, -0.3)	-0.3 (0.2)	(-0.7, 0.0)	0.071
		Placebo	80	71 (88.8)	-0.3 (0.1)	(-0.6, -0.0)			
>= 7	Week 10	CR845	106	85 (80.2)	-1.4 (0.1)	(-1.7, -1.1)	-0.4 (0.2)	(-0.7, -0.1)	0.019 *
		Placebo	109	96 (88.1)	-1.0 (0.1)	(-1.3, -0.7)			
>= 4 to < 7	Week 12	CR845	83	68 (81.9)	-0.7 (0.1)	(-0.9, -0.4)	-0.2 (0.2)	(-0.6, 0.1)	0.180
		Placebo	80	72 (90.0)	-0.4 (0.1)	(-0.7, -0.2)			
>= 7	Week 12	CR845	106	90 (84.9)	-1.4 (0.1)	(-1.7, -1.1)	-0.4 (0.2)	(-0.7, -0.0)	0.025 *
		Placebo	109	94 (86.2)	-1.0 (0.1)	(-1.3, -0.7)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DLC_ISCE: Change from baseline in 5-D duration score - MMRM results by specific medical condition
ITT

Change from baseline in 5-D duration score					Repeated measures analysis					
					Change from Baseline		Treatment Difference			
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value	
E: Presence of specific medical conditions									0.658	
No	Week 4	CR845	164	142 (86.6)	-0.8 (0.1)	(-1.0, -0.6)	-0.5 (0.1)	(-0.7, -0.2)	0.001	*
		Placebo	161	139 (86.3)	-0.4 (0.1)	(-0.5, -0.2)				
Yes	Week 4	CR845	25	24 (96.0)	-0.8 (0.3)	(-1.3, -0.3)	-0.4 (0.4)	(-1.1, 0.3)	0.290	
		Placebo	28	26 (92.9)	-0.4 (0.3)	(-0.9, 0.1)				
No	Week 8	CR845	164	133 (81.1)	-1.1 (0.1)	(-1.3, -0.9)	-0.5 (0.1)	(-0.7, -0.2)	0.001	*
		Placebo	161	143 (88.8)	-0.7 (0.1)	(-0.9, -0.5)				
Yes	Week 8	CR845	25	23 (92.0)	-0.9 (0.2)	(-1.4, -0.4)	-0.3 (0.3)	(-1.0, 0.4)	0.374	
		Placebo	28	27 (96.4)	-0.6 (0.2)	(-1.1, -0.2)				
No	Week 10	CR845	164	132 (80.5)	-1.1 (0.1)	(-1.3, -0.9)	-0.3 (0.1)	(-0.6, -0.1)	0.011	*
		Placebo	161	142 (88.2)	-0.8 (0.1)	(-1.0, -0.6)				
Yes	Week 10	CR845	25	22 (88.0)	-1.0 (0.3)	(-1.6, -0.5)	-0.5 (0.4)	(-1.2, 0.3)	0.198	
		Placebo	28	25 (89.3)	-0.6 (0.2)	(-1.1, -0.1)				
No	Week 12	CR845	164	134 (81.7)	-1.1 (0.1)	(-1.3, -0.9)	-0.3 (0.1)	(-0.5, 0.0)	0.059	
		Placebo	161	139 (86.3)	-0.8 (0.1)	(-1.0, -0.6)				
Yes	Week 12	CR845	25	24 (96.0)	-1.3 (0.2)	(-1.8, -0.9)	-0.6 (0.3)	(-1.2, -0.1)	0.033	*
		Placebo	28	27 (96.4)	-0.7 (0.2)	(-1.1, -0.3)				

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor previous use of anti-itch medication is also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DLC_ISCF: Change from baseline in 5-D duration score - MMRM results by use of concomitant itch medication
ITT

Change from baseline in 5-D duration score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
F: Use of concomitant itch medication									0.786
No	Week 4	CR845	117	106 (90.6)	-0.6 (0.1)	(-0.8, -0.3)	-0.3 (0.2)	(-0.7, -0.0)	0.031 *
		Placebo	111	94 (84.7)	-0.2 (0.1)	(-0.5, 0.0)			
Yes	Week 4	CR845	72	60 (83.3)	-1.0 (0.2)	(-1.3, -0.6)	-0.6 (0.2)	(-1.0, -0.1)	0.018 *
		Placebo	78	71 (91.0)	-0.4 (0.2)	(-0.8, -0.1)			
No	Week 8	CR845	117	100 (85.5)	-1.0 (0.1)	(-1.2, -0.7)	-0.6 (0.2)	(-0.9, -0.3)	<0.001 *
		Placebo	111	100 (90.1)	-0.4 (0.1)	(-0.6, -0.2)			
Yes	Week 8	CR845	72	56 (77.8)	-1.1 (0.2)	(-1.4, -0.7)	-0.1 (0.2)	(-0.6, 0.3)	0.546
		Placebo	78	70 (89.7)	-0.9 (0.2)	(-1.3, -0.6)			
No	Week 10	CR845	117	98 (83.8)	-0.9 (0.1)	(-1.2, -0.7)	-0.4 (0.2)	(-0.7, -0.1)	0.017 *
		Placebo	111	98 (88.3)	-0.5 (0.1)	(-0.8, -0.3)			
Yes	Week 10	CR845	72	56 (77.8)	-1.2 (0.2)	(-1.6, -0.9)	-0.3 (0.2)	(-0.7, 0.1)	0.160
		Placebo	78	69 (88.5)	-0.9 (0.2)	(-1.3, -0.6)			
No	Week 12	CR845	117	100 (85.5)	-0.9 (0.1)	(-1.2, -0.7)	-0.3 (0.2)	(-0.6, 0.0)	0.059
		Placebo	111	100 (90.1)	-0.6 (0.1)	(-0.9, -0.4)			
Yes	Week 12	CR845	72	58 (80.6)	-1.2 (0.2)	(-1.5, -0.9)	-0.3 (0.2)	(-0.7, 0.1)	0.160
		Placebo	78	66 (84.6)	-0.9 (0.2)	(-1.2, -0.6)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor presence of medical condition is also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DWC_ISCA: Change from baseline in 5-D direction score - MMRM results by age
ITT

Change from baseline in 5-D direction score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
A: Age									0.005 i
< 65 years	Week 4	CR845	135	117 (86.7)	-1.2 (0.1)	(-1.4, -1.1)	-0.6 (0.1)	(-0.8, -0.4)	<0.001 *
		Placebo	137	117 (85.4)	-0.6 (0.1)	(-0.8, -0.5)			
>= 65 years	Week 4	CR845	54	50 (92.6)	-1.0 (0.1)	(-1.3, -0.8)	-0.2 (0.2)	(-0.5, 0.1)	0.235
		Placebo	52	48 (92.3)	-0.9 (0.1)	(-1.1, -0.6)			
< 65 years	Week 8	CR845	135	109 (80.7)	-1.4 (0.1)	(-1.6, -1.3)	-0.6 (0.1)	(-0.9, -0.4)	<0.001 *
		Placebo	137	121 (88.3)	-0.8 (0.1)	(-1.0, -0.6)			
>= 65 years	Week 8	CR845	54	48 (88.9)	-1.0 (0.1)	(-1.3, -0.7)	0.1 (0.2)	(-0.3, 0.4)	0.602
		Placebo	52	49 (94.2)	-1.1 (0.1)	(-1.4, -0.8)			
< 65 years	Week 10	CR845	135	109 (80.7)	-1.5 (0.1)	(-1.6, -1.3)	-0.5 (0.1)	(-0.8, -0.3)	<0.001 *
		Placebo	137	118 (86.1)	-0.9 (0.1)	(-1.1, -0.8)			
>= 65 years	Week 10	CR845	54	46 (85.2)	-1.3 (0.1)	(-1.6, -1.0)	-0.2 (0.2)	(-0.5, 0.1)	0.185
		Placebo	52	49 (94.2)	-1.1 (0.1)	(-1.3, -0.8)			
< 65 years	Week 12	CR845	135	112 (83.0)	-1.5 (0.1)	(-1.6, -1.3)	-0.5 (0.1)	(-0.8, -0.3)	<0.001 *
		Placebo	137	118 (86.1)	-0.9 (0.1)	(-1.1, -0.7)			
>= 65 years	Week 12	CR845	54	47 (87.0)	-1.2 (0.1)	(-1.5, -0.9)	-0.1 (0.2)	(-0.4, 0.3)	0.672
		Placebo	52	48 (92.3)	-1.1 (0.1)	(-1.4, -0.8)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DWC_ISCB: Change from baseline in 5-D direction score - MMRM results by sex
ITT

Change from baseline in 5-D direction score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
B: Sex									0.830
Male	Week 4	CR845	112	97 (86.6)	-1.1 (0.1)	(-1.4, -0.9)	-0.5 (0.1)	(-0.7, -0.3)	<0.001 *
		Placebo	119	100 (84.0)	-0.6 (0.1)	(-0.8, -0.4)			
Female	Week 4	CR845	77	70 (90.9)	-1.2 (0.1)	(-1.4, -1.0)	-0.4 (0.1)	(-0.6, -0.1)	0.005 *
		Placebo	70	65 (92.9)	-0.9 (0.1)	(-1.1, -0.6)			
Male	Week 8	CR845	112	90 (80.4)	-1.2 (0.1)	(-1.4, -1.0)	-0.4 (0.1)	(-0.7, -0.2)	<0.001 *
		Placebo	119	106 (89.1)	-0.8 (0.1)	(-1.0, -0.6)			
Female	Week 8	CR845	77	67 (87.0)	-1.4 (0.1)	(-1.6, -1.2)	-0.4 (0.2)	(-0.7, -0.1)	0.014 *
		Placebo	70	64 (91.4)	-1.0 (0.1)	(-1.3, -0.8)			
Male	Week 10	CR845	112	90 (80.4)	-1.3 (0.1)	(-1.5, -1.1)	-0.4 (0.1)	(-0.6, -0.2)	<0.001 *
		Placebo	119	106 (89.1)	-1.0 (0.1)	(-1.1, -0.8)			
Female	Week 10	CR845	77	65 (84.4)	-1.5 (0.1)	(-1.8, -1.3)	-0.5 (0.2)	(-0.8, -0.2)	0.003 *
		Placebo	70	61 (87.1)	-1.0 (0.1)	(-1.3, -0.8)			
Male	Week 12	CR845	112	90 (80.4)	-1.3 (0.1)	(-1.6, -1.1)	-0.4 (0.1)	(-0.7, -0.2)	0.001 *
		Placebo	119	105 (88.2)	-0.9 (0.1)	(-1.1, -0.7)			
Female	Week 12	CR845	77	69 (89.6)	-1.4 (0.1)	(-1.7, -1.2)	-0.4 (0.2)	(-0.7, -0.0)	0.027 *
		Placebo	70	61 (87.1)	-1.1 (0.1)	(-1.3, -0.9)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DWC_ISCC: Change from baseline in 5-D direction score - MMRM results by race
ITT

Change from baseline in 5-D direction score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
C: Race									0.429
Black/African American	Week 4	CR845	82	69 (84.1)	-1.3 (0.1)	(-1.5, -1.1)	-0.6 (0.1)	(-0.9, -0.3)	<0.001 *
		Placebo	76	66 (86.8)	-0.7 (0.1)	(-0.9, -0.5)			
White	Week 4	CR845	91	83 (91.2)	-1.1 (0.1)	(-1.3, -0.9)	-0.3 (0.1)	(-0.6, -0.0)	0.023 *
		Placebo	93	81 (87.1)	-0.8 (0.1)	(-1.0, -0.6)			
Other	Week 4	CR845	15	14 (93.3)	-1.4 (0.3)	(-2.1, -0.7)	-0.6 (0.3)	(-1.3, 0.1)	0.081
		Placebo	18	16 (88.9)	-0.8 (0.3)	(-1.4, -0.2)			
Black/African American	Week 8	CR845	82	66 (80.5)	-1.4 (0.1)	(-1.7, -1.2)	-0.4 (0.1)	(-0.7, -0.1)	0.006 *
		Placebo	76	68 (89.5)	-1.0 (0.1)	(-1.3, -0.8)			
White	Week 8	CR845	91	76 (83.5)	-1.2 (0.1)	(-1.4, -1.0)	-0.4 (0.1)	(-0.6, -0.1)	0.006 *
		Placebo	93	83 (89.2)	-0.8 (0.1)	(-1.0, -0.6)			
Other	Week 8	CR845	15	14 (93.3)	-1.4 (0.3)	(-2.1, -0.7)	-0.6 (0.3)	(-1.3, 0.1)	0.076
		Placebo	18	17 (94.4)	-0.8 (0.3)	(-1.4, -0.1)			
Black/African American	Week 10	CR845	82	64 (78.0)	-1.6 (0.1)	(-1.8, -1.4)	-0.5 (0.1)	(-0.8, -0.3)	<0.001 *
		Placebo	76	66 (86.8)	-1.1 (0.1)	(-1.3, -0.9)			
White	Week 10	CR845	91	77 (84.6)	-1.3 (0.1)	(-1.5, -1.1)	-0.4 (0.1)	(-0.7, -0.1)	0.004 *
		Placebo	93	82 (88.2)	-0.9 (0.1)	(-1.1, -0.7)			
Other	Week 10	CR845	15	13 (86.7)	-1.4 (0.3)	(-2.1, -0.7)	-0.3 (0.3)	(-0.9, 0.4)	0.402
		Placebo	18	17 (94.4)	-1.1 (0.3)	(-1.7, -0.5)			
Black/African American	Week 12	CR845	82	66 (80.5)	-1.5 (0.1)	(-1.7, -1.3)	-0.5 (0.1)	(-0.8, -0.2)	<0.001 *
		Placebo	76	66 (86.8)	-1.0 (0.1)	(-1.2, -0.7)			
White	Week 12	CR845	91	79 (86.8)	-1.3 (0.1)	(-1.5, -1.1)	-0.4 (0.1)	(-0.7, -0.1)	0.005 *
		Placebo	93	80 (86.0)	-0.9 (0.1)	(-1.1, -0.7)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DWC_ISCC: Change from baseline in 5-D direction score - MMRM results by race
ITT

Change from baseline in 5-D direction score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Other	Week 12	CR845	15	13 (86.7)	-1.2 (0.4)	(-2.0, -0.4)	-0.1 (0.4)	(-0.9, 0.7)	0.811
		Placebo	18	18 (100.0)	-1.1 (0.3)	(-1.8, -0.4)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DWC_ISCD: Change from baseline in 5-D direction score - MMRM results by baseline WI-NRS
ITT

Change from baseline in 5-D direction score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
D: Baseline worst itching NRS score (WI-NRS)									0.955
>= 4 to < 7	Week 4	CR845	83	73 (88.0)	-1.3 (0.1)	(-1.5, -1.1)	-0.6 (0.1)	(-0.8, -0.3)	<0.001 *
		Placebo	80	70 (87.5)	-0.7 (0.1)	(-1.0, -0.5)			
>= 7	Week 4	CR845	106	94 (88.7)	-1.1 (0.1)	(-1.3, -1.0)	-0.4 (0.1)	(-0.6, -0.2)	<0.001 *
		Placebo	109	95 (87.2)	-0.7 (0.1)	(-0.9, -0.6)			
>= 4 to < 7	Week 8	CR845	83	69 (83.1)	-1.3 (0.1)	(-1.5, -1.1)	-0.4 (0.1)	(-0.7, -0.1)	0.005 *
		Placebo	80	72 (90.0)	-0.9 (0.1)	(-1.1, -0.7)			
>= 7	Week 8	CR845	106	88 (83.0)	-1.4 (0.1)	(-1.6, -1.2)	-0.5 (0.1)	(-0.7, -0.2)	<0.001 *
		Placebo	109	98 (89.9)	-0.9 (0.1)	(-1.1, -0.7)			
>= 4 to < 7	Week 10	CR845	83	69 (83.1)	-1.4 (0.1)	(-1.6, -1.2)	-0.4 (0.1)	(-0.7, -0.1)	0.002 *
		Placebo	80	71 (88.8)	-1.0 (0.1)	(-1.2, -0.8)			
>= 7	Week 10	CR845	106	86 (81.1)	-1.5 (0.1)	(-1.7, -1.3)	-0.5 (0.1)	(-0.7, -0.2)	<0.001 *
		Placebo	109	96 (88.1)	-1.0 (0.1)	(-1.2, -0.8)			
>= 4 to < 7	Week 12	CR845	83	68 (81.9)	-1.4 (0.1)	(-1.7, -1.2)	-0.4 (0.1)	(-0.7, -0.1)	0.012 *
		Placebo	80	72 (90.0)	-1.0 (0.1)	(-1.3, -0.8)			
>= 7	Week 12	CR845	106	91 (85.8)	-1.4 (0.1)	(-1.6, -1.2)	-0.4 (0.1)	(-0.7, -0.2)	<0.001 *
		Placebo	109	94 (86.2)	-1.0 (0.1)	(-1.2, -0.8)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DWC_ISCE: Change from baseline in 5-D direction score - MMRM results by specific medical condition
ITT

Change from baseline in 5-D direction score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
E: Presence of specific medical conditions									0.095
No	Week 4	CR845	164	143 (87.2)	-1.2 (0.1)	(-1.3, -1.1)	-0.4 (0.1)	(-0.6, -0.2)	<0.001 *
		Placebo	161	139 (86.3)	-0.8 (0.1)	(-0.9, -0.6)			
Yes	Week 4	CR845	25	24 (96.0)	-1.3 (0.2)	(-1.6, -0.9)	-0.6 (0.2)	(-1.1, -0.1)	0.024 *
		Placebo	28	26 (92.9)	-0.7 (0.2)	(-1.0, -0.4)			
No	Week 8	CR845	164	134 (81.7)	-1.3 (0.1)	(-1.4, -1.1)	-0.4 (0.1)	(-0.6, -0.2)	<0.001 *
		Placebo	161	143 (88.8)	-0.9 (0.1)	(-1.0, -0.7)			
Yes	Week 8	CR845	25	23 (92.0)	-1.7 (0.2)	(-2.0, -1.4)	-0.6 (0.2)	(-1.0, -0.1)	0.011 *
		Placebo	28	27 (96.4)	-1.1 (0.2)	(-1.4, -0.8)			
No	Week 10	CR845	164	133 (81.1)	-1.4 (0.1)	(-1.5, -1.3)	-0.4 (0.1)	(-0.6, -0.2)	<0.001 *
		Placebo	161	142 (88.2)	-1.0 (0.1)	(-1.1, -0.9)			
Yes	Week 10	CR845	25	22 (88.0)	-1.7 (0.2)	(-2.1, -1.3)	-0.8 (0.3)	(-1.3, -0.2)	0.009 *
		Placebo	28	25 (89.3)	-1.0 (0.2)	(-1.3, -0.6)			
No	Week 12	CR845	164	135 (82.3)	-1.3 (0.1)	(-1.5, -1.2)	-0.3 (0.1)	(-0.5, -0.1)	0.006 *
		Placebo	161	139 (86.3)	-1.0 (0.1)	(-1.2, -0.9)			
Yes	Week 12	CR845	25	24 (96.0)	-1.9 (0.2)	(-2.3, -1.6)	-1.0 (0.3)	(-1.6, -0.5)	<0.001 *
		Placebo	28	27 (96.4)	-0.9 (0.2)	(-1.3, -0.6)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor previous use of anti-itch medication is also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DWC_ISCF: Change from baseline in 5-D direction score - MMRM results by use of concomitant itch medication
ITT

Change from baseline in 5-D direction score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
F: Use of concomitant itch medication									0.415
No	Week 4	CR845	117	106 (90.6)	-1.1 (0.1)	(-1.2, -0.9)	-0.5 (0.1)	(-0.7, -0.3)	<0.001 *
		Placebo	111	94 (84.7)	-0.6 (0.1)	(-0.8, -0.4)			
Yes	Week 4	CR845	72	61 (84.7)	-1.4 (0.1)	(-1.6, -1.1)	-0.5 (0.2)	(-0.8, -0.2)	0.004 *
		Placebo	78	71 (91.0)	-0.9 (0.1)	(-1.1, -0.7)			
No	Week 8	CR845	117	100 (85.5)	-1.3 (0.1)	(-1.4, -1.1)	-0.4 (0.1)	(-0.6, -0.2)	<0.001 *
		Placebo	111	100 (90.1)	-0.9 (0.1)	(-1.0, -0.7)			
Yes	Week 8	CR845	72	57 (79.2)	-1.4 (0.1)	(-1.7, -1.1)	-0.5 (0.2)	(-0.8, -0.1)	0.007 *
		Placebo	78	70 (89.7)	-0.9 (0.1)	(-1.2, -0.7)			
No	Week 10	CR845	117	98 (83.8)	-1.3 (0.1)	(-1.5, -1.1)	-0.3 (0.1)	(-0.5, -0.1)	0.006 *
		Placebo	111	98 (88.3)	-1.0 (0.1)	(-1.2, -0.8)			
Yes	Week 10	CR845	72	57 (79.2)	-1.6 (0.1)	(-1.8, -1.3)	-0.6 (0.2)	(-0.9, -0.3)	<0.001 *
		Placebo	78	69 (88.5)	-1.0 (0.1)	(-1.2, -0.7)			
No	Week 12	CR845	117	100 (85.5)	-1.3 (0.1)	(-1.5, -1.1)	-0.4 (0.1)	(-0.6, -0.2)	0.001 *
		Placebo	111	100 (90.1)	-0.9 (0.1)	(-1.1, -0.7)			
Yes	Week 12	CR845	72	59 (81.9)	-1.5 (0.1)	(-1.7, -1.2)	-0.4 (0.2)	(-0.8, -0.1)	0.013 *
		Placebo	78	66 (84.6)	-1.1 (0.1)	(-1.3, -0.8)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor presence of medical condition is also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DNC_ISCA: Change from baseline in 5-D disability score - MMRM results by age
ITT

Change from baseline in 5-D disability score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
A: Age									0.020 i
< 65 years	Week 4	CR845	135	117 (86.7)	-0.6 (0.1)	(-0.8, -0.4)	-0.4 (0.1)	(-0.7, -0.2)	0.002 *
		Placebo	137	117 (85.4)	-0.2 (0.1)	(-0.4, 0.0)			
>= 65 years	Week 4	CR845	54	50 (92.6)	-0.6 (0.2)	(-0.9, -0.2)	0.1 (0.2)	(-0.3, 0.6)	0.616
		Placebo	52	48 (92.3)	-0.7 (0.2)	(-1.0, -0.3)			
< 65 years	Week 8	CR845	135	109 (80.7)	-0.8 (0.1)	(-1.1, -0.6)	-0.3 (0.1)	(-0.6, -0.1)	0.017 *
		Placebo	137	121 (88.3)	-0.5 (0.1)	(-0.7, -0.3)			
>= 65 years	Week 8	CR845	54	48 (88.9)	-0.7 (0.2)	(-1.1, -0.3)	0.1 (0.2)	(-0.3, 0.6)	0.633
		Placebo	52	49 (94.2)	-0.8 (0.2)	(-1.2, -0.4)			
< 65 years	Week 10	CR845	135	109 (80.7)	-1.0 (0.1)	(-1.3, -0.8)	-0.3 (0.1)	(-0.6, -0.0)	0.023 *
		Placebo	137	118 (86.1)	-0.7 (0.1)	(-0.9, -0.5)			
>= 65 years	Week 10	CR845	54	46 (85.2)	-0.7 (0.2)	(-1.1, -0.3)	0.2 (0.2)	(-0.3, 0.7)	0.403
		Placebo	52	49 (94.2)	-0.9 (0.2)	(-1.3, -0.5)			
< 65 years	Week 12	CR845	135	112 (83.0)	-1.1 (0.1)	(-1.3, -0.8)	-0.3 (0.2)	(-0.6, 0.0)	0.099
		Placebo	137	118 (86.1)	-0.8 (0.1)	(-1.1, -0.6)			
>= 65 years	Week 12	CR845	54	47 (87.0)	-0.9 (0.2)	(-1.2, -0.5)	0.1 (0.2)	(-0.3, 0.6)	0.582
		Placebo	52	48 (92.3)	-1.0 (0.2)	(-1.3, -0.7)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DNC_ISCB: Change from baseline in 5-D disability score - MMRM results by sex
ITT

Change from baseline in 5-D disability score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
B: Sex									0.729
Male	Week 4	CR845	112	97 (86.6)	-0.5 (0.1)	(-0.8, -0.3)	-0.3 (0.1)	(-0.6, -0.0)	0.037 *
		Placebo	119	100 (84.0)	-0.2 (0.1)	(-0.5, 0.0)			
Female	Week 4	CR845	77	70 (90.9)	-0.8 (0.1)	(-1.0, -0.5)	-0.2 (0.2)	(-0.6, 0.2)	0.317
		Placebo	70	65 (92.9)	-0.6 (0.1)	(-0.9, -0.3)			
Male	Week 8	CR845	112	90 (80.4)	-0.7 (0.1)	(-1.0, -0.5)	-0.2 (0.2)	(-0.5, 0.1)	0.200
		Placebo	119	106 (89.1)	-0.5 (0.1)	(-0.8, -0.3)			
Female	Week 8	CR845	77	67 (87.0)	-0.9 (0.1)	(-1.2, -0.6)	-0.2 (0.2)	(-0.6, 0.1)	0.222
		Placebo	70	64 (91.4)	-0.7 (0.1)	(-1.0, -0.4)			
Male	Week 10	CR845	112	90 (80.4)	-0.8 (0.1)	(-1.1, -0.5)	0.0 (0.2)	(-0.3, 0.3)	0.895
		Placebo	119	106 (89.1)	-0.8 (0.1)	(-1.1, -0.5)			
Female	Week 10	CR845	77	65 (84.4)	-1.2 (0.2)	(-1.5, -0.9)	-0.5 (0.2)	(-0.9, -0.1)	0.020 *
		Placebo	70	61 (87.1)	-0.7 (0.2)	(-1.0, -0.4)			
Male	Week 12	CR845	112	90 (80.4)	-0.9 (0.1)	(-1.2, -0.6)	-0.1 (0.2)	(-0.4, 0.2)	0.618
		Placebo	119	105 (88.2)	-0.8 (0.1)	(-1.1, -0.6)			
Female	Week 12	CR845	77	69 (89.6)	-1.2 (0.2)	(-1.5, -0.9)	-0.2 (0.2)	(-0.6, 0.2)	0.270
		Placebo	70	61 (87.1)	-1.0 (0.2)	(-1.3, -0.7)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DNC_ISCC: Change from baseline in 5-D disability score - MMRM results by race
ITT

Change from baseline in 5-D disability score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
C: Race									0.465
Black/African American	Week 4	CR845	82	69 (84.1)	-0.7 (0.1)	(-1.0, -0.4)	-0.4 (0.2)	(-0.8, -0.0)	0.043 *
		Placebo	76	66 (86.8)	-0.3 (0.2)	(-0.6, 0.0)			
White	Week 4	CR845	91	83 (91.2)	-0.5 (0.1)	(-0.8, -0.3)	-0.1 (0.2)	(-0.4, 0.2)	0.445
		Placebo	93	81 (87.1)	-0.4 (0.1)	(-0.7, -0.2)			
Other	Week 4	CR845	15	14 (93.3)	-1.0 (0.4)	(-1.8, -0.1)	-0.6 (0.4)	(-1.5, 0.3)	0.194
		Placebo	18	16 (88.9)	-0.4 (0.4)	(-1.2, 0.4)			
Black/African American	Week 8	CR845	82	66 (80.5)	-0.9 (0.2)	(-1.2, -0.6)	-0.3 (0.2)	(-0.7, 0.1)	0.092
		Placebo	76	68 (89.5)	-0.6 (0.2)	(-0.9, -0.3)			
White	Week 8	CR845	91	76 (83.5)	-0.7 (0.1)	(-1.0, -0.4)	-0.1 (0.2)	(-0.5, 0.2)	0.524
		Placebo	93	83 (89.2)	-0.6 (0.1)	(-0.8, -0.3)			
Other	Week 8	CR845	15	14 (93.3)	-0.8 (0.4)	(-1.6, 0.0)	-0.2 (0.4)	(-1.0, 0.6)	0.547
		Placebo	18	17 (94.4)	-0.6 (0.4)	(-1.3, 0.2)			
Black/African American	Week 10	CR845	82	64 (78.0)	-1.1 (0.2)	(-1.4, -0.8)	-0.2 (0.2)	(-0.6, 0.2)	0.316
		Placebo	76	66 (86.8)	-0.9 (0.2)	(-1.2, -0.6)			
White	Week 10	CR845	91	77 (84.6)	-0.7 (0.1)	(-1.0, -0.5)	-0.0 (0.2)	(-0.4, 0.3)	0.850
		Placebo	93	82 (88.2)	-0.7 (0.1)	(-1.0, -0.4)			
Other	Week 10	CR845	15	13 (86.7)	-1.7 (0.4)	(-2.5, -0.8)	-1.0 (0.4)	(-1.9, -0.1)	0.029 *
		Placebo	18	17 (94.4)	-0.7 (0.4)	(-1.4, 0.1)			
Black/African American	Week 12	CR845	82	66 (80.5)	-1.2 (0.2)	(-1.5, -0.9)	-0.4 (0.2)	(-0.8, 0.0)	0.083
		Placebo	76	66 (86.8)	-0.9 (0.2)	(-1.2, -0.5)			
White	Week 12	CR845	91	79 (86.8)	-0.9 (0.1)	(-1.2, -0.7)	-0.1 (0.2)	(-0.5, 0.2)	0.410
		Placebo	93	80 (86.0)	-0.8 (0.1)	(-1.1, -0.5)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DNC_ISCC: Change from baseline in 5-D disability score - MMRM results by race
ITT

Change from baseline in 5-D disability score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Other	Week 12	CR845	15	13 (86.7)	-0.9 (0.5)	(-1.8, 0.0)	0.4 (0.5)	(-0.6, 1.4)	0.436
		Placebo	18	18 (100.0)	-1.3 (0.4)	(-2.1, -0.5)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DNC_ISCD: Change from baseline in 5-D disability score - MMRM results by baseline WI-NRS
ITT

Change from baseline in 5-D disability score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
D: Baseline worst itching NRS score (WI-NRS)									0.317
>= 4 to < 7	Week 4	CR845	83	73 (88.0)	-0.7 (0.2)	(-1.0, -0.4)	-0.5 (0.2)	(-0.9, -0.2)	0.005 *
		Placebo	80	70 (87.5)	-0.2 (0.2)	(-0.5, 0.1)			
>= 7	Week 4	CR845	106	94 (88.7)	-0.6 (0.1)	(-0.8, -0.3)	-0.1 (0.1)	(-0.4, 0.2)	0.537
		Placebo	109	95 (87.2)	-0.5 (0.1)	(-0.7, -0.2)			
>= 4 to < 7	Week 8	CR845	83	69 (83.1)	-0.7 (0.2)	(-1.0, -0.4)	-0.2 (0.2)	(-0.6, 0.1)	0.241
		Placebo	80	72 (90.0)	-0.5 (0.1)	(-0.8, -0.2)			
>= 7	Week 8	CR845	106	88 (83.0)	-0.9 (0.1)	(-1.2, -0.6)	-0.2 (0.2)	(-0.5, 0.1)	0.177
		Placebo	109	98 (89.9)	-0.7 (0.1)	(-0.9, -0.4)			
>= 4 to < 7	Week 10	CR845	83	69 (83.1)	-0.8 (0.2)	(-1.2, -0.5)	-0.2 (0.2)	(-0.6, 0.1)	0.184
		Placebo	80	71 (88.8)	-0.6 (0.2)	(-0.9, -0.3)			
>= 7	Week 10	CR845	106	86 (81.1)	-1.1 (0.1)	(-1.4, -0.8)	-0.1 (0.2)	(-0.5, 0.2)	0.404
		Placebo	109	96 (88.1)	-0.9 (0.1)	(-1.2, -0.7)			
>= 4 to < 7	Week 12	CR845	83	68 (81.9)	-1.0 (0.2)	(-1.3, -0.7)	-0.2 (0.2)	(-0.5, 0.2)	0.407
		Placebo	80	72 (90.0)	-0.9 (0.2)	(-1.2, -0.6)			
>= 7	Week 12	CR845	106	91 (85.8)	-1.1 (0.1)	(-1.4, -0.8)	-0.2 (0.2)	(-0.5, 0.2)	0.357
		Placebo	109	94 (86.2)	-0.9 (0.1)	(-1.2, -0.7)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DNC_ISCE: Change from baseline in 5-D disability score - MMRM results by specific medical condition
ITT

Change from baseline in 5-D disability score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
E: Presence of specific medical conditions									0.663
No	Week 4	CR845	164	143 (87.2)	-0.8 (0.1)	(-0.9, -0.6)	-0.3 (0.1)	(-0.5, -0.1)	0.016 *
		Placebo	161	139 (86.3)	-0.5 (0.1)	(-0.6, -0.3)			
Yes	Week 4	CR845	25	24 (96.0)	-0.4 (0.2)	(-0.8, 0.1)	-0.0 (0.3)	(-0.7, 0.6)	0.886
		Placebo	28	26 (92.9)	-0.3 (0.2)	(-0.7, 0.1)			
No	Week 8	CR845	164	134 (81.7)	-0.9 (0.1)	(-1.1, -0.7)	-0.2 (0.1)	(-0.5, 0.0)	0.101
		Placebo	161	143 (88.8)	-0.7 (0.1)	(-0.8, -0.5)			
Yes	Week 8	CR845	25	23 (92.0)	-0.9 (0.2)	(-1.2, -0.5)	-0.2 (0.2)	(-0.7, 0.3)	0.527
		Placebo	28	27 (96.4)	-0.7 (0.2)	(-1.1, -0.4)			
No	Week 10	CR845	164	133 (81.1)	-1.1 (0.1)	(-1.3, -0.9)	-0.2 (0.1)	(-0.5, 0.1)	0.168
		Placebo	161	142 (88.2)	-0.9 (0.1)	(-1.1, -0.7)			
Yes	Week 10	CR845	25	22 (88.0)	-1.0 (0.2)	(-1.4, -0.5)	-0.1 (0.3)	(-0.7, 0.5)	0.828
		Placebo	28	25 (89.3)	-0.9 (0.2)	(-1.3, -0.5)			
No	Week 12	CR845	164	135 (82.3)	-1.1 (0.1)	(-1.3, -0.9)	-0.1 (0.1)	(-0.4, 0.2)	0.440
		Placebo	161	139 (86.3)	-1.0 (0.1)	(-1.2, -0.8)			
Yes	Week 12	CR845	25	24 (96.0)	-1.3 (0.2)	(-1.7, -0.9)	-0.4 (0.3)	(-0.9, 0.2)	0.167
		Placebo	28	27 (96.4)	-0.9 (0.2)	(-1.3, -0.6)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor previous use of anti-itch medication is also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DNC_ISCF: Change from baseline in 5-D disability score - MMRM results by use of concomitant itch medication
ITT

Change from baseline in 5-D disability score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
F: Use of concomitant itch medication									0.986
No	Week 4	CR845	117	106 (90.6)	-0.6 (0.1)	(-0.8, -0.3)	-0.3 (0.1)	(-0.5, 0.0)	0.070
		Placebo	111	94 (84.7)	-0.3 (0.1)	(-0.5, -0.1)			
Yes	Week 4	CR845	72	61 (84.7)	-0.7 (0.2)	(-1.1, -0.4)	-0.3 (0.2)	(-0.7, 0.1)	0.157
		Placebo	78	71 (91.0)	-0.4 (0.2)	(-0.7, -0.1)			
No	Week 8	CR845	117	100 (85.5)	-0.8 (0.1)	(-1.0, -0.5)	-0.2 (0.2)	(-0.5, 0.1)	0.149
		Placebo	111	100 (90.1)	-0.5 (0.1)	(-0.8, -0.3)			
Yes	Week 8	CR845	72	57 (79.2)	-0.9 (0.2)	(-1.2, -0.6)	-0.2 (0.2)	(-0.6, 0.2)	0.343
		Placebo	78	70 (89.7)	-0.7 (0.1)	(-1.0, -0.4)			
No	Week 10	CR845	117	98 (83.8)	-1.0 (0.1)	(-1.3, -0.7)	-0.3 (0.2)	(-0.6, 0.1)	0.113
		Placebo	111	98 (88.3)	-0.7 (0.1)	(-1.0, -0.5)			
Yes	Week 10	CR845	72	57 (79.2)	-0.9 (0.2)	(-1.2, -0.6)	-0.0 (0.2)	(-0.4, 0.4)	0.873
		Placebo	78	69 (88.5)	-0.9 (0.2)	(-1.2, -0.6)			
No	Week 12	CR845	117	100 (85.5)	-1.0 (0.1)	(-1.2, -0.7)	-0.1 (0.2)	(-0.4, 0.3)	0.752
		Placebo	111	100 (90.1)	-0.9 (0.1)	(-1.2, -0.7)			
Yes	Week 12	CR845	72	59 (81.9)	-1.2 (0.2)	(-1.5, -0.9)	-0.3 (0.2)	(-0.7, 0.1)	0.140
		Placebo	78	66 (84.6)	-0.9 (0.2)	(-1.2, -0.6)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor presence of medical condition is also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DVC_ISCA: Change from baseline in 5-D distribution score - MMRM results by age
ITT

Change from baseline in 5-D distribution score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
A: Age									0.436
< 65 years	Week 4	CR845	135	117 (86.7)	-0.3 (0.1)	(-0.5, -0.1)	-0.3 (0.1)	(-0.5, -0.1)	0.012 *
		Placebo	137	117 (85.4)	-0.0 (0.1)	(-0.2, 0.2)			
>= 65 years	Week 4	CR845	54	50 (92.6)	-0.2 (0.2)	(-0.5, 0.1)	-0.1 (0.2)	(-0.5, 0.3)	0.577
		Placebo	52	48 (92.3)	-0.1 (0.2)	(-0.4, 0.2)			
< 65 years	Week 8	CR845	135	109 (80.7)	-0.5 (0.1)	(-0.7, -0.3)	-0.3 (0.1)	(-0.6, -0.0)	0.022 *
		Placebo	137	121 (88.3)	-0.2 (0.1)	(-0.4, 0.1)			
>= 65 years	Week 8	CR845	54	48 (88.9)	-0.4 (0.2)	(-0.7, -0.1)	-0.3 (0.2)	(-0.6, 0.1)	0.167
		Placebo	52	49 (94.2)	-0.2 (0.1)	(-0.4, 0.1)			
< 65 years	Week 10	CR845	135	109 (80.7)	-0.5 (0.1)	(-0.7, -0.3)	-0.2 (0.1)	(-0.5, 0.1)	0.119
		Placebo	137	118 (86.1)	-0.3 (0.1)	(-0.5, -0.1)			
>= 65 years	Week 10	CR845	54	46 (85.2)	-0.4 (0.2)	(-0.7, -0.1)	-0.1 (0.2)	(-0.6, 0.3)	0.510
		Placebo	52	49 (94.2)	-0.3 (0.2)	(-0.6, 0.1)			
< 65 years	Week 12	CR845	135	112 (83.0)	-0.6 (0.1)	(-0.8, -0.4)	-0.4 (0.1)	(-0.7, -0.1)	0.004 *
		Placebo	137	118 (86.1)	-0.2 (0.1)	(-0.4, 0.0)			
>= 65 years	Week 12	CR845	54	47 (87.0)	-0.4 (0.2)	(-0.7, -0.0)	-0.2 (0.2)	(-0.6, 0.2)	0.402
		Placebo	52	48 (92.3)	-0.2 (0.2)	(-0.5, 0.1)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DVC_ISCB: Change from baseline in 5-D distribution score - MMRM results by sex
ITT

Change from baseline in 5-D distribution score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
B: Sex									0.449
Male	Week 4	CR845	112	97 (86.6)	-0.3 (0.1)	(-0.5, -0.0)	-0.3 (0.1)	(-0.5, -0.0)	0.049 *
		Placebo	119	100 (84.0)	0.0 (0.1)	(-0.2, 0.2)			
Female	Week 4	CR845	77	70 (90.9)	-0.4 (0.1)	(-0.7, -0.2)	-0.2 (0.2)	(-0.6, 0.1)	0.159
		Placebo	70	65 (92.9)	-0.2 (0.1)	(-0.4, 0.1)			
Male	Week 8	CR845	112	90 (80.4)	-0.5 (0.1)	(-0.8, -0.3)	-0.4 (0.1)	(-0.7, -0.1)	0.003 *
		Placebo	119	106 (89.1)	-0.1 (0.1)	(-0.3, 0.2)			
Female	Week 8	CR845	77	67 (87.0)	-0.5 (0.1)	(-0.8, -0.2)	-0.1 (0.2)	(-0.5, 0.2)	0.516
		Placebo	70	64 (91.4)	-0.4 (0.1)	(-0.6, -0.1)			
Male	Week 10	CR845	112	90 (80.4)	-0.5 (0.1)	(-0.8, -0.2)	-0.3 (0.2)	(-0.6, 0.0)	0.068
		Placebo	119	106 (89.1)	-0.2 (0.1)	(-0.5, 0.0)			
Female	Week 10	CR845	77	65 (84.4)	-0.6 (0.1)	(-0.8, -0.3)	-0.1 (0.2)	(-0.4, 0.3)	0.664
		Placebo	70	61 (87.1)	-0.5 (0.1)	(-0.8, -0.2)			
Male	Week 12	CR845	112	90 (80.4)	-0.5 (0.1)	(-0.8, -0.3)	-0.4 (0.1)	(-0.7, -0.1)	0.006 *
		Placebo	119	105 (88.2)	-0.1 (0.1)	(-0.4, 0.1)			
Female	Week 12	CR845	77	69 (89.6)	-0.6 (0.1)	(-0.9, -0.3)	-0.2 (0.2)	(-0.6, 0.1)	0.247
		Placebo	70	61 (87.1)	-0.4 (0.1)	(-0.7, -0.1)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DVC_ISCC: Change from baseline in 5-D distribution score - MMRM results by race
ITT

Change from baseline in 5-D distribution score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
C: Race									0.110
Black/African American	Week 4	CR845	82	69 (84.1)	-0.3 (0.1)	(-0.6, -0.0)	-0.4 (0.2)	(-0.8, -0.1)	0.007 *
		Placebo	76	66 (86.8)	0.1 (0.1)	(-0.1, 0.4)			
White	Week 4	CR845	91	83 (91.2)	-0.3 (0.1)	(-0.5, -0.0)	0.0 (0.1)	(-0.3, 0.3)	0.865
		Placebo	93	81 (87.1)	-0.3 (0.1)	(-0.5, -0.0)			
Other	Week 4	CR845	15	14 (93.3)	-0.7 (0.3)	(-1.3, -0.0)	-1.0 (0.3)	(-1.6, -0.4)	0.003 *
		Placebo	18	16 (88.9)	0.3 (0.3)	(-0.3, 0.9)			
Black/African American	Week 8	CR845	82	66 (80.5)	-0.5 (0.1)	(-0.7, -0.2)	-0.3 (0.2)	(-0.7, 0.0)	0.085
		Placebo	76	68 (89.5)	-0.2 (0.1)	(-0.4, 0.1)			
White	Week 8	CR845	91	76 (83.5)	-0.5 (0.1)	(-0.8, -0.3)	-0.3 (0.2)	(-0.6, 0.0)	0.086
		Placebo	93	83 (89.2)	-0.2 (0.1)	(-0.5, 0.0)			
Other	Week 8	CR845	15	14 (93.3)	-0.3 (0.4)	(-1.0, 0.4)	-0.4 (0.4)	(-1.2, 0.3)	0.266
		Placebo	18	17 (94.4)	0.1 (0.3)	(-0.5, 0.8)			
Black/African American	Week 10	CR845	82	64 (78.0)	-0.6 (0.1)	(-0.9, -0.3)	-0.3 (0.2)	(-0.7, 0.1)	0.093
		Placebo	76	66 (86.8)	-0.3 (0.2)	(-0.5, 0.0)			
White	Week 10	CR845	91	77 (84.6)	-0.4 (0.1)	(-0.7, -0.2)	-0.1 (0.2)	(-0.4, 0.3)	0.712
		Placebo	93	82 (88.2)	-0.4 (0.1)	(-0.6, -0.1)			
Other	Week 10	CR845	15	13 (86.7)	-0.5 (0.3)	(-1.2, 0.2)	-0.5 (0.3)	(-1.2, 0.2)	0.157
		Placebo	18	17 (94.4)	-0.0 (0.3)	(-0.6, 0.6)			
Black/African American	Week 12	CR845	82	66 (80.5)	-0.6 (0.1)	(-0.9, -0.4)	-0.6 (0.2)	(-0.9, -0.2)	0.003 *
		Placebo	76	66 (86.8)	-0.1 (0.1)	(-0.4, 0.2)			
White	Week 12	CR845	91	79 (86.8)	-0.5 (0.1)	(-0.8, -0.3)	-0.2 (0.2)	(-0.5, 0.1)	0.204
		Placebo	93	80 (86.0)	-0.3 (0.1)	(-0.6, -0.1)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DVC_ISCC: Change from baseline in 5-D distribution score - MMRM results by race
ITT

Change from baseline in 5-D distribution score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Other	Week 12	CR845	15	13 (86.7)	-0.3 (0.4)	(-1.1, 0.5)	-0.3 (0.4)	(-1.1, 0.6)	0.531
		Placebo	18	18 (100.0)	-0.1 (0.3)	(-0.7, 0.6)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DVC_ISCD: Change from baseline in 5-D distribution score - MMRM results by baseline WI-NRS
ITT

Change from baseline in 5-D distribution score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
D: Baseline worst itching NRS score (WI-NRS)									0.379
>= 4 to < 7	Week 4	CR845	83	73 (88.0)	-0.3 (0.1)	(-0.6, -0.1)	-0.4 (0.1)	(-0.7, -0.1)	0.007 *
		Placebo	80	70 (87.5)	0.1 (0.1)	(-0.2, 0.3)			
>= 7	Week 4	CR845	106	94 (88.7)	-0.3 (0.1)	(-0.6, -0.1)	-0.2 (0.1)	(-0.5, 0.1)	0.278
		Placebo	109	95 (87.2)	-0.2 (0.1)	(-0.4, 0.1)			
>= 4 to < 7	Week 8	CR845	83	69 (83.1)	-0.4 (0.1)	(-0.7, -0.1)	-0.3 (0.2)	(-0.7, -0.0)	0.031 *
		Placebo	80	72 (90.0)	-0.1 (0.1)	(-0.3, 0.2)			
>= 7	Week 8	CR845	106	88 (83.0)	-0.6 (0.1)	(-0.8, -0.3)	-0.3 (0.2)	(-0.6, 0.0)	0.076
		Placebo	109	98 (89.9)	-0.3 (0.1)	(-0.5, -0.0)			
>= 4 to < 7	Week 10	CR845	83	69 (83.1)	-0.5 (0.1)	(-0.8, -0.2)	-0.4 (0.2)	(-0.8, -0.1)	0.008 *
		Placebo	80	71 (88.8)	-0.1 (0.1)	(-0.4, 0.2)			
>= 7	Week 10	CR845	106	86 (81.1)	-0.5 (0.1)	(-0.8, -0.3)	-0.0 (0.2)	(-0.3, 0.3)	0.871
		Placebo	109	96 (88.1)	-0.5 (0.1)	(-0.7, -0.2)			
>= 4 to < 7	Week 12	CR845	83	68 (81.9)	-0.4 (0.1)	(-0.7, -0.2)	-0.3 (0.2)	(-0.6, -0.0)	0.042 *
		Placebo	80	72 (90.0)	-0.1 (0.1)	(-0.4, 0.1)			
>= 7	Week 12	CR845	106	91 (85.8)	-0.7 (0.1)	(-0.9, -0.4)	-0.4 (0.2)	(-0.7, -0.0)	0.033 *
		Placebo	109	94 (86.2)	-0.3 (0.1)	(-0.6, -0.1)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DVC_ISCE: Change from baseline in 5-D distribution score - MMRM results by specific medical condition
ITT

Change from baseline in 5-D distribution score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
E: Presence of specific medical conditions									0.279
No	Week 4	CR845	164	143 (87.2)	-0.4 (0.1)	(-0.6, -0.3)	-0.3 (0.1)	(-0.5, -0.1)	0.007 *
		Placebo	161	139 (86.3)	-0.1 (0.1)	(-0.3, 0.1)			
Yes	Week 4	CR845	25	24 (96.0)	-0.2 (0.2)	(-0.5, 0.2)	0.0 (0.3)	(-0.5, 0.5)	0.998
		Placebo	28	26 (92.9)	-0.2 (0.2)	(-0.5, 0.2)			
No	Week 8	CR845	164	134 (81.7)	-0.6 (0.1)	(-0.8, -0.4)	-0.4 (0.1)	(-0.7, -0.2)	<0.001 *
		Placebo	161	143 (88.8)	-0.2 (0.1)	(-0.4, -0.0)			
Yes	Week 8	CR845	25	23 (92.0)	-0.1 (0.2)	(-0.6, 0.3)	0.3 (0.3)	(-0.3, 0.9)	0.301
		Placebo	28	27 (96.4)	-0.4 (0.2)	(-0.8, -0.0)			
No	Week 10	CR845	164	133 (81.1)	-0.6 (0.1)	(-0.8, -0.4)	-0.2 (0.1)	(-0.5, 0.0)	0.057
		Placebo	161	142 (88.2)	-0.4 (0.1)	(-0.5, -0.2)			
Yes	Week 10	CR845	25	22 (88.0)	-0.4 (0.2)	(-0.8, 0.1)	0.0 (0.3)	(-0.6, 0.6)	0.978
		Placebo	28	25 (89.3)	-0.4 (0.2)	(-0.8, 0.0)			
No	Week 12	CR845	164	135 (82.3)	-0.6 (0.1)	(-0.8, -0.4)	-0.3 (0.1)	(-0.6, -0.1)	0.014 *
		Placebo	161	139 (86.3)	-0.3 (0.1)	(-0.5, -0.1)			
Yes	Week 12	CR845	25	24 (96.0)	-0.7 (0.2)	(-1.1, -0.3)	-0.5 (0.3)	(-1.0, 0.1)	0.075
		Placebo	28	27 (96.4)	-0.3 (0.2)	(-0.6, 0.1)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor previous use of anti-itch medication is also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DVC_ISCF: Change from baseline in 5-D distribution score - MMRM results by use of concomitant itch medication
ITT

Change from baseline in 5-D distribution score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
F: Use of concomitant itch medication									0.732
No	Week 4	CR845	117	106 (90.6)	-0.3 (0.1)	(-0.5, -0.0)	-0.3 (0.1)	(-0.6, -0.0)	0.023 *
		Placebo	111	94 (84.7)	0.0 (0.1)	(-0.2, 0.3)			
Yes	Week 4	CR845	72	61 (84.7)	-0.4 (0.1)	(-0.6, -0.1)	-0.2 (0.2)	(-0.5, 0.1)	0.278
		Placebo	78	71 (91.0)	-0.2 (0.1)	(-0.4, 0.1)			
No	Week 8	CR845	117	100 (85.5)	-0.5 (0.1)	(-0.7, -0.2)	-0.4 (0.1)	(-0.6, -0.1)	0.014 *
		Placebo	111	100 (90.1)	-0.1 (0.1)	(-0.4, 0.1)			
Yes	Week 8	CR845	72	57 (79.2)	-0.5 (0.1)	(-0.8, -0.2)	-0.2 (0.2)	(-0.6, 0.1)	0.244
		Placebo	78	70 (89.7)	-0.2 (0.1)	(-0.5, 0.0)			
No	Week 10	CR845	117	98 (83.8)	-0.5 (0.1)	(-0.7, -0.2)	-0.2 (0.1)	(-0.5, 0.1)	0.244
		Placebo	111	98 (88.3)	-0.3 (0.1)	(-0.6, -0.1)			
Yes	Week 10	CR845	72	57 (79.2)	-0.5 (0.1)	(-0.8, -0.2)	-0.2 (0.2)	(-0.6, 0.1)	0.217
		Placebo	78	69 (88.5)	-0.3 (0.1)	(-0.6, -0.0)			
No	Week 12	CR845	117	100 (85.5)	-0.5 (0.1)	(-0.8, -0.3)	-0.3 (0.2)	(-0.6, -0.0)	0.025 *
		Placebo	111	100 (90.1)	-0.2 (0.1)	(-0.4, 0.1)			
Yes	Week 12	CR845	72	59 (81.9)	-0.6 (0.1)	(-0.9, -0.4)	-0.3 (0.2)	(-0.7, 0.0)	0.063
		Placebo	78	66 (84.6)	-0.3 (0.1)	(-0.6, -0.0)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor presence of medical condition is also included in the model.
Source Data: afived, created on: 17FEB2022

Table AT2DTCD5_ISPA: Decrease of 5-D total score of at least 5 points by age
ITT

Decrease of 5-D total score of at least 5 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	A: Age										0.260
	< 65 years	135	111 (82.2)	56 (41.5) [33.1, 50.3]	137	118 (86.1)	48 (35.0) [27.1, 43.6]	1.184 [0.874, 1.604]	1.314 [0.805, 2.146]	6.4 [-5.8, 18.7]	0.275
	>= 65 years	54	47 (87.0)	25 (46.3) [32.6, 60.4]	52	48 (92.3)	27 (51.9) [37.6, 66.0]	0.892 [0.605, 1.315]	0.798 [0.372, 1.712]	-5.6 [-26.5, 15.3]	0.564

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table AT2DTCD5_ISPB: Decrease of 5-D total score of at least 5 points by sex
ITT

Decrease of 5-D total score of at least 5 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	B: Sex										0.773
	Male	112	90 (80.4)	43 (38.4) [29.4, 48.1]	119	105 (88.2)	44 (37.0) [28.3, 46.3]	1.038 [0.745, 1.447]	1.062 [0.624, 1.809]	1.4 [-12.0, 14.8]	0.824
	Female	77	68 (88.3)	38 (49.4) [37.8, 61.0]	70	61 (87.1)	31 (44.3) [32.4, 56.7]	1.114 [0.788, 1.576]	1.226 [0.640, 2.347]	5.1 [-12.4, 22.6]	0.540

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table AT2DTCD5_ISPC: Decrease of 5-D total score of at least 5 points by race
ITT

Decrease of 5-D total score of at least 5 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	C: Race										0.223
	Black/African American	82	65 (79.3)	35 (42.7) [31.8, 54.1]	76	66 (86.8)	24 (31.6) [21.4, 43.3]	1.352 [0.892, 2.047]	1.613 [0.840, 3.098]	11.1 [-5.1, 27.3]	0.151
	White	91	79 (86.8)	40 (44.0) [33.6, 54.8]	93	80 (86.0)	39 (41.9) [31.8, 52.6]	1.048 [0.751, 1.463]	1.086 [0.606, 1.947]	2.0 [-13.4, 17.4]	0.782
	Other	15	13 (86.7)	6 (40.0) [16.3, 67.7]	18	18 (100.0)	11 (61.1) [35.7, 82.7]	0.655 [0.318, 1.346]	0.424 [0.104, 1.724]	-21.1 [-60.7, 18.5]	0.234

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table AT2DTCD5_ISPD: Decrease of 5-D total score of at least 5 points by baseline WI-NRS
ITT

Decrease of 5-D total score of at least 5 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.527
	>= 4 to < 7	83	68 (81.9)	24 (28.9) [19.5, 39.9]	80	72 (90.0)	24 (30.0) [20.3, 41.3]	0.964 [0.599, 1.550]	0.949 [0.484, 1.862]	-1.1 [-16.3, 14.1]	0.880
	>= 7	106	90 (84.9)	57 (53.8) [43.8, 63.5]	109	94 (86.2)	51 (46.8) [37.2, 56.6]	1.149 [0.880, 1.501]	1.323 [0.774, 2.261]	7.0 [-7.3, 21.3]	0.307

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table AT2DTCD5_ISPE: Decrease of 5-D total score of at least 5 points by specific medical condition
ITT

Decrease of 5-D total score of at least 5 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	E: Presence of specific medical conditions										0.064	
	No	164	134 (81.7)	65 (39.6) [32.1, 47.6]	161	139 (86.3)	65 (40.4) [32.7, 48.4]	0.982 [0.752, 1.281]	0.970 [0.622, 1.511]	-0.7 [-12.0, 10.5]	0.892	
	Yes	25	24 (96.0)	16 (64.0) [42.5, 82.0]	28	27 (96.4)	10 (35.7) [18.6, 55.9]	1.792 [1.006, 3.192]	3.200 [1.039, 9.852]	28.3 [-1.4, 57.9]	0.042	*

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table AT2DTCD5_ISPF: Decrease of 5-D total score of at least 5 points by use of concomitant itch medication
ITT

Decrease of 5-D total score of at least 5 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	F: Use of concomitant itch medication										0.383
	No	117	100 (85.5)	48 (41.0) [32.0, 50.5]	111	100 (90.1)	46 (41.4) [32.2, 51.2]	0.990 [0.726, 1.350]	0.983 [0.580, 1.666]	-0.4 [-14.1, 13.2]	0.949
	Yes	72	58 (80.6)	33 (45.8) [34.0, 58.0]	78	66 (84.6)	29 (37.2) [26.5, 48.9]	1.233 [0.841, 1.807]	1.430 [0.745, 2.746]	8.7 [-8.4, 25.7]	0.284

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table AT2DDCD1_ISPA: Decrease of 5-D degree score of at least 1 point by age
ITT

Decrease of 5-D degree score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	A: Age										0.521
	< 65 years	135	112 (83.0)	76 (56.3) [47.5, 64.8]	137	118 (86.1)	66 (48.2) [39.6, 56.9]	1.169 [0.930, 1.469]	1.386 [0.860, 2.234]	8.1 [-4.4, 20.7]	0.181
	>= 65 years	54	47 (87.0)	32 (59.3) [45.0, 72.4]	52	48 (92.3)	30 (57.7) [43.2, 71.3]	1.027 [0.745, 1.416]	1.067 [0.492, 2.310]	1.6 [-19.1, 22.2]	0.871

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table AT2DDCD1_ISPB: Decrease of 5-D degree score of at least 1 point by sex
ITT

Decrease of 5-D degree score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	B: Sex										0.258
	Male	112	90 (80.4)	60 (53.6) [43.9, 63.0]	119	105 (88.2)	62 (52.1) [42.8, 61.3]	1.028 [0.806, 1.312]	1.061 [0.633, 1.779]	1.5 [-12.3, 15.2]	0.823
	Female	77	69 (89.6)	48 (62.3) [50.6, 73.1]	70	61 (87.1)	34 (48.6) [36.4, 60.8]	1.283 [0.954, 1.727]	1.753 [0.908, 3.382]	13.8 [-3.5, 31.1]	0.094

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table AT2DDCD1_ISPC: Decrease of 5-D degree score of at least 1 point by race
ITT

Decrease of 5-D degree score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	C: Race										0.406
	Black/African American	82	66 (80.5)	46 (56.1) [44.7, 67.0]	76	66 (86.8)	34 (44.7) [33.3, 56.6]	1.254 [0.915, 1.718]	1.578 [0.842, 2.958]	11.4 [-5.4, 28.1]	0.155
	White	91	79 (86.8)	53 (58.2) [47.4, 68.5]	93	80 (86.0)	48 (51.6) [41.0, 62.1]	1.128 [0.868, 1.467]	1.308 [0.730, 2.341]	6.6 [-8.8, 22.1]	0.368
	Other	15	13 (86.7)	8 (53.3) [26.6, 78.7]	18	18 (100.0)	12 (66.7) [41.0, 86.7]	0.800 [0.450, 1.422]	0.571 [0.139, 2.342]	-13.3 [-52.8, 26.1]	0.442

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table AT2DDCD1_ISPD: Decrease of 5-D degree score of at least 1 point by baseline WI-NRS
ITT

Decrease of 5-D degree score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.697
	>= 4 to < 7	83	68 (81.9)	39 (47.0) [35.9, 58.3]	80	72 (90.0)	35 (43.8) [32.7, 55.3]	1.074 [0.766, 1.505]	1.140 [0.615, 2.113]	3.2 [-13.3, 19.7]	0.679
	>= 7	106	91 (85.8)	69 (65.1) [55.2, 74.1]	109	94 (86.2)	61 (56.0) [46.1, 65.5]	1.163 [0.936, 1.445]	1.467 [0.847, 2.543]	9.1 [-4.8, 23.1]	0.172

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table AT2DDCD1_ISPE: Decrease of 5-D degree score of at least 1 point by specific medical condition
ITT

Decrease of 5-D degree score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	E: Presence of specific medical conditions										0.242
	No	164	135 (82.3)	89 (54.3) [46.3, 62.1]	161	139 (86.3)	81 (50.3) [42.3, 58.3]	1.079 [0.876, 1.328]	1.172 [0.758, 1.812]	4.0 [-7.5, 15.4]	0.476
	Yes	25	24 (96.0)	19 (76.0) [54.9, 90.6]	28	27 (96.4)	15 (53.6) [33.9, 72.5]	1.419 [0.942, 2.136]	2.744 [0.843, 8.938]	22.4 [-6.3, 51.1]	0.092

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table AT2DDCD1_ISPF: Decrease of 5-D degree score of at least 1 point by use of concomitant itch medication
ITT

Decrease of 5-D degree score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	F: Use of concomitant itch medication										0.171
	No	117	100 (85.5)	64 (54.7) [45.2, 63.9]	111	100 (90.1)	60 (54.1) [44.3, 63.6]	1.012 [0.798, 1.284]	1.026 [0.609, 1.729]	0.6 [-13.2, 14.5]	0.922
	Yes	72	59 (81.9)	44 (61.1) [48.9, 72.4]	78	66 (84.6)	36 (46.2) [34.8, 57.8]	1.324 [0.979, 1.792]	1.833 [0.957, 3.512]	15.0 [-2.2, 32.1]	0.067

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table AT2DLCD1_ISPA: Decrease of 5-D duration score of at least 1 point by age
ITT

Decrease of 5-D duration score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	A: Age										0.156
	< 65 years	135	111 (82.2)	61 (45.2) [36.6, 54.0]	137	118 (86.1)	71 (51.8) [43.1, 60.4]	0.872 [0.682, 1.115]	0.766 [0.476, 1.234]	-6.6 [-19.2, 5.9]	0.274
	>= 65 years	54	47 (87.0)	35 (64.8) [50.6, 77.3]	52	48 (92.3)	29 (55.8) [41.3, 69.5]	1.162 [0.851, 1.587]	1.461 [0.668, 3.193]	9.0 [-11.4, 29.5]	0.343

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table AT2DLCD1_ISPB: Decrease of 5-D duration score of at least 1 point by sex
ITT

Decrease of 5-D duration score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	B: Sex										0.402
	Male	112	90 (80.4)	51 (45.5) [36.1, 55.2]	119	105 (88.2)	61 (51.3) [41.9, 60.5]	0.888 [0.680, 1.161]	0.795 [0.474, 1.333]	-5.7 [-19.5, 8.0]	0.385
	Female	77	68 (88.3)	45 (58.4) [46.6, 69.6]	70	61 (87.1)	39 (55.7) [43.3, 67.6]	1.049 [0.792, 1.390]	1.118 [0.581, 2.150]	2.7 [-14.7, 20.1]	0.739

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table AT2DLCD1_ISPC: Decrease of 5-D duration score of at least 1 point by race
ITT

Decrease of 5-D duration score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	C: Race										0.163
	Black/African American	82	65 (79.3)	41 (50.0) [38.7, 61.3]	76	66 (86.8)	40 (52.6) [40.8, 64.2]	0.950 [0.701, 1.287]	0.900 [0.482, 1.681]	-2.6 [-19.5, 14.2]	0.742
	White	91	79 (86.8)	50 (54.9) [44.2, 65.4]	93	80 (86.0)	46 (49.5) [38.9, 60.0]	1.111 [0.842, 1.466]	1.246 [0.698, 2.224]	5.5 [-10.0, 21.0]	0.458
	Other	15	13 (86.7)	5 (33.3) [11.8, 61.6]	18	18 (100.0)	12 (66.7) [41.0, 86.7]	0.500 [0.228, 1.098]	0.250 [0.058, 1.070]	-33.3 [-71.7, 5.1]	0.060

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table AT2DLCD1_ISPD: Decrease of 5-D duration score of at least 1 point by baseline WI-NRS
ITT

Decrease of 5-D duration score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.062
	>= 4 to < 7	83	68 (81.9)	29 (34.9) [24.8, 46.2]	80	72 (90.0)	38 (47.5) [36.2, 59.0]	0.736 [0.506, 1.068]	0.594 [0.316, 1.114]	-12.6 [-28.8, 3.7]	0.104
	>= 7	106	90 (84.9)	67 (63.2) [53.3, 72.4]	109	94 (86.2)	62 (56.9) [47.0, 66.3]	1.111 [0.893, 1.383]	1.302 [0.753, 2.251]	6.3 [-7.7, 20.3]	0.345

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table AT2DLCD1_ISPE: Decrease of 5-D duration score of at least 1 point by specific medical condition
ITT

Decrease of 5-D duration score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	E: Presence of specific medical conditions										0.933
	No	164	134 (81.7)	82 (50.0) [42.1, 57.9]	161	139 (86.3)	84 (52.2) [44.2, 60.1]	0.958 [0.775, 1.186]	0.917 [0.593, 1.416]	-2.2 [-13.7, 9.3]	0.696
	Yes	25	24 (96.0)	14 (56.0) [34.9, 75.6]	28	27 (96.4)	16 (57.1) [37.2, 75.5]	0.980 [0.611, 1.573]	0.955 [0.322, 2.834]	-1.1 [-31.7, 29.4]	0.934

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table AT2DLCD1_ISPF: Decrease of 5-D duration score of at least 1 point by use of concomitant itch medication
ITT

Decrease of 5-D duration score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	F: Use of concomitant itch medication										0.378
	No	117	100 (85.5)	60 (51.3) [41.9, 60.6]	111	100 (90.1)	55 (49.5) [39.9, 59.2]	1.035 [0.800, 1.339]	1.072 [0.638, 1.802]	1.7 [-12.1, 15.6]	0.794
	Yes	72	58 (80.6)	36 (50.0) [38.0, 62.0]	78	66 (84.6)	45 (57.7) [46.0, 68.8]	0.867 [0.643, 1.169]	0.733 [0.385, 1.397]	-7.7 [-25.0, 9.6]	0.347

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table AT2DNCD1_ISPA: Decrease of 5-D disability score of at least 1 point by age
ITT

Decrease of 5-D disability score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	A: Age										0.088
	< 65 years	135	112 (83.0)	75 (55.6) [46.8, 64.1]	137	118 (86.1)	68 (49.6) [41.0, 58.3]	1.119 [0.893, 1.404]	1.268 [0.787, 2.043]	5.9 [-6.7, 18.5]	0.329
	>= 65 years	54	47 (87.0)	28 (51.9) [37.8, 65.7]	52	48 (92.3)	34 (65.4) [50.9, 78.0]	0.793 [0.573, 1.097]	0.570 [0.261, 1.246]	-13.5 [-34.0, 6.9]	0.159

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table AT2DNCD1_ISPB: Decrease of 5-D disability score of at least 1 point by sex
ITT

Decrease of 5-D disability score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	B: Sex										0.430
	Male	112	90 (80.4)	57 (50.9) [41.3, 60.5]	119	105 (88.2)	64 (53.8) [44.4, 63.0]	0.946 [0.739, 1.211]	0.891 [0.531, 1.493]	-2.9 [-16.6, 10.9]	0.661
	Female	77	69 (89.6)	46 (59.7) [47.9, 70.8]	70	61 (87.1)	38 (54.3) [41.9, 66.3]	1.100 [0.830, 1.460]	1.250 [0.649, 2.405]	5.5 [-11.9, 22.8]	0.506

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table AT2DNCD1_ISPC: Decrease of 5-D disability score of at least 1 point by race
ITT

Decrease of 5-D disability score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	C: Race										0.469
	Black/African American	82	66 (80.5)	44 (53.7) [42.3, 64.7]	76	66 (86.8)	40 (52.6) [40.8, 64.2]	1.020 [0.760, 1.367]	1.042 [0.558, 1.948]	1.0 [-15.8, 17.9]	0.897
	White	91	79 (86.8)	51 (56.0) [45.2, 66.4]	93	80 (86.0)	48 (51.6) [41.0, 62.1]	1.086 [0.831, 1.420]	1.195 [0.669, 2.136]	4.4 [-11.0, 19.9]	0.548
	Other	15	13 (86.7)	8 (53.3) [26.6, 78.7]	18	18 (100.0)	13 (72.2) [46.5, 90.3]	0.738 [0.425, 1.284]	0.440 [0.103, 1.868]	-18.9 [-57.6, 19.9]	0.269

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table AT2DNCD1_ISPD: Decrease of 5-D disability score of at least 1 point by baseline WI-NRS
ITT

Decrease of 5-D disability score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.526
	>= 4 to < 7	83	68 (81.9)	43 (51.8) [40.6, 62.9]	80	72 (90.0)	44 (55.0) [43.5, 66.2]	0.942 [0.707, 1.255]	0.880 [0.475, 1.628]	-3.2 [-19.7, 13.3]	0.684
	>= 7	106	91 (85.8)	60 (56.6) [46.6, 66.2]	109	94 (86.2)	58 (53.2) [43.4, 62.8]	1.064 [0.835, 1.356]	1.147 [0.670, 1.964]	3.4 [-10.8, 17.6]	0.618

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table AT2DNCD1_ISPE: Decrease of 5-D disability score of at least 1 point by specific medical condition
ITT

Decrease of 5-D disability score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	E: Presence of specific medical conditions										0.602
	No	164	135 (82.3)	86 (52.4) [44.5, 60.3]	161	139 (86.3)	85 (52.8) [44.8, 60.7]	0.993 [0.808, 1.221]	0.986 [0.638, 1.524]	-0.4 [-11.8, 11.1]	0.949
	Yes	25	24 (96.0)	17 (68.0) [46.5, 85.1]	28	27 (96.4)	17 (60.7) [40.6, 78.5]	1.120 [0.750, 1.673]	1.375 [0.443, 4.265]	7.3 [-22.2, 36.8]	0.584

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table AT2DNCD1_ISPF: Decrease of 5-D disability score of at least 1 point by use of concomitant itch medication
ITT

Decrease of 5-D disability score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	F: Use of concomitant itch medication										0.302
	No	117	100 (85.5)	60 (51.3) [41.9, 60.6]	111	100 (90.1)	61 (55.0) [45.2, 64.4]	0.933 [0.731, 1.191]	0.863 [0.513, 1.452]	-3.7 [-17.5, 10.2]	0.579
	Yes	72	59 (81.9)	43 (59.7) [47.5, 71.1]	78	66 (84.6)	41 (52.6) [40.9, 64.0]	1.136 [0.856, 1.509]	1.338 [0.700, 2.557]	7.2 [-10.0, 24.3]	0.379

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table AT2DVCD1_ISPA: Decrease of 5-D distribution score of at least 1 point by age
ITT

Decrease of 5-D distribution score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	A: Age										0.725
	< 65 years	135	112 (83.0)	54 (40.0) [31.7, 48.8]	137	118 (86.1)	46 (33.6) [25.7, 42.1]	1.191 [0.871, 1.630]	1.319 [0.805, 2.162]	6.4 [-5.8, 18.6]	0.273
	>= 65 years	54	47 (87.0)	20 (37.0) [24.3, 51.3]	52	48 (92.3)	18 (34.6) [22.0, 49.1]	1.070 [0.642, 1.782]	1.111 [0.502, 2.460]	2.4 [-17.7, 22.6]	0.796

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table AT2DVCD1_ISPB: Decrease of 5-D distribution score of at least 1 point by sex
ITT

Decrease of 5-D distribution score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	B: Sex										0.860
	Male	112	90 (80.4)	42 (37.5) [28.5, 47.1]	119	105 (88.2)	38 (31.9) [23.7, 41.1]	1.174 [0.823, 1.675]	1.279 [0.743, 2.201]	5.6 [-7.6, 18.7]	0.375
	Female	77	69 (89.6)	32 (41.6) [30.4, 53.4]	70	61 (87.1)	26 (37.1) [25.9, 49.5]	1.119 [0.747, 1.675]	1.203 [0.620, 2.337]	4.4 [-12.7, 21.6]	0.586

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table AT2DVCD1_ISPC: Decrease of 5-D distribution score of at least 1 point by race
ITT

Decrease of 5-D distribution score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	C: Race										0.348
	Black/African American	82	66 (80.5)	33 (40.2) [29.6, 51.7]	76	66 (86.8)	21 (27.6) [18.0, 39.1]	1.456 [0.929, 2.283]	1.764 [0.903, 3.444]	12.6 [-3.3, 28.5]	0.096
	White	91	79 (86.8)	34 (37.4) [27.4, 48.1]	93	80 (86.0)	33 (35.5) [25.8, 46.1]	1.053 [0.719, 1.543]	1.085 [0.595, 1.977]	1.9 [-13.1, 16.9]	0.792
	Other	15	13 (86.7)	6 (40.0) [16.3, 67.7]	18	18 (100.0)	9 (50.0) [26.0, 74.0]	0.800 [0.369, 1.733]	0.667 [0.167, 2.666]	-10.0 [-50.0, 30.0]	0.572

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table AT2DVCD1_ISPD: Decrease of 5-D distribution score of at least 1 point by baseline WI-NRS
ITT

Decrease of 5-D distribution score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.680
	>= 4 to < 7	83	68 (81.9)	28 (33.7) [23.7, 44.9]	80	72 (90.0)	25 (31.3) [21.3, 42.6]	1.080 [0.693, 1.682]	1.120 [0.581, 2.159]	2.5 [-13.1, 18.1]	0.736
	>= 7	106	91 (85.8)	46 (43.4) [33.8, 53.4]	109	94 (86.2)	39 (35.8) [26.8, 45.5]	1.213 [0.870, 1.691]	1.376 [0.795, 2.382]	7.6 [-6.4, 21.6]	0.255

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table AT2DVCD1_ISPE: Decrease of 5-D distribution score of at least 1 point by specific medical condition
ITT

Decrease of 5-D distribution score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	E: Presence of specific medical conditions										0.424
	No	164	135 (82.3)	62 (37.8) [30.4, 45.7]	161	139 (86.3)	55 (34.2) [26.9, 42.0]	1.107 [0.827, 1.480]	1.171 [0.744, 1.844]	3.6 [-7.4, 14.7]	0.495
	Yes	25	24 (96.0)	12 (48.0) [27.8, 68.7]	28	27 (96.4)	9 (32.1) [15.9, 52.4]	1.493 [0.760, 2.934]	1.949 [0.639, 5.946]	15.9 [-14.1, 45.8]	0.243

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table AT2DVCD1_ISPF: Decrease of 5-D distribution score of at least 1 point by use of concomitant itch medication
ITT

Decrease of 5-D distribution score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	F: Use of concomitant itch medication										0.861
	No	117	100 (85.5)	46 (39.3) [30.4, 48.8]	111	100 (90.1)	37 (33.3) [24.7, 42.9]	1.179 [0.834, 1.668]	1.296 [0.754, 2.227]	6.0 [-7.4, 19.3]	0.349
	Yes	72	59 (81.9)	28 (38.9) [27.6, 51.1]	78	66 (84.6)	27 (34.6) [24.2, 46.2]	1.123 [0.738, 1.711]	1.202 [0.618, 2.337]	4.3 [-12.5, 21.0]	0.589

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table AT2DWCD1_ISPA: Decrease of 5-D direction score of at least 1 point by age
ITT

Decrease of 5-D direction score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	A: Age										0.039	i
	< 65 years	135	112 (83.0)	96 (71.1) [62.7, 78.6]	137	118 (86.1)	77 (56.2) [47.5, 64.7]	1.265 [1.054, 1.519]	1.918 [1.161, 3.170]	14.9 [2.9, 26.9]	0.011	*
	>= 65 years	54	47 (87.0)	36 (66.7) [52.5, 78.9]	52	48 (92.3)	38 (73.1) [59.0, 84.4]	0.912 [0.710, 1.172]	0.737 [0.320, 1.697]	-6.4 [-25.7, 12.9]	0.474	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table AT2DWCD1_ISPB: Decrease of 5-D direction score of at least 1 point by sex
ITT

Decrease of 5-D direction score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	B: Sex										0.751
	Male	112	90 (80.4)	75 (67.0) [57.4, 75.6]	119	105 (88.2)	71 (59.7) [50.3, 68.6]	1.122 [0.922, 1.367]	1.370 [0.800, 2.346]	7.3 [-6.0, 20.6]	0.251
	Female	77	69 (89.6)	57 (74.0) [62.8, 83.4]	70	61 (87.1)	44 (62.9) [50.5, 74.1]	1.178 [0.942, 1.473]	1.684 [0.834, 3.402]	11.2 [-5.2, 27.5]	0.146

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table AT2DWCD1_ISPC: Decrease of 5-D direction score of at least 1 point by race
ITT

Decrease of 5-D direction score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	C: Race										0.395
	Black/African American	82	66 (80.5)	56 (68.3) [57.1, 78.1]	76	66 (86.8)	45 (59.2) [47.3, 70.4]	1.153 [0.909, 1.463]	1.484 [0.773, 2.849]	9.1 [-7.1, 25.3]	0.236
	White	91	79 (86.8)	67 (73.6) [63.3, 82.3]	93	80 (86.0)	56 (60.2) [49.5, 70.2]	1.223 [0.995, 1.502]	1.844 [0.988, 3.444]	13.4 [-1.1, 27.9]	0.054
	Other	15	13 (86.7)	8 (53.3) [26.6, 78.7]	18	18 (100.0)	12 (66.7) [41.0, 86.7]	0.800 [0.450, 1.422]	0.571 [0.139, 2.342]	-13.3 [-52.8, 26.1]	0.442

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table AT2DWCD1_ISPD: Decrease of 5-D direction score of at least 1 point by baseline WI-NRS
ITT

Decrease of 5-D direction score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.812
	>= 4 to < 7	83	68 (81.9)	56 (67.5) [56.3, 77.4]	80	72 (90.0)	48 (60.0) [48.4, 70.8]	1.124 [0.891, 1.420]	1.383 [0.728, 2.625]	7.5 [-8.5, 23.4]	0.323
	>= 7	106	91 (85.8)	76 (71.7) [62.1, 80.0]	109	94 (86.2)	67 (61.5) [51.7, 70.6]	1.166 [0.964, 1.412]	1.588 [0.896, 2.814]	10.2 [-3.2, 23.7]	0.113

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table AT2DWCD1_ISPE: Decrease of 5-D direction score of at least 1 point by specific medical condition
ITT

Decrease of 5-D direction score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	E: Presence of specific medical conditions										0.020	i
	No	164	135 (82.3)	109 (66.5) [58.7, 73.6]	161	139 (86.3)	100 (62.1) [54.1, 69.6]	1.070 [0.910, 1.259]	1.209 [0.767, 1.904]	4.4 [-6.7, 15.4]	0.414	
	Yes	25	24 (96.0)	23 (92.0) [74.0, 99.0]	28	27 (96.4)	15 (53.6) [33.9, 72.5]	1.717 [1.194, 2.471]	9.967 [1.963, 50.595]	38.4 [13.3, 63.5]	0.002	*

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table AT2DWCD1_ISPF: Decrease of 5-D direction score of at least 1 point by use of concomitant itch medication
ITT

Decrease of 5-D direction score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	F: Use of concomitant itch medication										0.731
	No	117	100 (85.5)	85 (72.6) [63.6, 80.5]	111	100 (90.1)	69 (62.2) [52.5, 71.2]	1.169 [0.973, 1.403]	1.617 [0.925, 2.827]	10.5 [-2.5, 23.5]	0.092
	Yes	72	59 (81.9)	47 (65.3) [53.1, 76.1]	78	66 (84.6)	46 (59.0) [47.3, 70.0]	1.107 [0.862, 1.422]	1.308 [0.674, 2.537]	6.3 [-10.5, 23.1]	0.428

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table AT2PGI_ISPA: Relevant improvement in PGIC by age
ITT

		CR845			Placebo						
Relevant improvement in PGIC		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	A: Age										0.079
	< 65 years	135	124 (91.9)	78 (57.8) [49.0, 66.2]	137	129 (94.2)	43 (31.4) [23.7, 39.9]	1.841 [1.382, 2.452]	2.991 [1.820, 4.916]	26.4 [14.3, 38.5]	<0.001 *
	>= 65 years	54	50 (92.6)	30 (55.6) [41.4, 69.1]	52	48 (92.3)	24 (46.2) [32.2, 60.5]	1.204 [0.825, 1.757]	1.458 [0.679, 3.134]	9.4 [-11.4, 30.2]	0.335

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. PGIC = patient global impression of change.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: apgic, created on: 24FEB2022

Table AT2PGI_ISPB: Relevant improvement in PGIC by sex
ITT

		CR845			Placebo						
Relevant improvement in PGIC		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	B: Sex										0.920
	Male	112	101 (90.2)	61 (54.5) [44.8, 63.9]	119	112 (94.1)	40 (33.6) [25.2, 42.8]	1.620 [1.196, 2.196]	2.362 [1.388, 4.021]	20.9 [7.5, 34.3]	0.001 *
	Female	77	73 (94.8)	47 (61.0) [49.2, 72.0]	70	65 (92.9)	27 (38.6) [27.2, 51.0]	1.582 [1.120, 2.235]	2.495 [1.284, 4.849]	22.5 [5.3, 39.6]	0.007 *

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. PGIC = patient global impression of change.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: apgic, created on: 24FEB2022

Table AT2PGI_ISPC: Relevant improvement in PGIC by race
ITT

			CR845			Placebo						
Relevant improvement in PGIC		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	C: Race										0.080	
	Black/African American	82	75 (91.5)	46 (56.1) [44.7, 67.0]	76	70 (92.1)	31 (40.8) [29.6, 52.7]	1.375 [0.987, 1.916]	1.855 [0.986, 3.490]	15.3 [-1.4, 32.0]	0.055	
	White	91	84 (92.3)	55 (60.4) [49.6, 70.5]	93	87 (93.5)	27 (29.0) [20.1, 39.4]	2.082 [1.454, 2.980]	3.735 [2.021, 6.901]	31.4 [16.7, 46.1]	<0.001	*
	Other	15	14 (93.3)	7 (46.7) [21.3, 73.4]	18	18 (100.0)	9 (50.0) [26.0, 74.0]	0.933 [0.458, 1.901]	0.875 [0.222, 3.451]	-3.3 [-43.7, 37.0]	0.851	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. PGIC = patient global impression of change.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: apgic, created on: 24FEB2022

Table AT2PGI_ISPD: Relevant improvement in PGIC by baseline WI-NRS
ITT

		CR845			Placebo						
Relevant improvement in PGIC		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.165
	>= 4 to < 7	83	77 (92.8)	54 (65.1) [53.8, 75.2]	80	76 (95.0)	27 (33.8) [23.6, 45.2]	1.928 [1.365, 2.722]	3.655 [1.914, 6.979]	31.3 [15.5, 47.1]	<0.001 *
	>= 7	106	97 (91.5)	54 (50.9) [41.0, 60.8]	109	101 (92.7)	40 (36.7) [27.7, 46.5]	1.388 [1.019, 1.891]	1.791 [1.039, 3.089]	14.2 [0.2, 28.3]	0.036 *

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. PGIC = patient global impression of change.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: apgic, created on: 24FEB2022

Table AT2PGI_ISPE: Relevant improvement in PGIC by specific medical condition
ITT

Relevant improvement in PGIC		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	E: Presence of specific medical conditions										0.134	
	No	164	150 (91.5)	90 (54.9) [46.9, 62.6]	161	149 (92.5)	59 (36.6) [29.2, 44.6]	1.498 [1.171, 1.915]	2.103 [1.348, 3.279]	18.2 [7.0, 29.5]	<0.001	*
	Yes	25	24 (96.0)	18 (72.0) [50.6, 87.9]	28	28 (100.0)	8 (28.6) [13.2, 48.7]	2.520 [1.336, 4.753]	6.429 [1.941, 21.294]	43.4 [15.4, 71.5]	0.002	*

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. PGIC = patient global impression of change.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: apgic, created on: 24FEB2022

Table AT2PGI_ISPF: Relevant improvement in PGIC by use of concomitant itch medication
ITT

Relevant improvement in PGIC		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	F: Use of concomitant itch medication										0.214	
	No	117	107 (91.5)	65 (55.6) [46.1, 64.7]	111	103 (92.8)	43 (38.7) [29.6, 48.5]	1.434 [1.079, 1.906]	1.977 [1.166, 3.352]	16.8 [3.2, 30.5]	0.011	*
	Yes	72	67 (93.1)	43 (59.7) [47.5, 71.1]	78	74 (94.9)	24 (30.8) [20.8, 42.2]	1.941 [1.323, 2.847]	3.336 [1.702, 6.540]	29.0 [12.3, 45.6]	<0.001	*

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. PGIC = patient global impression of change.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: apgic, created on: 24FEB2022

Table AT2STC_ISHA: Change from baseline in Skindex-10 total score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
< 65 years	Skindex-10 total score	Baseline	CR845	135	130 (96.3)	35.4 (13.8)	4	36.0	60	
			Placebo	137	133 (97.1)	37.7 (15.2)	4	39.0	60	
		Week 4	CR845	135	118 (87.4)	26.0 (14.7)	0	24.0	60	
			Placebo	137	115 (83.9)	31.2 (15.7)	0	31.0	60	
		Week 8	CR845	135	108 (80.0)	22.6 (16.4)	0	19.5	60	
			Placebo	137	119 (86.9)	29.2 (17.7)	0	26.0	60	
		Week 10	CR845	135	110 (81.5)	19.9 (15.3)	0	16.5	60	
			Placebo	137	117 (85.4)	27.5 (17.9)	0	26.0	60	
		Week 12	CR845	135	111 (82.2)	17.7 (14.5)	0	14.0	60	
			Placebo	137	116 (84.7)	26.3 (18.0)	0	24.5	60	
	Change from baseline in Skindex-10 total score	Week 4	CR845	135	114 (84.4)	-9.5 (12.3)	-41	-8.0	22	-0.18 [-0.44, 0.08]
			Placebo	137	111 (81.0)	-7.1 (14.5)	-50	-5.0	30	
		Week 8	CR845	135	104 (77.0)	-12.1 (13.4)	-41	-11.0	30	-0.20 [-0.47, 0.07]
			Placebo	137	115 (83.9)	-9.2 (15.4)	-60	-8.0	30	
		Week 10	CR845	135	107 (79.3)	-15.3 (13.6)	-46	-14.0	25	-0.29 [-0.55, -0.02]
			Placebo	137	113 (82.5)	-10.7 (17.7)	-60	-8.0	32	
		Week 12	CR845	135	108 (80.0)	-17.2 (13.8)	-44	-16.5	26	-0.36 [-0.62, -0.09]
			Placebo	137	113 (82.5)	-11.7 (16.3)	-60	-11.0	32	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2STC_ISHA: Change from baseline in Skindex-10 total score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 65 years	Skindex-10 total score	Baseline	CR845	54	53 (98.1)	38.0 (15.7)	2	37.0	60	
			Placebo	52	52 (100.0)	39.8 (15.9)	8	43.5	60	
		Week 4	CR845	54	49 (90.7)	26.6 (17.6)	0	26.0	55	
			Placebo	52	47 (90.4)	29.9 (17.8)	2	28.0	60	
		Week 8	CR845	54	48 (88.9)	22.0 (15.5)	0	20.0	57	
			Placebo	52	47 (90.4)	26.0 (16.3)	0	26.0	60	
		Week 10	CR845	54	45 (83.3)	20.4 (16.4)	0	15.0	58	
			Placebo	52	48 (92.3)	22.4 (16.4)	0	20.0	60	
		Week 12	CR845	54	47 (87.0)	20.8 (16.9)	0	15.0	60	
			Placebo	52	45 (86.5)	22.2 (15.7)	0	20.0	60	
	Change from baseline in Skindex-10 total score	Week 4	CR845	54	48 (88.9)	-11.8 (17.7)	-59	-7.0	18	-0.05 [-0.45, 0.35]
			Placebo	52	47 (90.4)	-11.0 (11.3)	-43	-9.0	9	
		Week 8	CR845	54	47 (87.0)	-16.3 (16.0)	-54	-12.0	8	-0.14 [-0.54, 0.27]
			Placebo	52	47 (90.4)	-14.3 (13.8)	-60	-13.0	22	
		Week 10	CR845	54	45 (83.3)	-17.3 (18.4)	-57	-12.0	24	-0.01 [-0.42, 0.40]
			Placebo	52	48 (92.3)	-17.1 (12.4)	-42	-16.5	3	
		Week 12	CR845	54	46 (85.2)	-18.8 (19.7)	-57	-15.5	30	-0.09 [-0.50, 0.32]
			Placebo	52	45 (86.5)	-17.4 (13.2)	-51	-15.0	6	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2STC_ISHB: Change from baseline in Skindex-10 total score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Male	Skindex-10 total score	Baseline	CR845	112	109 (97.3)	35.7 (14.3)	2	36.0	60	
			Placebo	119	116 (97.5)	36.4 (15.8)	4	37.5	60	
		Week 4	CR845	112	97 (86.6)	25.3 (14.4)	0	24.0	60	
			Placebo	119	97 (81.5)	30.2 (16.6)	2	32.0	60	
		Week 8	CR845	112	89 (79.5)	22.5 (15.7)	0	20.0	57	
			Placebo	119	104 (87.4)	28.8 (17.3)	0	24.5	60	
		Week 10	CR845	112	91 (81.3)	21.5 (15.4)	0	19.0	60	
			Placebo	119	105 (88.2)	26.5 (17.6)	0	24.0	60	
		Week 12	CR845	112	91 (81.3)	18.5 (15.3)	0	15.0	60	
			Placebo	119	103 (86.6)	25.1 (17.3)	0	22.0	60	
	Change from baseline in Skindex-10 total score	Week 4	CR845	112	95 (84.8)	-10.2 (13.6)	-59	-8.0	22	-0.20 [-0.49, 0.08]
			Placebo	119	94 (79.0)	-7.6 (12.4)	-46	-6.0	30	
		Week 8	CR845	112	87 (77.7)	-12.7 (14.5)	-54	-12.0	30	-0.26 [-0.55, 0.03]
			Placebo	119	101 (84.9)	-8.9 (14.8)	-60	-8.0	30	
		Week 10	CR845	112	90 (80.4)	-14.2 (14.7)	-55	-12.0	24	-0.22 [-0.51, 0.06]
			Placebo	119	102 (85.7)	-10.7 (15.9)	-60	-8.0	25	
		Week 12	CR845	112	89 (79.5)	-16.9 (15.6)	-57	-16.0	26	-0.33 [-0.62, -0.04]
			Placebo	119	101 (84.9)	-11.8 (15.4)	-60	-11.0	17	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2STC_ISHB: Change from baseline in Skindex-10 total score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Female	Skindex-10 total score	Baseline	CR845	77	74 (96.1)	36.9 (14.6)	4	37.0	60	
			Placebo	70	69 (98.6)	41.4 (14.3)	9	45.0	60	
		Week 4	CR845	77	70 (90.9)	27.3 (17.1)	0	25.5	58	
			Placebo	70	65 (92.9)	31.7 (16.0)	0	30.0	60	
		Week 8	CR845	77	67 (87.0)	22.3 (16.6)	0	19.0	60	
			Placebo	70	62 (88.6)	27.3 (17.5)	0	26.0	60	
		Week 10	CR845	77	64 (83.1)	18.0 (15.8)	0	14.0	56	
			Placebo	70	60 (85.7)	25.4 (17.7)	0	22.5	60	
		Week 12	CR845	77	67 (87.0)	18.7 (15.3)	0	15.0	56	
			Placebo	70	58 (82.9)	25.1 (17.9)	0	24.0	60	
	Change from baseline in Skindex-10 total score	Week 4	CR845	77	67 (87.0)	-10.1 (14.9)	-50	-8.0	19	-0.06 [-0.40, 0.29]
			Placebo	70	64 (91.4)	-9.3 (15.4)	-50	-7.0	30	
		Week 8	CR845	77	64 (83.1)	-14.4 (14.3)	-53	-11.0	21	-0.05 [-0.40, 0.30]
			Placebo	70	61 (87.1)	-13.7 (15.3)	-60	-13.0	27	
		Week 10	CR845	77	62 (80.5)	-18.3 (15.5)	-57	-15.5	25	-0.15 [-0.50, 0.21]
			Placebo	70	59 (84.3)	-16.0 (17.1)	-58	-16.0	32	
		Week 12	CR845	77	65 (84.4)	-18.8 (16.0)	-56	-17.0	30	-0.17 [-0.52, 0.19]
			Placebo	70	57 (81.4)	-16.1 (16.0)	-58	-15.0	32	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2STC_ISHC: Change from baseline in Skindex-10 total score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Black/African American	Skindex-10 total score	Baseline	CR845	82	81 (98.8)	33.8 (14.4)	4	33.0	60	
			Placebo	76	75 (98.7)	36.8 (14.7)	4	36.0	60	
		Week 4	CR845	82	69 (84.1)	23.2 (16.0)	0	20.0	58	
			Placebo	76	65 (85.5)	28.9 (14.6)	4	29.0	60	
		Week 8	CR845	82	65 (79.3)	20.3 (15.6)	0	17.0	57	
			Placebo	76	67 (88.2)	25.6 (17.6)	0	21.0	60	
		Week 10	CR845	82	63 (76.8)	16.5 (14.2)	0	12.0	60	
			Placebo	76	65 (85.5)	24.6 (17.3)	0	23.0	60	
		Week 12	CR845	82	64 (78.0)	16.1 (14.7)	0	13.0	56	
			Placebo	76	65 (85.5)	23.5 (16.7)	0	21.0	60	
	Change from baseline in Skindex-10 total score	Week 4	CR845	82	68 (82.9)	-11.1 (15.3)	-59	-8.5	21	-0.21 [-0.55, 0.14]
			Placebo	76	64 (84.2)	-8.1 (13.5)	-47	-6.5	21	
		Week 8	CR845	82	64 (78.0)	-14.8 (14.3)	-54	-12.5	30	-0.17 [-0.51, 0.18]
			Placebo	76	66 (86.8)	-12.3 (14.8)	-60	-11.0	30	
		Week 10	CR845	82	63 (76.8)	-17.2 (14.7)	-55	-15.0	13	-0.24 [-0.59, 0.11]
			Placebo	76	64 (84.2)	-13.4 (17.2)	-60	-13.0	25	
		Week 12	CR845	82	63 (76.8)	-18.3 (16.6)	-57	-18.0	30	-0.29 [-0.64, 0.06]
			Placebo	76	64 (84.2)	-13.8 (15.2)	-60	-13.0	15	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2STC_ISHC: Change from baseline in Skindex-10 total score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
White	Skindex-10 total score	Baseline	CR845	91	86 (94.5)	38.2 (14.4)	2	38.0	60	
			Placebo	93	91 (97.8)	39.0 (16.1)	5	42.0	60	
		Week 4	CR845	91	83 (91.2)	27.9 (15.1)	0	26.0	60	
			Placebo	93	79 (84.9)	31.7 (17.1)	0	33.0	60	
		Week 8	CR845	91	76 (83.5)	23.8 (16.3)	0	21.0	60	
			Placebo	93	81 (87.1)	29.3 (16.9)	0	29.0	60	
		Week 10	CR845	91	78 (85.7)	22.4 (16.1)	0	19.5	60	
			Placebo	93	81 (87.1)	26.3 (17.6)	0	23.0	60	
		Week 12	CR845	91	80 (87.9)	20.0 (15.0)	0	15.5	60	
			Placebo	93	77 (82.8)	26.6 (17.6)	0	27.0	60	
	Change from baseline in Skindex-10 total score	Week 4	CR845	91	79 (86.8)	-9.9 (13.2)	-50	-9.0	22	-0.13 [-0.45, 0.18]
			Placebo	93	77 (82.8)	-8.1 (13.7)	-43	-7.0	30	
		Week 8	CR845	91	72 (79.1)	-12.4 (14.0)	-50	-10.0	21	-0.20 [-0.52, 0.12]
			Placebo	93	79 (84.9)	-9.4 (15.5)	-60	-8.0	28	
		Week 10	CR845	91	75 (82.4)	-15.2 (15.4)	-53	-13.0	25	-0.15 [-0.47, 0.16]
			Placebo	93	79 (84.9)	-12.7 (16.9)	-49	-10.0	32	
		Week 12	CR845	91	77 (84.6)	-17.6 (14.9)	-53	-15.0	26	-0.34 [-0.66, -0.02]
			Placebo	93	75 (80.6)	-12.3 (16.0)	-45	-12.0	32	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2STC_ISHC: Change from baseline in Skindex-10 total score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Other	Skindex-10 total score	Baseline	CR845	15	15 (100.0)	37.5 (13.0)	13	31.0	57	
			Placebo	18	18 (100.0)	40.3 (15.3)	18	38.0	60	
		Week 4	CR845	15	14 (93.3)	30.0 (15.5)	7	27.5	53	
			Placebo	18	16 (88.9)	31.4 (17.7)	2	28.5	60	
		Week 8	CR845	15	14 (93.3)	24.4 (17.2)	0	27.0	48	
			Placebo	18	16 (88.9)	31.3 (16.9)	0	31.0	60	
		Week 10	CR845	15	13 (86.7)	21.8 (16.8)	0	20.0	54	
			Placebo	18	17 (94.4)	30.1 (19.6)	4	28.0	60	
		Week 12	CR845	15	13 (86.7)	20.9 (18.9)	0	23.0	60	
			Placebo	18	18 (100.0)	24.8 (20.1)	0	19.0	60	
	Change from baseline in Skindex-10 total score	Week 4	CR845	15	14 (93.3)	-8.0 (13.9)	-48	-4.0	7	0.15 [-0.57, 0.87]
			Placebo	18	16 (88.9)	-10.2 (15.4)	-50	-6.5	11	
		Week 8	CR845	15	14 (93.3)	-13.6 (16.9)	-53	-7.5	8	-0.21 [-0.93, 0.51]
			Placebo	18	16 (88.9)	-10.3 (15.4)	-36	-7.5	13	
		Week 10	CR845	15	13 (86.7)	-15.0 (15.6)	-57	-12.0	4	-0.42 [-1.15, 0.31]
			Placebo	18	17 (94.4)	-9.2 (12.2)	-34	-5.0	2	
		Week 12	CR845	15	13 (86.7)	-16.6 (17.3)	-56	-11.0	5	-0.07 [-0.78, 0.64]
			Placebo	18	18 (100.0)	-15.4 (16.4)	-51	-12.0	8	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2STC_ISHD: Change from baseline in Skindex-10 total score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 4 to < 7	Skindex-10 total score	Baseline	CR845	83	81 (97.6)	29.8 (13.5)	2	31.0	60	
			Placebo	80	79 (98.8)	29.8 (14.2)	4	28.0	59	
		Week 4	CR845	83	71 (85.5)	19.3 (12.5)	0	18.0	58	
			Placebo	80	67 (83.8)	24.0 (15.6)	0	21.0	59	
		Week 8	CR845	83	68 (81.9)	17.1 (13.6)	0	15.0	57	
			Placebo	80	68 (85.0)	20.7 (15.3)	0	15.0	57	
		Week 10	CR845	83	69 (83.1)	15.7 (12.0)	0	14.0	60	
			Placebo	80	70 (87.5)	19.9 (16.5)	0	13.0	60	
		Week 12	CR845	83	67 (80.7)	13.7 (10.5)	0	13.0	48	
			Placebo	80	69 (86.3)	20.0 (16.1)	0	16.0	60	
	Change from baseline in Skindex-10 total score	Week 4	CR845	83	70 (84.3)	-9.4 (13.1)	-59	-7.0	18	-0.30 [-0.64, 0.04]
			Placebo	80	66 (82.5)	-5.6 (12.2)	-29	-5.0	30	
		Week 8	CR845	83	67 (80.7)	-12.8 (12.3)	-54	-11.0	11	-0.32 [-0.66, 0.02]
			Placebo	80	67 (83.8)	-8.9 (12.1)	-48	-8.0	27	
		Week 10	CR845	83	68 (81.9)	-13.7 (12.8)	-55	-12.5	24	-0.30 [-0.64, 0.03]
			Placebo	80	69 (86.3)	-9.5 (15.4)	-47	-9.0	32	
		Week 12	CR845	83	66 (79.5)	-15.6 (12.2)	-57	-13.0	13	-0.50 [-0.85, -0.16]
			Placebo	80	68 (85.0)	-9.0 (14.1)	-39	-10.0	32	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2STC_ISHD: Change from baseline in Skindex-10 total score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 7	Skindex-10 total score	Baseline	CR845	106	102 (96.2)	41.2 (13.0)	15	42.0	60	
			Placebo	109	106 (97.2)	44.6 (13.1)	5	47.5	60	
		Week 4	CR845	106	96 (90.6)	31.2 (15.8)	0	30.0	60	
			Placebo	109	95 (87.2)	35.6 (15.1)	4	36.0	60	
		Week 8	CR845	106	88 (83.0)	26.5 (16.7)	0	23.0	60	
			Placebo	109	98 (89.9)	33.5 (16.7)	0	32.5	60	
		Week 10	CR845	106	86 (81.1)	23.5 (17.3)	0	19.5	60	
			Placebo	109	95 (87.2)	30.6 (17.0)	0	29.0	60	
		Week 12	CR845	106	91 (85.8)	22.2 (17.2)	0	20.0	60	
			Placebo	109	92 (84.4)	29.0 (17.5)	0	28.5	60	
	Change from baseline in Skindex-10 total score	Week 4	CR845	106	92 (86.8)	-10.7 (14.9)	-50	-10.0	22	-0.04 [-0.33, 0.25]
			Placebo	109	92 (84.4)	-10.2 (14.4)	-50	-8.0	30	
		Week 8	CR845	106	84 (79.2)	-14.0 (15.9)	-53	-12.0	30	-0.12 [-0.42, 0.17]
			Placebo	109	95 (87.2)	-12.0 (16.9)	-60	-10.0	30	
		Week 10	CR845	106	84 (79.2)	-17.6 (16.7)	-57	-14.5	25	-0.15 [-0.45, 0.14]
			Placebo	109	92 (84.4)	-15.0 (17.0)	-60	-13.0	19	
		Week 12	CR845	106	88 (83.0)	-19.2 (17.9)	-56	-18.0	30	-0.15 [-0.45, 0.14]
			Placebo	109	90 (82.6)	-16.6 (16.1)	-60	-15.5	17	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2STC_ISHE: Change from baseline in Skindex-10 total score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	Skindex-10 total score	Baseline	CR845	164	159 (97.0)	36.2 (14.2)	2	36.0	60	
			Placebo	161	159 (98.8)	37.5 (15.8)	4	39.0	60	
		Week 4	CR845	164	143 (87.2)	25.3 (15.4)	0	24.0	60	
			Placebo	161	138 (85.7)	29.7 (16.2)	0	30.0	60	
		Week 8	CR845	164	133 (81.1)	21.7 (15.9)	0	19.0	60	
			Placebo	161	140 (87.0)	27.3 (17.4)	0	24.0	60	
		Week 10	CR845	164	133 (81.1)	19.7 (15.3)	0	16.0	60	
			Placebo	161	141 (87.6)	25.7 (17.5)	0	23.0	60	
		Week 12	CR845	164	134 (81.7)	18.2 (15.1)	0	14.5	60	
			Placebo	161	135 (83.9)	24.3 (17.4)	0	21.0	60	
	Change from baseline in Skindex-10 total score	Week 4	CR845	164	139 (84.8)	-10.9 (14.2)	-59	-8.0	22	-0.19 [-0.43, 0.05]
			Placebo	161	136 (84.5)	-8.2 (13.9)	-50	-6.5	30	
		Week 8	CR845	164	129 (78.7)	-13.9 (14.8)	-54	-12.0	30	-0.23 [-0.47, 0.01]
			Placebo	161	138 (85.7)	-10.4 (15.4)	-60	-10.0	30	
		Week 10	CR845	164	130 (79.3)	-16.3 (15.1)	-57	-14.0	24	-0.27 [-0.51, -0.03]
			Placebo	161	139 (86.3)	-11.9 (16.6)	-60	-10.0	32	
		Week 12	CR845	164	131 (79.9)	-17.9 (16.2)	-57	-17.0	30	-0.33 [-0.57, -0.08]
			Placebo	161	134 (83.2)	-12.7 (15.7)	-60	-12.0	32	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2STC_ISHE: Change from baseline in Skindex-10 total score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	Skindex-10 total score	Baseline	CR845	25	24 (96.0)	36.0 (15.4)	12	35.5	60	
			Placebo	28	26 (92.9)	43.2 (12.1)	19	46.0	60	
		Week 4	CR845	25	24 (96.0)	31.3 (15.8)	3	30.0	58	
			Placebo	28	24 (85.7)	37.2 (16.0)	10	40.0	60	
		Week 8	CR845	25	23 (92.0)	26.7 (16.7)	4	26.0	55	
			Placebo	28	26 (92.9)	33.3 (16.1)	6	32.5	60	
		Week 10	CR845	25	22 (88.0)	22.5 (17.4)	0	15.5	55	
			Placebo	28	24 (85.7)	28.4 (17.9)	3	26.0	60	
		Week 12	CR845	25	24 (96.0)	21.0 (16.3)	0	19.0	56	
			Placebo	28	26 (92.9)	29.3 (17.3)	5	25.5	60	
	Change from baseline in Skindex-10 total score	Week 4	CR845	25	23 (92.0)	-5.6 (12.6)	-30	-8.0	21	0.22 [-0.37, 0.81]
			Placebo	28	22 (78.6)	-8.4 (12.5)	-35	-6.0	8	
		Week 8	CR845	25	22 (88.0)	-10.9 (11.4)	-34	-9.5	21	0.10 [-0.48, 0.68]
			Placebo	28	24 (85.7)	-12.1 (13.3)	-34	-11.0	18	
		Week 10	CR845	25	22 (88.0)	-13.5 (15.3)	-42	-12.5	25	0.25 [-0.34, 0.84]
			Placebo	28	22 (78.6)	-17.3 (15.1)	-42	-18.5	12	
		Week 12	CR845	25	23 (92.0)	-16.6 (13.3)	-42	-15.0	14	0.04 [-0.53, 0.61]
			Placebo	28	24 (85.7)	-17.2 (15.4)	-51	-17.5	15	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2STC_ISHF: Change from baseline in Skindex-10 total score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	Skindex-10 total score	Baseline	CR845	117	112 (95.7)	35.6 (14.6)	5	36.0	60	
			Placebo	111	110 (99.1)	38.1 (15.3)	4	39.0	60	
		Week 4	CR845	117	105 (89.7)	25.0 (15.3)	0	23.0	60	
			Placebo	111	92 (82.9)	30.5 (16.3)	2	30.0	60	
		Week 8	CR845	117	101 (86.3)	20.5 (16.0)	0	17.0	60	
			Placebo	111	98 (88.3)	27.9 (16.5)	0	25.0	60	
		Week 10	CR845	117	98 (83.8)	20.0 (15.8)	0	15.0	60	
			Placebo	111	98 (88.3)	24.8 (17.4)	0	21.5	60	
		Week 12	CR845	117	100 (85.5)	18.1 (15.4)	0	14.5	60	
			Placebo	111	98 (88.3)	23.8 (16.6)	0	22.5	60	
	Change from baseline in Skindex-10 total score	Week 4	CR845	117	101 (86.3)	-10.6 (14.1)	-50	-7.0	19	-0.17 [-0.46, 0.11]
			Placebo	111	91 (82.0)	-8.1 (14.7)	-50	-6.0	30	
		Week 8	CR845	117	97 (82.9)	-14.6 (14.8)	-53	-12.0	21	-0.28 [-0.56, 0.01]
			Placebo	111	97 (87.4)	-10.4 (15.6)	-60	-9.0	28	
		Week 10	CR845	117	96 (82.1)	-15.6 (15.5)	-57	-12.5	25	-0.15 [-0.43, 0.14]
			Placebo	111	97 (87.4)	-13.2 (17.8)	-60	-10.0	32	
		Week 12	CR845	117	97 (82.9)	-18.0 (16.3)	-56	-16.0	30	-0.26 [-0.54, 0.02]
			Placebo	111	97 (87.4)	-13.8 (16.1)	-60	-12.0	32	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2STC_ISHF: Change from baseline in Skindex-10 total score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	Skindex-10 total score	Baseline	CR845	72	71 (98.6)	37.1 (14.0)	2	37.0	60	
			Placebo	78	75 (96.2)	38.5 (15.6)	5	41.0	60	
		Week 4	CR845	72	62 (86.1)	28.2 (16.0)	0	28.0	60	
			Placebo	78	70 (89.7)	31.3 (16.4)	0	32.0	60	
		Week 8	CR845	72	55 (76.4)	25.9 (15.8)	0	21.0	56	
			Placebo	78	68 (87.2)	28.8 (18.6)	0	30.0	60	
		Week 10	CR845	72	57 (79.2)	20.1 (15.4)	0	16.0	60	
			Placebo	78	67 (85.9)	28.0 (17.8)	0	28.0	60	
		Week 12	CR845	72	58 (80.6)	19.5 (15.3)	0	15.0	60	
			Placebo	78	63 (80.8)	27.2 (18.5)	0	25.0	60	
	Change from baseline in Skindex-10 total score	Week 4	CR845	72	61 (84.7)	-9.5 (14.2)	-59	-8.0	22	-0.07 [-0.42, 0.27]
			Placebo	78	67 (85.9)	-8.5 (12.3)	-43	-7.0	21	
		Week 8	CR845	72	54 (75.0)	-11.3 (13.3)	-54	-10.0	30	-0.01 [-0.37, 0.35]
			Placebo	78	65 (83.3)	-11.2 (14.5)	-60	-10.0	30	
		Week 10	CR845	72	56 (77.8)	-16.3 (14.6)	-55	-14.5	24	-0.31 [-0.67, 0.05]
			Placebo	78	64 (82.1)	-11.8 (14.4)	-47	-10.5	19	
		Week 12	CR845	72	57 (79.2)	-17.1 (15.0)	-57	-17.0	18	-0.30 [-0.66, 0.07]
			Placebo	78	61 (78.2)	-12.6 (15.0)	-51	-13.0	17	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SDC_ISHA: Change from baseline in Skindex-10 disease score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
< 65 years	Skindex-10 disease score	Baseline	CR845	135	132 (97.8)	13.0 (3.9)	4	13.5	18	
			Placebo	137	136 (99.3)	13.7 (4.0)	2	15.0	18	
		Week 4	CR845	135	118 (87.4)	9.7 (4.5)	0	9.0	18	
			Placebo	137	116 (84.7)	11.5 (4.4)	0	11.0	18	
		Week 8	CR845	135	110 (81.5)	8.5 (4.9)	0	8.0	18	
			Placebo	137	120 (87.6)	10.4 (5.0)	0	10.0	18	
		Week 10	CR845	135	110 (81.5)	7.8 (4.7)	0	7.5	18	
			Placebo	137	117 (85.4)	9.9 (5.3)	0	10.0	18	
		Week 12	CR845	135	111 (82.2)	6.6 (4.5)	0	6.0	18	
			Placebo	137	116 (84.7)	9.8 (5.4)	0	10.0	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	135	116 (85.9)	-3.4 (4.2)	-14	-3.0	8	-0.30 [-0.56, -0.04]
			Placebo	137	115 (83.9)	-2.2 (4.2)	-15	-2.0	7	
		Week 8	CR845	135	108 (80.0)	-4.4 (4.9)	-16	-4.0	11	-0.25 [-0.51, 0.01]
			Placebo	137	119 (86.9)	-3.2 (4.8)	-18	-3.0	7	
		Week 10	CR845	135	108 (80.0)	-5.2 (5.1)	-18	-5.0	9	-0.28 [-0.55, -0.02]
			Placebo	137	116 (84.7)	-3.7 (5.2)	-18	-3.0	7	
		Week 12	CR845	135	110 (81.5)	-6.2 (4.9)	-18	-6.0	7	-0.47 [-0.74, -0.21]
			Placebo	137	115 (83.9)	-3.9 (5.0)	-18	-3.0	9	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SDC_ISHA: Change from baseline in Skindex-10 disease score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 65 years	Skindex-10 disease score	Baseline	CR845	54	54 (100.0)	14.0 (3.9)	2	15.0	18	
			Placebo	52	52 (100.0)	14.1 (3.5)	3	15.5	18	
		Week 4	CR845	54	50 (92.6)	10.3 (5.0)	0	10.5	18	
			Placebo	52	48 (92.3)	10.8 (5.0)	0	11.5	18	
		Week 8	CR845	54	48 (88.9)	8.7 (4.5)	0	8.0	17	
			Placebo	52	48 (92.3)	9.9 (4.5)	0	9.5	18	
		Week 10	CR845	54	46 (85.2)	8.3 (4.9)	0	7.0	18	
			Placebo	52	48 (92.3)	8.8 (4.9)	0	8.0	18	
		Week 12	CR845	54	47 (87.0)	8.4 (5.3)	0	8.0	18	
			Placebo	52	46 (88.5)	8.5 (4.6)	0	8.0	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	54	50 (92.6)	-3.6 (5.0)	-17	-3.5	10	0.02 [-0.37, 0.42]
			Placebo	52	48 (92.3)	-3.7 (4.0)	-15	-4.0	5	
		Week 8	CR845	54	48 (88.9)	-5.2 (4.7)	-16	-5.0	4	-0.15 [-0.55, 0.25]
			Placebo	52	48 (92.3)	-4.5 (4.4)	-18	-3.5	3	
		Week 10	CR845	54	46 (85.2)	-5.7 (5.7)	-18	-5.0	5	-0.08 [-0.48, 0.32]
			Placebo	52	48 (92.3)	-5.3 (4.4)	-13	-5.5	7	
		Week 12	CR845	54	47 (87.0)	-5.9 (6.1)	-18	-6.0	9	-0.01 [-0.42, 0.39]
			Placebo	52	46 (88.5)	-5.8 (3.9)	-14	-5.5	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SDC_ISHB: Change from baseline in Skindex-10 disease score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Male	Skindex-10 disease score	Baseline	CR845	112	110 (98.2)	12.9 (4.2)	2	13.0	18	
			Placebo	119	119 (100.0)	13.5 (3.7)	3	14.0	18	
		Week 4	CR845	112	97 (86.6)	9.7 (4.3)	0	9.0	18	
			Placebo	119	99 (83.2)	11.6 (4.6)	2	12.0	18	
		Week 8	CR845	112	90 (80.4)	8.4 (5.0)	0	8.0	18	
			Placebo	119	106 (89.1)	10.6 (4.7)	0	10.5	18	
		Week 10	CR845	112	91 (81.3)	8.3 (4.6)	0	8.0	18	
			Placebo	119	105 (88.2)	9.8 (5.1)	0	9.0	18	
		Week 12	CR845	112	91 (81.3)	7.0 (4.6)	0	6.0	18	
			Placebo	119	104 (87.4)	9.5 (5.2)	0	9.0	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	112	96 (85.7)	-3.0 (4.3)	-17	-3.0	8	-0.20 [-0.48, 0.08]
			Placebo	119	99 (83.2)	-2.2 (4.0)	-15	-2.0	7	
		Week 8	CR845	112	89 (79.5)	-4.2 (5.1)	-16	-4.0	11	-0.23 [-0.51, 0.05]
			Placebo	119	106 (89.1)	-3.1 (4.4)	-18	-2.5	7	
		Week 10	CR845	112	90 (80.4)	-4.5 (5.2)	-18	-4.0	9	-0.12 [-0.40, 0.16]
			Placebo	119	105 (88.2)	-3.9 (4.7)	-18	-3.0	7	
		Week 12	CR845	112	90 (80.4)	-5.8 (5.3)	-18	-6.0	7	-0.33 [-0.61, -0.05]
			Placebo	119	104 (87.4)	-4.1 (4.6)	-18	-4.0	9	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SDC_ISHB: Change from baseline in Skindex-10 disease score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Female	Skindex-10 disease score	Baseline	CR845	77	76 (98.7)	14.0 (3.4)	4	15.0	18	
			Placebo	70	69 (98.6)	14.2 (4.0)	2	15.0	18	
		Week 4	CR845	77	71 (92.2)	10.1 (5.1)	0	10.0	18	
			Placebo	70	65 (92.9)	10.9 (4.6)	0	11.0	18	
		Week 8	CR845	77	68 (88.3)	8.8 (4.6)	0	8.0	18	
			Placebo	70	62 (88.6)	9.7 (5.2)	0	9.0	18	
		Week 10	CR845	77	65 (84.4)	7.5 (5.0)	0	7.0	18	
			Placebo	70	60 (85.7)	9.3 (5.3)	0	8.5	18	
		Week 12	CR845	77	67 (87.0)	7.4 (5.0)	0	6.0	18	
			Placebo	70	58 (82.9)	9.3 (5.4)	0	9.5	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	77	70 (90.9)	-4.1 (4.6)	-15	-4.0	10	-0.18 [-0.52, 0.16]
			Placebo	70	64 (91.4)	-3.3 (4.4)	-15	-3.0	7	
		Week 8	CR845	77	67 (87.0)	-5.3 (4.4)	-16	-5.0	2	-0.18 [-0.53, 0.16]
			Placebo	70	61 (87.1)	-4.4 (5.1)	-18	-3.0	4	
		Week 10	CR845	77	64 (83.1)	-6.6 (5.2)	-18	-6.0	4	-0.34 [-0.69, 0.02]
			Placebo	70	59 (84.3)	-4.8 (5.5)	-18	-4.0	7	
		Week 12	CR845	77	67 (87.0)	-6.6 (5.3)	-18	-6.0	9	-0.31 [-0.67, 0.04]
			Placebo	70	57 (81.4)	-5.0 (5.0)	-18	-4.0	5	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SDC_ISHC: Change from baseline in Skindex-10 disease score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Black/African American	Skindex-10 disease score	Baseline	CR845	82	82 (100.0)	13.0 (3.9)	4	14.0	18	
			Placebo	76	76 (100.0)	13.4 (3.9)	2	14.0	18	
		Week 4	CR845	82	69 (84.1)	9.4 (4.9)	0	9.0	18	
			Placebo	76	65 (85.5)	11.1 (4.6)	0	10.0	18	
		Week 8	CR845	82	66 (80.5)	8.3 (4.6)	0	8.0	18	
			Placebo	76	68 (89.5)	9.6 (5.0)	0	9.0	18	
		Week 10	CR845	82	63 (76.8)	7.6 (4.6)	0	7.0	18	
			Placebo	76	65 (85.5)	9.4 (5.2)	0	9.0	18	
		Week 12	CR845	82	64 (78.0)	7.0 (5.0)	0	6.0	18	
			Placebo	76	66 (86.8)	9.3 (5.1)	0	9.0	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	82	69 (84.1)	-3.7 (4.8)	-17	-3.0	8	-0.34 [-0.68, 0.01]
			Placebo	76	65 (85.5)	-2.2 (4.1)	-12	-2.0	7	
		Week 8	CR845	82	66 (80.5)	-5.0 (5.0)	-16	-5.0	11	-0.24 [-0.58, 0.10]
			Placebo	76	68 (89.5)	-3.8 (4.9)	-18	-3.0	7	
		Week 10	CR845	82	63 (76.8)	-5.3 (5.7)	-18	-5.0	9	-0.23 [-0.57, 0.12]
			Placebo	76	65 (85.5)	-4.1 (5.5)	-18	-4.0	7	
		Week 12	CR845	82	64 (78.0)	-6.0 (5.8)	-18	-6.0	9	-0.33 [-0.68, 0.01]
			Placebo	76	66 (86.8)	-4.2 (5.0)	-18	-4.0	9	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SDC_ISHC: Change from baseline in Skindex-10 disease score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
White	Skindex-10 disease score	Baseline	CR845	91	88 (96.7)	13.6 (4.0)	2	14.0	18	
			Placebo	93	92 (98.9)	14.0 (3.8)	3	15.0	18	
		Week 4	CR845	91	84 (92.3)	10.1 (4.6)	0	10.0	18	
			Placebo	93	81 (87.1)	11.3 (4.6)	0	12.0	18	
		Week 8	CR845	91	77 (84.6)	8.8 (4.9)	0	8.0	18	
			Placebo	93	82 (88.2)	10.5 (4.8)	0	10.0	18	
		Week 10	CR845	91	79 (86.8)	8.2 (4.9)	0	7.0	18	
			Placebo	93	81 (87.1)	9.6 (5.3)	0	9.0	18	
		Week 12	CR845	91	80 (87.9)	7.1 (4.3)	0	6.0	18	
			Placebo	93	77 (82.8)	9.7 (5.3)	0	9.0	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	91	82 (90.1)	-3.5 (4.2)	-15	-3.5	10	-0.15 [-0.45, 0.16]
			Placebo	93	80 (86.0)	-2.9 (4.1)	-15	-2.5	7	
		Week 8	CR845	91	75 (82.4)	-4.4 (4.7)	-16	-4.0	7	-0.21 [-0.53, 0.10]
			Placebo	93	81 (87.1)	-3.4 (4.5)	-18	-3.0	7	
		Week 10	CR845	91	77 (84.6)	-5.5 (5.0)	-18	-5.0	6	-0.22 [-0.53, 0.09]
			Placebo	93	80 (86.0)	-4.4 (4.8)	-14	-4.0	7	
		Week 12	CR845	91	79 (86.8)	-6.4 (4.8)	-18	-6.0	7	-0.46 [-0.78, -0.14]
			Placebo	93	76 (81.7)	-4.3 (4.6)	-15	-4.0	7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SDC_ISHC: Change from baseline in Skindex-10 disease score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Other	Skindex-10 disease score	Baseline	CR845	15	15 (100.0)	13.2 (3.2)	7	14.0	18	
			Placebo	18	18 (100.0)	14.5 (3.9)	7	16.0	18	
		Week 4	CR845	15	14 (93.3)	10.6 (4.1)	4	11.0	16	
			Placebo	18	16 (88.9)	11.3 (4.9)	2	12.0	18	
		Week 8	CR845	15	14 (93.3)	8.8 (5.4)	0	8.5	16	
			Placebo	18	16 (88.9)	11.0 (4.6)	0	11.0	18	
		Week 10	CR845	15	13 (86.7)	8.2 (5.5)	0	9.0	15	
			Placebo	18	17 (94.4)	10.2 (5.1)	3	9.0	18	
		Week 12	CR845	15	13 (86.7)	8.2 (6.2)	0	8.0	18	
			Placebo	18	18 (100.0)	8.4 (5.6)	0	7.5	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	15	14 (93.3)	-2.6 (3.5)	-8	-3.0	4	0.23 [-0.49, 0.95]
			Placebo	18	16 (88.9)	-3.6 (4.9)	-15	-3.0	5	
		Week 8	CR845	15	14 (93.3)	-4.7 (5.0)	-13	-4.0	4	-0.17 [-0.89, 0.55]
			Placebo	18	16 (88.9)	-3.9 (5.0)	-16	-3.0	2	
		Week 10	CR845	15	13 (86.7)	-5.2 (5.0)	-17	-5.0	2	-0.24 [-0.96, 0.48]
			Placebo	18	17 (94.4)	-4.1 (4.2)	-13	-3.0	1	
		Week 12	CR845	15	13 (86.7)	-5.2 (5.4)	-16	-5.0	3	0.20 [-0.52, 0.91]
			Placebo	18	18 (100.0)	-6.1 (4.4)	-14	-6.5	0	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SDC_ISHD: Change from baseline in Skindex-10 disease score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 4 to < 7	Skindex-10 disease score	Baseline	CR845	83	82 (98.8)	11.3 (3.9)	2	11.0	18	
			Placebo	80	79 (98.8)	11.6 (3.9)	2	12.0	18	
		Week 4	CR845	83	72 (86.7)	7.8 (4.0)	0	8.0	18	
			Placebo	80	69 (86.3)	9.7 (4.6)	0	9.0	18	
		Week 8	CR845	83	69 (83.1)	6.8 (4.4)	0	6.0	18	
			Placebo	80	70 (87.5)	8.6 (4.4)	0	7.5	18	
		Week 10	CR845	83	69 (83.1)	6.6 (3.9)	0	6.0	18	
			Placebo	80	70 (87.5)	7.8 (5.0)	0	6.5	18	
		Week 12	CR845	83	67 (80.7)	5.8 (3.3)	0	6.0	15	
			Placebo	80	70 (87.5)	8.0 (5.1)	0	7.0	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	83	72 (86.7)	-3.2 (4.5)	-17	-2.5	10	-0.28 [-0.61, 0.06]
			Placebo	80	68 (85.0)	-2.0 (3.9)	-10	-1.5	7	
		Week 8	CR845	83	69 (83.1)	-4.6 (4.7)	-16	-4.0	8	-0.35 [-0.69, -0.02]
			Placebo	80	69 (86.3)	-3.0 (4.2)	-13	-3.0	7	
		Week 10	CR845	83	69 (83.1)	-4.6 (4.8)	-16	-5.0	5	-0.17 [-0.51, 0.16]
			Placebo	80	69 (86.3)	-3.8 (4.9)	-14	-3.0	7	
		Week 12	CR845	83	67 (80.7)	-5.3 (4.5)	-17	-6.0	4	-0.36 [-0.70, -0.02]
			Placebo	80	69 (86.3)	-3.7 (4.7)	-14	-3.0	9	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SDC_ISHD: Change from baseline in Skindex-10 disease score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 7	Skindex-10 disease score	Baseline	CR845	106	104 (98.1)	14.9 (3.1)	4	16.0	18	
			Placebo	109	109 (100.0)	15.4 (2.9)	5	16.0	18	
		Week 4	CR845	106	96 (90.6)	11.4 (4.5)	0	11.5	18	
			Placebo	109	95 (87.2)	12.5 (4.2)	0	13.0	18	
		Week 8	CR845	106	89 (84.0)	10.0 (4.6)	0	9.0	18	
			Placebo	109	98 (89.9)	11.4 (4.8)	0	12.0	18	
		Week 10	CR845	106	87 (82.1)	9.0 (5.2)	0	9.0	18	
			Placebo	109	95 (87.2)	10.9 (4.9)	0	11.0	18	
		Week 12	CR845	106	91 (85.8)	8.2 (5.4)	0	8.0	18	
			Placebo	109	92 (84.4)	10.5 (5.0)	0	12.0	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	106	94 (88.7)	-3.7 (4.3)	-15	-4.0	8	-0.15 [-0.44, 0.13]
			Placebo	109	95 (87.2)	-3.0 (4.3)	-15	-2.0	7	
		Week 8	CR845	106	87 (82.1)	-4.7 (5.0)	-16	-5.0	11	-0.15 [-0.44, 0.14]
			Placebo	109	98 (89.9)	-4.0 (5.0)	-18	-3.0	7	
		Week 10	CR845	106	85 (80.2)	-6.0 (5.6)	-18	-5.0	9	-0.27 [-0.57, 0.02]
			Placebo	109	95 (87.2)	-4.5 (5.1)	-18	-4.0	7	
		Week 12	CR845	106	90 (84.9)	-6.7 (5.7)	-18	-6.0	9	-0.33 [-0.62, -0.03]
			Placebo	109	92 (84.4)	-5.0 (4.8)	-18	-4.0	7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SDC_ISHE: Change from baseline in Skindex-10 disease score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	Skindex-10 disease score	Baseline	CR845	164	161 (98.2)	13.2 (4.0)	2	14.0	18	
			Placebo	161	160 (99.4)	13.6 (4.0)	2	15.0	18	
		Week 4	CR845	164	144 (87.8)	9.6 (4.7)	0	9.0	18	
			Placebo	161	138 (85.7)	11.0 (4.5)	0	11.0	18	
		Week 8	CR845	164	135 (82.3)	8.4 (4.9)	0	8.0	18	
			Placebo	161	141 (87.6)	10.0 (4.8)	0	10.0	18	
		Week 10	CR845	164	134 (81.7)	7.9 (4.8)	0	7.0	18	
			Placebo	161	141 (87.6)	9.5 (5.2)	0	9.0	18	
		Week 12	CR845	164	134 (81.7)	7.2 (4.8)	0	6.0	18	
			Placebo	161	136 (84.5)	9.2 (5.2)	0	9.0	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	164	142 (86.6)	-3.7 (4.6)	-17	-3.0	10	-0.22 [-0.46, 0.01]
			Placebo	161	137 (85.1)	-2.7 (4.2)	-15	-2.0	7	
		Week 8	CR845	164	133 (81.1)	-4.7 (5.0)	-16	-4.0	11	-0.23 [-0.47, 0.01]
			Placebo	161	140 (87.0)	-3.6 (4.8)	-18	-3.0	7	
		Week 10	CR845	164	132 (80.5)	-5.4 (5.3)	-18	-5.0	9	-0.26 [-0.49, -0.02]
			Placebo	161	140 (87.0)	-4.1 (5.0)	-18	-3.5	7	
		Week 12	CR845	164	133 (81.1)	-6.0 (5.4)	-18	-6.0	9	-0.32 [-0.56, -0.08]
			Placebo	161	135 (83.9)	-4.4 (4.8)	-18	-4.0	9	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SDC_ISHE: Change from baseline in Skindex-10 disease score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	Skindex-10 disease score	Baseline	CR845	25	25 (100.0)	13.8 (3.4)	6	14.0	18	
			Placebo	28	28 (100.0)	15.0 (2.7)	10	15.5	18	
		Week 4	CR845	25	24 (96.0)	11.2 (4.5)	2	11.5	18	
			Placebo	28	26 (92.9)	12.9 (4.6)	0	14.0	18	
		Week 8	CR845	25	23 (92.0)	9.5 (4.1)	4	8.0	18	
			Placebo	28	27 (96.4)	11.7 (4.9)	4	11.0	18	
		Week 10	CR845	25	22 (88.0)	8.5 (4.6)	0	7.5	17	
			Placebo	28	24 (85.7)	10.3 (5.3)	1	8.0	18	
		Week 12	CR845	25	24 (96.0)	7.2 (4.9)	0	6.5	15	
			Placebo	28	26 (92.9)	10.6 (5.2)	3	10.0	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	25	24 (96.0)	-2.5 (2.9)	-7	-3.0	3	-0.04 [-0.60, 0.51]
			Placebo	28	26 (92.9)	-2.3 (3.9)	-12	-1.0	4	
		Week 8	CR845	25	23 (92.0)	-4.2 (3.2)	-10	-4.0	2	-0.20 [-0.75, 0.36]
			Placebo	28	27 (96.4)	-3.4 (4.4)	-11	-2.0	7	
		Week 10	CR845	25	22 (88.0)	-5.0 (5.0)	-18	-4.0	3	-0.03 [-0.60, 0.55]
			Placebo	28	24 (85.7)	-4.9 (5.0)	-13	-6.0	7	
		Week 12	CR845	25	24 (96.0)	-6.5 (4.3)	-18	-6.5	0	-0.44 [-1.00, 0.13]
			Placebo	28	26 (92.9)	-4.6 (4.7)	-14	-4.5	7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SDC_ISHF: Change from baseline in Skindex-10 disease score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	Skindex-10 disease score	Baseline	CR845	117	115 (98.3)	12.9 (3.9)	4	13.0	18	
			Placebo	111	110 (99.1)	13.5 (3.7)	3	14.0	18	
		Week 4	CR845	117	106 (90.6)	9.6 (4.5)	0	9.0	18	
			Placebo	111	93 (83.8)	11.2 (4.6)	0	11.0	18	
		Week 8	CR845	117	101 (86.3)	7.9 (4.8)	0	8.0	18	
			Placebo	111	99 (89.2)	10.3 (4.6)	0	10.0	18	
		Week 10	CR845	117	99 (84.6)	7.9 (4.9)	0	7.0	18	
			Placebo	111	98 (88.3)	9.4 (5.1)	0	9.0	18	
		Week 12	CR845	117	100 (85.5)	6.8 (4.7)	0	6.0	18	
			Placebo	111	98 (88.3)	8.9 (5.0)	0	9.0	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	117	105 (89.7)	-3.3 (4.2)	-15	-3.0	10	-0.21 [-0.49, 0.07]
			Placebo	111	92 (82.9)	-2.4 (4.4)	-15	-2.0	7	
		Week 8	CR845	117	100 (85.5)	-4.8 (4.7)	-16	-5.0	8	-0.35 [-0.63, -0.06]
			Placebo	111	98 (88.3)	-3.2 (4.8)	-18	-3.0	7	
		Week 10	CR845	117	98 (83.8)	-5.1 (5.2)	-17	-5.0	6	-0.19 [-0.47, 0.09]
			Placebo	111	97 (87.4)	-4.1 (5.4)	-18	-4.0	7	
		Week 12	CR845	117	100 (85.5)	-6.2 (5.2)	-16	-6.0	9	-0.32 [-0.60, -0.04]
			Placebo	111	97 (87.4)	-4.6 (4.6)	-18	-4.0	7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SDC_ISHF: Change from baseline in Skindex-10 disease score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	Skindex-10 disease score	Baseline	CR845	72	71 (98.6)	13.9 (3.8)	2	14.0	18	
			Placebo	78	78 (100.0)	14.2 (4.0)	2	16.0	18	
		Week 4	CR845	72	62 (86.1)	10.3 (4.9)	0	11.0	18	
			Placebo	78	71 (91.0)	11.4 (4.6)	0	11.0	18	
		Week 8	CR845	72	57 (79.2)	9.7 (4.7)	0	9.0	18	
			Placebo	78	69 (88.5)	10.2 (5.3)	0	9.0	18	
		Week 10	CR845	72	57 (79.2)	7.9 (4.7)	0	7.0	18	
			Placebo	78	67 (85.9)	9.9 (5.3)	0	10.0	18	
		Week 12	CR845	72	58 (80.6)	7.8 (4.9)	0	7.5	18	
			Placebo	78	64 (82.1)	10.1 (5.4)	0	11.0	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	72	61 (84.7)	-3.8 (4.8)	-17	-4.0	8	-0.21 [-0.55, 0.13]
			Placebo	78	71 (91.0)	-2.9 (3.8)	-12	-2.0	7	
		Week 8	CR845	72	56 (77.8)	-4.3 (5.0)	-16	-4.0	11	-0.05 [-0.40, 0.30]
			Placebo	78	69 (88.5)	-4.1 (4.6)	-18	-3.0	4	
		Week 10	CR845	72	56 (77.8)	-5.8 (5.3)	-18	-5.0	9	-0.29 [-0.65, 0.06]
			Placebo	78	67 (85.9)	-4.4 (4.5)	-14	-4.0	4	
		Week 12	CR845	72	57 (79.2)	-6.0 (5.4)	-18	-6.0	5	-0.35 [-0.71, 0.01]
			Placebo	78	64 (82.1)	-4.2 (5.0)	-14	-4.0	9	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SMC_ISHA: Change from baseline in Skindex-10 mood/emotional distress score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
< 65 years	Skindex-10 mood/emotional distress score	Baseline	CR845	135	130 (96.3)	11.4 (4.5)	0	12.0	18	
			Placebo	137	135 (98.5)	11.9 (4.9)	0	12.0	18	
		Week 4	CR845	135	119 (88.1)	8.4 (4.9)	0	8.0	18	
			Placebo	137	116 (84.7)	9.9 (5.1)	0	10.0	18	
		Week 8	CR845	135	110 (81.5)	6.8 (5.5)	0	6.0	18	
			Placebo	137	119 (86.9)	9.1 (5.7)	0	9.0	18	
		Week 10	CR845	135	111 (82.2)	5.9 (5.1)	0	4.0	18	
			Placebo	137	118 (86.1)	8.7 (5.7)	0	8.0	18	
		Week 12	CR845	135	112 (83.0)	5.3 (4.8)	0	5.0	18	
			Placebo	137	118 (86.1)	8.2 (5.9)	0	8.0	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	135	115 (85.2)	-3.0 (4.6)	-15	-3.0	10	-0.20 [-0.46, 0.06]
			Placebo	137	114 (83.2)	-2.1 (4.9)	-17	-2.0	10	
		Week 8	CR845	135	106 (78.5)	-4.5 (5.3)	-18	-4.0	14	-0.32 [-0.58, -0.06]
			Placebo	137	117 (85.4)	-2.9 (5.0)	-18	-2.0	9	
		Week 10	CR845	135	108 (80.0)	-5.6 (5.0)	-17	-6.0	10	-0.42 [-0.68, -0.15]
			Placebo	137	116 (84.7)	-3.3 (5.7)	-18	-2.0	10	
		Week 12	CR845	135	109 (80.7)	-6.0 (4.8)	-18	-6.0	6	-0.41 [-0.67, -0.15]
			Placebo	137	116 (84.7)	-3.8 (5.8)	-18	-4.0	14	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SMC_ISHA: Change from baseline in Skindex-10 mood/emotional distress score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 65 years	Skindex-10 mood/emotional distress score	Baseline	CR845	54	54 (100.0)	12.1 (4.7)	0	12.0	18	
			Placebo	52	52 (100.0)	12.3 (5.3)	0	13.5	18	
		Week 4	CR845	54	50 (92.6)	8.4 (5.8)	0	9.0	18	
			Placebo	52	47 (90.4)	9.0 (6.0)	0	8.0	18	
		Week 8	CR845	54	48 (88.9)	6.6 (5.3)	0	5.0	18	
			Placebo	52	48 (92.3)	8.1 (5.5)	0	8.0	18	
		Week 10	CR845	54	45 (83.3)	6.1 (5.3)	0	5.0	18	
			Placebo	52	48 (92.3)	6.9 (5.6)	0	6.0	18	
		Week 12	CR845	54	47 (87.0)	6.1 (5.6)	0	5.0	18	
			Placebo	52	47 (90.4)	7.0 (5.4)	0	6.0	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	54	50 (92.6)	-3.7 (6.1)	-18	-2.0	12	-0.01 [-0.41, 0.39]
			Placebo	52	47 (90.4)	-3.7 (3.8)	-12	-3.0	2	
		Week 8	CR845	54	48 (88.9)	-5.5 (5.8)	-18	-5.0	4	-0.22 [-0.62, 0.18]
			Placebo	52	48 (92.3)	-4.3 (4.7)	-18	-4.5	8	
		Week 10	CR845	54	45 (83.3)	-5.9 (5.8)	-17	-4.0	9	-0.10 [-0.51, 0.30]
			Placebo	52	48 (92.3)	-5.4 (4.6)	-14	-6.0	5	
		Week 12	CR845	54	47 (87.0)	-6.2 (6.2)	-17	-5.0	6	-0.18 [-0.58, 0.23]
			Placebo	52	47 (90.4)	-5.3 (4.5)	-16	-4.0	5	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SMC_ISHB: Change from baseline in Skindex-10 mood/emotional distress score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Male	Skindex-10 mood/emotional distress score	Baseline	CR845	112	109 (97.3)	11.6 (4.5)	0	12.0	18	
			Placebo	119	118 (99.2)	11.4 (5.2)	0	12.0	18	
		Week 4	CR845	112	98 (87.5)	8.0 (4.7)	0	8.0	18	
			Placebo	119	98 (82.4)	9.3 (5.5)	0	10.0	18	
		Week 8	CR845	112	90 (80.4)	7.0 (5.3)	0	6.0	18	
			Placebo	119	104 (87.4)	9.0 (5.7)	0	9.0	18	
		Week 10	CR845	112	91 (81.3)	6.4 (5.1)	0	5.0	18	
			Placebo	119	105 (88.2)	8.3 (5.8)	0	8.0	18	
		Week 12	CR845	112	91 (81.3)	5.5 (5.0)	0	5.0	18	
			Placebo	119	104 (87.4)	7.9 (5.7)	0	7.0	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	112	96 (85.7)	-3.6 (4.8)	-18	-3.5	8	-0.27 [-0.55, 0.01]
			Placebo	119	97 (81.5)	-2.4 (4.4)	-17	-2.0	10	
		Week 8	CR845	112	88 (78.6)	-4.7 (5.4)	-18	-4.5	14	-0.40 [-0.69, -0.11]
			Placebo	119	103 (86.6)	-2.7 (4.7)	-18	-2.0	9	
		Week 10	CR845	112	90 (80.4)	-5.3 (5.3)	-17	-5.5	10	-0.38 [-0.67, -0.10]
			Placebo	119	104 (87.4)	-3.3 (5.2)	-18	-2.0	8	
		Week 12	CR845	112	89 (79.5)	-6.1 (5.2)	-17	-6.0	6	-0.48 [-0.77, -0.19]
			Placebo	119	103 (86.6)	-3.6 (5.5)	-18	-3.0	14	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SMC_ISHB: Change from baseline in Skindex-10 mood/emotional distress score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Female	Skindex-10 mood/emotional distress score	Baseline	CR845	77	75 (97.4)	11.6 (4.7)	0	12.0	18	
			Placebo	70	69 (98.6)	13.0 (4.4)	0	13.0	18	
		Week 4	CR845	77	71 (92.2)	9.0 (5.7)	0	9.0	18	
			Placebo	70	65 (92.9)	10.2 (5.2)	0	9.0	18	
		Week 8	CR845	77	68 (88.3)	6.5 (5.6)	0	6.0	18	
			Placebo	70	63 (90.0)	8.5 (5.6)	0	8.0	18	
		Week 10	CR845	77	65 (84.4)	5.3 (5.2)	0	4.0	18	
			Placebo	70	61 (87.1)	8.0 (5.6)	0	8.0	18	
		Week 12	CR845	77	68 (88.3)	5.6 (5.1)	0	5.0	18	
			Placebo	70	61 (87.1)	7.8 (5.9)	0	7.0	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	77	69 (89.6)	-2.7 (5.5)	-16	-2.0	12	0.02 [-0.32, 0.36]
			Placebo	70	64 (91.4)	-2.8 (5.1)	-15	-2.0	8	
		Week 8	CR845	77	66 (85.7)	-5.0 (5.5)	-18	-4.0	8	-0.12 [-0.47, 0.22]
			Placebo	70	62 (88.6)	-4.4 (5.1)	-18	-3.5	8	
		Week 10	CR845	77	63 (81.8)	-6.2 (5.2)	-17	-6.0	10	-0.22 [-0.57, 0.13]
			Placebo	70	60 (85.7)	-5.0 (5.9)	-17	-5.5	10	
		Week 12	CR845	77	67 (87.0)	-6.0 (5.5)	-18	-6.0	6	-0.12 [-0.47, 0.23]
			Placebo	70	60 (85.7)	-5.3 (5.4)	-17	-5.0	9	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SMC_ISHC: Change from baseline in Skindex-10 mood/emotional distress score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Black/African American	Skindex-10 mood/emotional distress score	Baseline	CR845	82	82 (100.0)	11.0 (4.7)	0	11.0	18	
			Placebo	76	76 (100.0)	11.9 (4.8)	0	12.0	18	
		Week 4	CR845	82	69 (84.1)	7.7 (5.6)	0	7.0	18	
			Placebo	76	66 (86.8)	9.4 (5.0)	0	9.0	18	
		Week 8	CR845	82	66 (80.5)	6.0 (5.4)	0	5.0	18	
			Placebo	76	67 (88.2)	8.3 (5.8)	0	8.0	18	
		Week 10	CR845	82	64 (78.0)	4.7 (4.9)	0	3.0	18	
			Placebo	76	66 (86.8)	8.0 (5.8)	0	8.0	18	
		Week 12	CR845	82	65 (79.3)	4.5 (4.7)	0	3.0	18	
			Placebo	76	65 (85.5)	7.5 (5.7)	0	7.0	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	82	69 (84.1)	-3.4 (6.1)	-18	-3.0	12	-0.17 [-0.51, 0.17]
			Placebo	76	66 (86.8)	-2.5 (4.4)	-15	-2.0	7	
		Week 8	CR845	82	66 (80.5)	-5.6 (5.9)	-18	-5.0	14	-0.31 [-0.65, 0.03]
			Placebo	76	67 (88.2)	-3.9 (4.7)	-18	-3.0	8	
		Week 10	CR845	82	64 (78.0)	-6.5 (5.5)	-17	-7.0	10	-0.44 [-0.79, -0.09]
			Placebo	76	66 (86.8)	-4.0 (5.8)	-18	-3.5	10	
		Week 12	CR845	82	65 (79.3)	-6.6 (5.7)	-18	-7.0	6	-0.41 [-0.75, -0.06]
			Placebo	76	65 (85.5)	-4.4 (5.3)	-18	-4.0	14	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SMC_ISHC: Change from baseline in Skindex-10 mood/emotional distress score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
White	Skindex-10 mood/emotional distress score	Baseline	CR845	91	86 (94.5)	12.2 (4.4)	0	12.0	18	
			Placebo	93	91 (97.8)	11.9 (5.3)	0	13.0	18	
		Week 4	CR845	91	85 (93.4)	8.8 (4.7)	0	8.0	18	
			Placebo	93	79 (84.9)	9.6 (5.7)	0	10.0	18	
		Week 8	CR845	91	77 (84.6)	7.2 (5.3)	0	6.0	18	
			Placebo	93	81 (87.1)	8.9 (5.6)	0	9.0	18	
		Week 10	CR845	91	78 (85.7)	6.9 (5.1)	0	6.0	18	
			Placebo	93	81 (87.1)	7.8 (5.7)	0	7.0	18	
		Week 12	CR845	91	80 (87.9)	6.2 (5.0)	0	6.0	18	
			Placebo	93	80 (86.0)	8.2 (5.9)	0	8.5	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	91	81 (89.0)	-3.2 (4.2)	-15	-3.0	9	-0.14 [-0.45, 0.17]
			Placebo	93	77 (82.8)	-2.6 (4.9)	-17	-2.0	10	
		Week 8	CR845	91	73 (80.2)	-4.4 (5.0)	-15	-4.0	8	-0.28 [-0.60, 0.03]
			Placebo	93	79 (84.9)	-3.0 (5.0)	-18	-2.0	9	
		Week 10	CR845	91	75 (82.4)	-5.2 (5.1)	-17	-5.0	10	-0.19 [-0.51, 0.13]
			Placebo	93	79 (84.9)	-4.2 (5.5)	-16	-3.0	9	
		Week 12	CR845	91	77 (84.6)	-5.8 (4.8)	-17	-5.0	6	-0.37 [-0.69, -0.05]
			Placebo	93	78 (83.9)	-3.9 (5.5)	-14	-4.0	10	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SMC_ISHC: Change from baseline in Skindex-10 mood/emotional distress score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Other	Skindex-10 mood/emotional distress score	Baseline	CR845	15	15 (100.0)	11.7 (4.4)	5	10.0	18	
			Placebo	18	18 (100.0)	12.5 (4.6)	3	12.0	18	
		Week 4	CR845	15	14 (93.3)	9.2 (5.4)	0	8.0	18	
			Placebo	18	16 (88.9)	9.7 (5.7)	0	9.5	18	
		Week 8	CR845	15	14 (93.3)	8.2 (6.3)	0	9.5	17	
			Placebo	18	17 (94.4)	9.8 (5.6)	0	9.0	18	
		Week 10	CR845	15	13 (86.7)	6.7 (5.7)	0	5.0	18	
			Placebo	18	17 (94.4)	9.6 (5.7)	0	10.0	18	
		Week 12	CR845	15	13 (86.7)	5.8 (6.3)	0	7.0	18	
			Placebo	18	18 (100.0)	7.8 (6.1)	0	6.0	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	15	14 (93.3)	-2.7 (5.0)	-16	-1.5	4	0.09 [-0.62, 0.81]
			Placebo	18	16 (88.9)	-3.2 (5.0)	-15	-2.0	3	
		Week 8	CR845	15	14 (93.3)	-3.7 (5.5)	-16	-2.0	4	-0.18 [-0.89, 0.53]
			Placebo	18	17 (94.4)	-2.8 (5.1)	-10	-3.0	8	
		Week 10	CR845	15	13 (86.7)	-4.8 (4.7)	-16	-4.0	3	-0.50 [-1.23, 0.24]
			Placebo	18	17 (94.4)	-2.6 (4.4)	-11	-1.0	4	
		Week 12	CR845	15	13 (86.7)	-5.6 (5.4)	-16	-4.0	1	-0.16 [-0.88, 0.55]
			Placebo	18	18 (100.0)	-4.7 (6.1)	-16	-4.0	5	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SMC_ISHD: Change from baseline in Skindex-10 mood/emotional distress score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 4 to < 7	Skindex-10 mood/emotional distress score	Baseline	CR845	83	81 (97.6)	9.9 (4.7)	0	10.0	18	
			Placebo	80	79 (98.8)	9.2 (4.9)	0	10.0	18	
		Week 4	CR845	83	73 (88.0)	6.3 (4.4)	0	6.0	18	
			Placebo	80	68 (85.0)	7.5 (5.4)	0	6.5	18	
		Week 8	CR845	83	69 (83.1)	5.1 (4.7)	0	4.0	18	
			Placebo	80	69 (86.3)	6.0 (5.0)	0	5.0	18	
		Week 10	CR845	83	69 (83.1)	4.7 (4.1)	0	4.0	18	
			Placebo	80	70 (87.5)	5.9 (5.4)	0	4.5	18	
		Week 12	CR845	83	67 (80.7)	4.2 (3.7)	0	3.0	14	
			Placebo	80	71 (88.8)	6.3 (5.5)	0	5.0	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	83	72 (86.7)	-3.3 (4.6)	-18	-3.0	12	-0.34 [-0.68, -0.01]
			Placebo	80	67 (83.8)	-1.8 (4.4)	-11	-2.0	8	
		Week 8	CR845	83	68 (81.9)	-4.9 (4.9)	-15	-4.5	7	-0.36 [-0.70, -0.02]
			Placebo	80	68 (85.0)	-3.2 (4.7)	-15	-3.0	8	
		Week 10	CR845	83	68 (81.9)	-5.1 (4.6)	-16	-6.0	9	-0.39 [-0.73, -0.05]
			Placebo	80	69 (86.3)	-3.2 (5.3)	-15	-3.0	9	
		Week 12	CR845	83	66 (79.5)	-5.5 (4.4)	-16	-6.0	6	-0.57 [-0.92, -0.23]
			Placebo	80	70 (87.5)	-2.7 (5.4)	-14	-3.0	14	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SMC_ISHD: Change from baseline in Skindex-10 mood/emotional distress score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 7	Skindex-10 mood/emotional distress score	Baseline	CR845	106	103 (97.2)	13.0 (4.0)	3	13.0	18	
			Placebo	109	108 (99.1)	14.0 (4.0)	0	15.0	18	
		Week 4	CR845	106	96 (90.6)	10.0 (5.1)	0	11.0	18	
			Placebo	109	95 (87.2)	11.1 (4.9)	0	11.0	18	
		Week 8	CR845	106	89 (84.0)	8.1 (5.6)	0	7.0	18	
			Placebo	109	98 (89.9)	10.8 (5.2)	0	11.5	18	
		Week 10	CR845	106	87 (82.1)	7.0 (5.7)	0	6.0	18	
			Placebo	109	96 (88.1)	9.8 (5.4)	0	10.0	18	
		Week 12	CR845	106	92 (86.8)	6.5 (5.6)	0	6.0	18	
			Placebo	109	94 (86.2)	9.0 (5.7)	0	9.0	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	106	93 (87.7)	-3.2 (5.5)	-17	-2.0	10	-0.01 [-0.30, 0.27]
			Placebo	109	94 (86.2)	-3.1 (4.8)	-17	-2.0	10	
		Week 8	CR845	106	86 (81.1)	-4.8 (5.9)	-18	-4.0	14	-0.25 [-0.54, 0.04]
			Placebo	109	97 (89.0)	-3.4 (5.1)	-18	-3.0	9	
		Week 10	CR845	106	85 (80.2)	-6.1 (5.7)	-17	-6.0	10	-0.29 [-0.59, 0.00]
			Placebo	109	95 (87.2)	-4.5 (5.6)	-18	-4.0	10	
		Week 12	CR845	106	90 (84.9)	-6.4 (5.8)	-18	-7.0	6	-0.20 [-0.49, 0.09]
			Placebo	109	93 (85.3)	-5.3 (5.3)	-18	-5.0	7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SMC_ISHE: Change from baseline in Skindex-10 mood/emotional distress score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	Skindex-10 mood/emotional distress score	Baseline	CR845	164	159 (97.0)	11.6 (4.6)	0	12.0	18	
			Placebo	161	160 (99.4)	11.6 (5.1)	0	12.0	18	
		Week 4	CR845	164	145 (88.4)	8.1 (5.1)	0	8.0	18	
			Placebo	161	139 (86.3)	9.3 (5.4)	0	9.0	18	
		Week 8	CR845	164	135 (82.3)	6.6 (5.5)	0	6.0	18	
			Placebo	161	141 (87.6)	8.5 (5.7)	0	8.0	18	
		Week 10	CR845	164	134 (81.7)	5.9 (5.0)	0	5.0	18	
			Placebo	161	142 (88.2)	7.9 (5.7)	0	7.5	18	
		Week 12	CR845	164	135 (82.3)	5.3 (4.9)	0	5.0	18	
			Placebo	161	138 (85.7)	7.6 (5.7)	0	7.0	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	164	141 (86.0)	-3.6 (5.1)	-18	-3.0	12	-0.22 [-0.45, 0.02]
			Placebo	161	138 (85.7)	-2.5 (4.7)	-17	-2.0	10	
		Week 8	CR845	164	131 (79.9)	-5.0 (5.6)	-18	-4.0	14	-0.33 [-0.57, -0.09]
			Placebo	161	140 (87.0)	-3.2 (5.0)	-18	-3.0	9	
		Week 10	CR845	164	131 (79.9)	-5.8 (5.3)	-17	-6.0	10	-0.39 [-0.63, -0.15]
			Placebo	161	141 (87.6)	-3.7 (5.5)	-18	-3.0	10	
		Week 12	CR845	164	132 (80.5)	-6.2 (5.4)	-18	-6.0	6	-0.42 [-0.67, -0.18]
			Placebo	161	137 (85.1)	-3.9 (5.4)	-18	-4.0	14	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SMC_ISHE: Change from baseline in Skindex-10 mood/emotional distress score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	Skindex-10 mood/emotional distress score	Baseline	CR845	25	25 (100.0)	11.5 (4.7)	3	11.0	18	
			Placebo	28	27 (96.4)	14.2 (3.8)	5	16.0	18	
		Week 4	CR845	25	24 (96.0)	10.2 (5.5)	1	10.0	18	
			Placebo	28	24 (85.7)	11.6 (4.9)	2	13.0	18	
		Week 8	CR845	25	23 (92.0)	7.8 (5.1)	0	7.0	17	
			Placebo	28	26 (92.9)	10.7 (5.1)	0	11.5	18	
		Week 10	CR845	25	22 (88.0)	6.6 (6.0)	0	5.5	18	
			Placebo	28	24 (85.7)	9.5 (5.7)	0	11.0	18	
		Week 12	CR845	25	24 (96.0)	6.5 (5.7)	0	5.0	18	
			Placebo	28	27 (96.4)	9.1 (5.8)	1	8.0	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	25	24 (96.0)	-1.3 (4.9)	-12	-1.0	9	0.34 [-0.24, 0.91]
			Placebo	28	23 (82.1)	-3.0 (4.7)	-13	-1.0	4	
		Week 8	CR845	25	23 (92.0)	-3.9 (4.4)	-12	-4.0	8	-0.02 [-0.58, 0.55]
			Placebo	28	25 (89.3)	-3.8 (4.1)	-11	-3.0	1	
		Week 10	CR845	25	22 (88.0)	-4.8 (5.2)	-14	-5.0	10	0.06 [-0.53, 0.64]
			Placebo	28	23 (82.1)	-5.1 (5.3)	-15	-5.0	4	
		Week 12	CR845	25	24 (96.0)	-5.0 (4.7)	-13	-5.0	3	0.11 [-0.45, 0.67]
			Placebo	28	26 (92.9)	-5.6 (5.6)	-16	-4.0	7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SMC_ISHF: Change from baseline in Skindex-10 mood/emotional distress score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	Skindex-10 mood/emotional distress score	Baseline	CR845	117	113 (96.6)	11.5 (4.7)	0	12.0	18	
			Placebo	111	110 (99.1)	11.9 (4.9)	0	12.0	18	
		Week 4	CR845	117	107 (91.5)	8.0 (5.1)	0	8.0	18	
			Placebo	111	93 (83.8)	9.5 (5.3)	0	9.0	18	
		Week 8	CR845	117	101 (86.3)	6.2 (5.4)	0	5.0	18	
			Placebo	111	99 (89.2)	8.6 (5.1)	0	9.0	18	
		Week 10	CR845	117	98 (83.8)	6.0 (5.2)	0	5.0	18	
			Placebo	111	98 (88.3)	7.7 (5.5)	0	6.5	18	
		Week 12	CR845	117	100 (85.5)	5.5 (5.1)	0	5.0	18	
			Placebo	111	100 (90.1)	7.5 (5.5)	0	7.0	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	117	104 (88.9)	-3.5 (4.8)	-17	-3.0	12	-0.16 [-0.44, 0.12]
			Placebo	111	92 (82.9)	-2.7 (4.6)	-15	-2.0	10	
		Week 8	CR845	117	98 (83.8)	-5.1 (5.4)	-17	-4.0	8	-0.35 [-0.63, -0.07]
			Placebo	111	98 (88.3)	-3.3 (4.7)	-18	-3.0	9	
		Week 10	CR845	117	96 (82.1)	-5.7 (5.1)	-17	-5.0	10	-0.25 [-0.54, 0.03]
			Placebo	111	97 (87.4)	-4.3 (5.6)	-18	-4.0	9	
		Week 12	CR845	117	98 (83.8)	-6.0 (5.2)	-17	-6.0	6	-0.33 [-0.61, -0.05]
			Placebo	111	99 (89.2)	-4.3 (5.2)	-18	-4.0	14	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SMC_ISHF: Change from baseline in Skindex-10 mood/emotional distress score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	Skindex-10 mood/emotional distress score	Baseline	CR845	72	71 (98.6)	11.7 (4.5)	0	12.0	18	
			Placebo	78	77 (98.7)	12.1 (5.3)	0	13.0	18	
		Week 4	CR845	72	62 (86.1)	9.1 (5.2)	0	9.0	18	
			Placebo	78	70 (89.7)	9.8 (5.6)	0	11.0	18	
		Week 8	CR845	72	57 (79.2)	7.8 (5.3)	0	7.0	18	
			Placebo	78	68 (87.2)	9.1 (6.4)	0	10.0	18	
		Week 10	CR845	72	58 (80.6)	5.9 (5.1)	0	4.0	18	
			Placebo	78	68 (87.2)	8.9 (5.9)	0	8.0	18	
		Week 12	CR845	72	59 (81.9)	5.5 (5.0)	0	5.0	18	
			Placebo	78	65 (83.3)	8.3 (6.2)	0	8.0	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	72	61 (84.7)	-2.8 (5.6)	-18	-2.0	10	-0.09 [-0.44, 0.25]
			Placebo	78	69 (88.5)	-2.3 (4.8)	-17	-2.0	7	
		Week 8	CR845	72	56 (77.8)	-4.3 (5.6)	-18	-3.5	14	-0.20 [-0.55, 0.16]
			Placebo	78	67 (85.9)	-3.2 (5.2)	-18	-2.0	8	
		Week 10	CR845	72	57 (79.2)	-5.7 (5.6)	-16	-6.0	10	-0.43 [-0.78, -0.07]
			Placebo	78	67 (85.9)	-3.3 (5.3)	-15	-3.0	10	
		Week 12	CR845	72	58 (80.6)	-6.1 (5.5)	-18	-6.0	6	-0.36 [-0.72, 0.00]
			Placebo	78	64 (82.1)	-4.0 (5.9)	-16	-4.0	10	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SSC_ISHA: Change from baseline in Skindex-10 social functioning score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
< 65 years	Skindex-10 social functioning score	Baseline	CR845	135	132 (97.8)	11.0 (7.2)	0	10.0	24	
			Placebo	137	135 (98.5)	12.3 (8.0)	0	12.0	24	
		Week 4	CR845	135	119 (88.1)	7.9 (7.0)	0	7.0	24	
			Placebo	137	117 (85.4)	9.8 (7.8)	0	9.0	24	
		Week 8	CR845	135	109 (80.7)	7.2 (7.2)	0	5.0	24	
			Placebo	137	120 (87.6)	9.6 (8.3)	0	8.0	24	
		Week 10	CR845	135	111 (82.2)	6.1 (6.8)	0	4.0	24	
			Placebo	137	118 (86.1)	8.8 (8.2)	0	7.0	24	
		Week 12	CR845	135	112 (83.0)	5.6 (6.5)	0	3.0	24	
			Placebo	137	118 (86.1)	8.2 (7.9)	0	5.5	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	135	117 (86.7)	-3.2 (5.6)	-20	-3.0	11	-0.08 [-0.34, 0.18]
			Placebo	137	115 (83.9)	-2.7 (7.1)	-23	-1.0	20	
		Week 8	CR845	135	107 (79.3)	-3.6 (5.9)	-19	-4.0	11	-0.11 [-0.37, 0.15]
			Placebo	137	118 (86.1)	-2.8 (7.7)	-24	-2.0	20	
		Week 10	CR845	135	109 (80.7)	-4.5 (5.9)	-19	-4.0	12	-0.16 [-0.42, 0.11]
			Placebo	137	116 (84.7)	-3.4 (8.3)	-24	-2.0	20	
		Week 12	CR845	135	111 (82.2)	-5.1 (6.5)	-21	-5.0	16	-0.14 [-0.40, 0.12]
			Placebo	137	116 (84.7)	-4.1 (7.6)	-24	-3.0	20	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SSC_ISHA: Change from baseline in Skindex-10 social functioning score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 65 years	Skindex-10 social functioning score	Baseline	CR845	54	53 (98.1)	12.0 (8.9)	0	12.0	24	
			Placebo	52	52 (100.0)	13.4 (8.5)	0	14.0	24	
		Week 4	CR845	54	49 (90.7)	7.9 (8.3)	0	4.0	24	
			Placebo	52	48 (92.3)	10.3 (8.3)	0	11.0	24	
		Week 8	CR845	54	48 (88.9)	6.6 (7.0)	0	5.0	23	
			Placebo	52	49 (94.2)	8.4 (7.6)	0	8.0	24	
		Week 10	CR845	54	46 (85.2)	6.4 (7.6)	0	3.5	23	
			Placebo	52	48 (92.3)	6.8 (6.9)	0	4.5	24	
		Week 12	CR845	54	47 (87.0)	6.3 (7.2)	0	4.0	24	
			Placebo	52	48 (92.3)	7.4 (7.3)	0	5.0	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	54	48 (88.9)	-4.2 (8.5)	-24	-2.0	9	-0.07 [-0.47, 0.33]
			Placebo	52	48 (92.3)	-3.7 (6.4)	-20	-2.5	9	
		Week 8	CR845	54	47 (87.0)	-5.5 (8.1)	-24	-2.0	6	-0.04 [-0.44, 0.36]
			Placebo	52	49 (94.2)	-5.2 (7.4)	-24	-5.0	17	
		Week 10	CR845	54	46 (85.2)	-5.5 (8.3)	-24	-2.0	10	0.12 [-0.28, 0.53]
			Placebo	52	48 (92.3)	-6.4 (6.4)	-20	-5.5	4	
		Week 12	CR845	54	46 (85.2)	-6.4 (9.4)	-24	-5.0	15	-0.03 [-0.44, 0.37]
			Placebo	52	48 (92.3)	-6.1 (6.8)	-23	-4.0	4	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SSC_ISHB: Change from baseline in Skindex-10 social functioning score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Male	Skindex-10 social functioning score	Baseline	CR845	112	110 (98.2)	11.3 (7.5)	0	10.5	24	
			Placebo	119	117 (98.3)	11.8 (8.3)	0	12.0	24	
		Week 4	CR845	112	98 (87.5)	7.6 (6.9)	0	7.0	24	
			Placebo	119	100 (84.0)	9.5 (7.8)	0	9.0	24	
		Week 8	CR845	112	90 (80.4)	7.1 (6.7)	0	5.0	24	
			Placebo	119	106 (89.1)	9.2 (8.2)	0	8.0	24	
		Week 10	CR845	112	91 (81.3)	6.8 (6.9)	0	4.0	24	
			Placebo	119	105 (88.2)	8.4 (8.1)	0	6.0	24	
		Week 12	CR845	112	91 (81.3)	6.1 (6.7)	0	4.0	24	
			Placebo	119	105 (88.2)	7.9 (7.8)	0	5.0	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	112	97 (86.6)	-3.7 (6.3)	-24	-3.0	11	-0.14 [-0.42, 0.14]
			Placebo	119	98 (82.4)	-2.8 (6.2)	-23	-1.0	18	
		Week 8	CR845	112	89 (79.5)	-4.1 (6.5)	-24	-4.0	10	-0.17 [-0.45, 0.12]
			Placebo	119	104 (87.4)	-2.9 (7.8)	-24	-2.0	20	
		Week 10	CR845	112	90 (80.4)	-4.4 (6.5)	-24	-5.0	12	-0.15 [-0.44, 0.13]
			Placebo	119	103 (86.6)	-3.3 (7.9)	-24	-2.0	17	
		Week 12	CR845	112	90 (80.4)	-5.2 (7.4)	-24	-5.0	16	-0.17 [-0.46, 0.11]
			Placebo	119	103 (86.6)	-3.9 (7.4)	-24	-3.0	13	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SSC_ISHB: Change from baseline in Skindex-10 social functioning score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Female	Skindex-10 social functioning score	Baseline	CR845	77	75 (97.4)	11.3 (8.2)	0	11.0	24	
			Placebo	70	70 (100.0)	14.0 (7.6)	0	14.5	24	
		Week 4	CR845	77	70 (90.9)	8.2 (8.0)	0	4.5	24	
			Placebo	70	65 (92.9)	10.6 (8.1)	0	10.0	24	
		Week 8	CR845	77	67 (87.0)	6.9 (7.7)	0	4.0	24	
			Placebo	70	63 (90.0)	9.3 (7.9)	0	8.0	24	
		Week 10	CR845	77	66 (85.7)	5.5 (7.1)	0	2.5	24	
			Placebo	70	61 (87.1)	7.9 (7.6)	0	7.0	24	
		Week 12	CR845	77	68 (88.3)	5.5 (6.8)	0	3.0	23	
			Placebo	70	61 (87.1)	8.2 (7.7)	0	7.0	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	77	68 (88.3)	-3.2 (7.0)	-24	-1.5	9	0.00 [-0.34, 0.34]
			Placebo	70	65 (92.9)	-3.2 (7.9)	-23	-2.0	20	
		Week 8	CR845	77	65 (84.4)	-4.3 (7.0)	-24	-3.0	11	0.03 [-0.31, 0.38]
			Placebo	70	63 (90.0)	-4.6 (7.3)	-24	-4.0	20	
		Week 10	CR845	77	65 (84.4)	-5.3 (6.9)	-24	-3.0	12	0.08 [-0.27, 0.43]
			Placebo	70	61 (87.1)	-5.9 (7.7)	-23	-5.0	20	
		Week 12	CR845	77	67 (87.0)	-5.8 (7.5)	-24	-6.0	15	0.02 [-0.33, 0.36]
			Placebo	70	61 (87.1)	-6.0 (7.2)	-23	-4.0	20	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SSC_ISHC: Change from baseline in Skindex-10 social functioning score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Black/African American	Skindex-10 social functioning score	Baseline	CR845	82	81 (98.8)	9.9 (7.7)	0	9.0	24	
			Placebo	76	75 (98.7)	11.7 (8.0)	0	13.0	24	
		Week 4	CR845	82	69 (84.1)	6.1 (7.3)	0	3.0	24	
			Placebo	76	66 (86.8)	8.2 (7.3)	0	7.5	24	
		Week 8	CR845	82	65 (79.3)	5.8 (7.0)	0	4.0	24	
			Placebo	76	68 (89.5)	7.7 (8.1)	0	4.0	24	
		Week 10	CR845	82	64 (78.0)	4.1 (6.4)	0	2.0	24	
			Placebo	76	66 (86.8)	7.1 (7.5)	0	5.0	24	
		Week 12	CR845	82	65 (79.3)	4.5 (6.2)	0	1.0	23	
			Placebo	76	66 (86.8)	7.0 (7.3)	0	4.5	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	82	68 (82.9)	-3.8 (6.6)	-24	-3.0	11	-0.05 [-0.39, 0.29]
			Placebo	76	65 (85.5)	-3.5 (7.3)	-23	-1.0	9	
		Week 8	CR845	82	64 (78.0)	-4.4 (6.4)	-24	-3.5	8	-0.01 [-0.35, 0.33]
			Placebo	76	67 (88.2)	-4.3 (7.5)	-24	-4.0	19	
		Week 10	CR845	82	64 (78.0)	-5.4 (6.3)	-24	-4.0	8	-0.07 [-0.42, 0.28]
			Placebo	76	65 (85.5)	-4.9 (7.8)	-24	-4.0	11	
		Week 12	CR845	82	64 (78.0)	-5.4 (7.5)	-24	-6.0	15	-0.05 [-0.40, 0.29]
			Placebo	76	65 (85.5)	-5.0 (6.8)	-24	-4.0	7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SSC_ISHC: Change from baseline in Skindex-10 social functioning score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
White	Skindex-10 social functioning score	Baseline	CR845	91	88 (96.7)	12.4 (7.7)	0	12.5	24	
			Placebo	93	93 (100.0)	13.2 (8.2)	0	14.0	24	
		Week 4	CR845	91	84 (92.3)	8.9 (7.2)	0	8.0	24	
			Placebo	93	81 (87.1)	10.9 (8.1)	0	12.0	24	
		Week 8	CR845	91	77 (84.6)	7.9 (7.3)	0	6.0	24	
			Placebo	93	82 (88.2)	9.9 (8.0)	0	10.0	24	
		Week 10	CR845	91	79 (86.8)	7.7 (7.2)	0	6.0	24	
			Placebo	93	81 (87.1)	8.9 (7.9)	0	8.0	24	
		Week 12	CR845	91	80 (87.9)	6.7 (6.8)	0	4.0	24	
			Placebo	93	80 (86.0)	8.8 (8.0)	0	7.0	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	91	82 (90.1)	-3.4 (6.5)	-20	-2.5	11	-0.13 [-0.44, 0.17]
			Placebo	93	81 (87.1)	-2.5 (6.6)	-20	-1.0	20	
		Week 8	CR845	91	75 (82.4)	-3.9 (6.9)	-20	-3.0	11	-0.11 [-0.42, 0.20]
			Placebo	93	82 (88.2)	-3.1 (7.8)	-24	-2.0	20	
		Week 10	CR845	91	77 (84.6)	-4.4 (6.9)	-20	-3.0	12	-0.05 [-0.36, 0.26]
			Placebo	93	81 (87.1)	-4.0 (8.4)	-24	-3.0	20	
		Week 12	CR845	91	79 (86.8)	-5.6 (7.5)	-21	-5.0	16	-0.17 [-0.48, 0.14]
			Placebo	93	80 (86.0)	-4.3 (7.8)	-24	-3.5	20	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SSC_ISHC: Change from baseline in Skindex-10 social functioning score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Other	Skindex-10 social functioning score	Baseline	CR845	15	15 (100.0)	12.6 (7.4)	0	12.0	24	
			Placebo	18	18 (100.0)	13.3 (8.2)	0	11.5	24	
		Week 4	CR845	15	14 (93.3)	10.2 (7.8)	0	9.0	22	
			Placebo	18	16 (88.9)	10.5 (8.2)	0	8.5	24	
		Week 8	CR845	15	14 (93.3)	7.4 (6.8)	0	7.0	18	
			Placebo	18	17 (94.4)	11.2 (7.5)	0	12.0	24	
		Week 10	CR845	15	13 (86.7)	6.8 (6.9)	0	7.0	21	
			Placebo	18	17 (94.4)	10.2 (9.2)	0	10.0	24	
		Week 12	CR845	15	13 (86.7)	6.8 (7.9)	0	6.0	24	
			Placebo	18	18 (100.0)	8.6 (8.7)	0	6.5	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	15	14 (93.3)	-2.6 (7.5)	-24	-1.0	8	0.10 [-0.62, 0.82]
			Placebo	18	16 (88.9)	-3.4 (7.0)	-20	-3.0	7	
		Week 8	CR845	15	14 (93.3)	-5.2 (7.6)	-24	-3.5	4	-0.36 [-1.08, 0.35]
			Placebo	18	17 (94.4)	-2.4 (8.0)	-15	-2.0	12	
		Week 10	CR845	15	13 (86.7)	-5.0 (7.1)	-24	-5.0	4	-0.38 [-1.11, 0.35]
			Placebo	18	17 (94.4)	-2.6 (5.7)	-16	-1.0	8	
		Week 12	CR845	15	13 (86.7)	-5.8 (7.7)	-24	-3.0	3	-0.16 [-0.87, 0.56]
			Placebo	18	18 (100.0)	-4.7 (7.5)	-21	-2.5	10	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SSC_ISHD: Change from baseline in Skindex-10 social functioning score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 4 to < 7	Skindex-10 social functioning score	Baseline	CR845	83	82 (98.8)	8.6 (6.7)	0	8.0	24	
			Placebo	80	80 (100.0)	9.0 (7.3)	0	8.0	24	
		Week 4	CR845	83	72 (86.7)	5.3 (5.6)	0	4.0	24	
			Placebo	80	70 (87.5)	7.1 (6.9)	0	4.0	24	
		Week 8	CR845	83	68 (81.9)	5.1 (5.6)	0	4.0	23	
			Placebo	80	71 (88.8)	6.5 (7.1)	0	4.0	24	
		Week 10	CR845	83	69 (83.1)	4.4 (5.1)	0	3.0	24	
			Placebo	80	70 (87.5)	6.1 (7.2)	0	4.0	24	
		Week 12	CR845	83	67 (80.7)	3.8 (4.7)	0	2.0	20	
			Placebo	80	72 (90.0)	5.9 (6.7)	0	3.5	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	83	72 (86.7)	-2.9 (5.8)	-24	-2.0	9	-0.14 [-0.47, 0.19]
			Placebo	80	70 (87.5)	-2.1 (6.2)	-19	-1.0	20	
		Week 8	CR845	83	68 (81.9)	-3.7 (5.6)	-24	-3.0	7	-0.19 [-0.53, 0.14]
			Placebo	80	71 (88.8)	-2.5 (6.2)	-20	-1.0	20	
		Week 10	CR845	83	69 (83.1)	-4.0 (5.7)	-24	-4.0	10	-0.21 [-0.54, 0.12]
			Placebo	80	70 (87.5)	-2.6 (7.7)	-22	-1.5	20	
		Week 12	CR845	83	67 (80.7)	-4.7 (5.9)	-24	-4.0	7	-0.27 [-0.60, 0.07]
			Placebo	80	72 (90.0)	-3.0 (6.6)	-19	-3.0	20	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SSC_ISHD: Change from baseline in Skindex-10 social functioning score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 7	Skindex-10 social functioning score	Baseline	CR845	106	103 (97.2)	13.4 (7.9)	0	13.0	24	
			Placebo	109	107 (98.2)	15.3 (7.6)	0	17.0	24	
		Week 4	CR845	106	96 (90.6)	9.8 (8.0)	0	8.0	24	
			Placebo	109	95 (87.2)	12.0 (8.1)	0	12.0	24	
		Week 8	CR845	106	89 (84.0)	8.5 (7.8)	0	6.0	24	
			Placebo	109	98 (89.9)	11.2 (8.2)	0	12.0	24	
		Week 10	CR845	106	88 (83.0)	7.6 (8.0)	0	5.0	24	
			Placebo	109	96 (88.1)	9.8 (8.1)	0	8.0	24	
		Week 12	CR845	106	92 (86.8)	7.3 (7.5)	0	4.0	24	
			Placebo	109	94 (86.2)	9.6 (8.1)	0	8.0	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	106	93 (87.7)	-3.9 (7.2)	-24	-3.0	11	-0.04 [-0.33, 0.25]
			Placebo	109	93 (85.3)	-3.6 (7.4)	-23	-2.0	18	
		Week 8	CR845	106	86 (81.1)	-4.6 (7.5)	-24	-4.0	11	-0.04 [-0.33, 0.25]
			Placebo	109	96 (88.1)	-4.3 (8.5)	-24	-4.0	20	
		Week 10	CR845	106	86 (81.1)	-5.4 (7.4)	-24	-4.5	12	0.01 [-0.28, 0.30]
			Placebo	109	94 (86.2)	-5.5 (7.9)	-24	-4.0	11	
		Week 12	CR845	106	90 (84.9)	-6.0 (8.4)	-24	-6.0	16	-0.01 [-0.30, 0.28]
			Placebo	109	92 (84.4)	-6.0 (7.7)	-24	-4.0	13	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SSC_ISHE: Change from baseline in Skindex-10 social functioning score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	Skindex-10 social functioning score	Baseline	CR845	164	161 (98.2)	11.4 (7.7)	0	11.0	24	
			Placebo	161	160 (99.4)	12.3 (8.2)	0	12.0	24	
		Week 4	CR845	164	144 (87.8)	7.5 (7.4)	0	6.0	24	
			Placebo	161	139 (86.3)	9.4 (7.8)	0	9.0	24	
		Week 8	CR845	164	134 (81.7)	6.6 (6.8)	0	4.5	24	
			Placebo	161	142 (88.2)	9.0 (8.2)	0	7.5	24	
		Week 10	CR845	164	135 (82.3)	6.0 (6.8)	0	4.0	24	
			Placebo	161	142 (88.2)	8.2 (7.9)	0	6.0	24	
		Week 12	CR845	164	135 (82.3)	5.6 (6.7)	0	3.0	24	
			Placebo	161	139 (86.3)	7.8 (7.8)	0	5.0	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	164	142 (86.6)	-3.8 (6.7)	-24	-3.0	11	-0.11 [-0.34, 0.13]
			Placebo	161	138 (85.7)	-3.1 (6.9)	-23	-2.0	20	
		Week 8	CR845	164	132 (80.5)	-4.5 (6.9)	-24	-3.5	10	-0.16 [-0.39, 0.08]
			Placebo	161	141 (87.6)	-3.3 (7.8)	-24	-3.0	20	
		Week 10	CR845	164	133 (81.1)	-5.0 (6.8)	-24	-4.0	12	-0.14 [-0.38, 0.10]
			Placebo	161	141 (87.6)	-3.9 (8.1)	-24	-2.0	20	
		Week 12	CR845	164	134 (81.7)	-5.6 (7.6)	-24	-5.5	16	-0.17 [-0.41, 0.07]
			Placebo	161	138 (85.7)	-4.4 (7.4)	-24	-3.5	20	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SSC_ISHE: Change from baseline in Skindex-10 social functioning score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	Skindex-10 social functioning score	Baseline	CR845	25	24 (96.0)	10.9 (8.3)	0	10.0	24	
			Placebo	28	27 (96.4)	14.4 (7.3)	1	16.0	24	
		Week 4	CR845	25	24 (96.0)	9.9 (7.3)	0	10.5	24	
			Placebo	28	26 (92.9)	12.8 (8.0)	0	13.0	24	
		Week 8	CR845	25	23 (92.0)	9.4 (8.4)	0	6.0	24	
			Placebo	28	27 (96.4)	10.7 (7.3)	0	11.0	24	
		Week 10	CR845	25	22 (88.0)	7.3 (8.1)	0	3.5	24	
			Placebo	28	24 (85.7)	8.6 (7.8)	0	7.5	24	
		Week 12	CR845	25	24 (96.0)	7.3 (6.9)	0	4.0	23	
			Placebo	28	27 (96.4)	9.0 (7.5)	0	7.0	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	25	23 (92.0)	-1.6 (6.0)	-14	0.0	11	0.12 [-0.44, 0.69]
			Placebo	28	25 (89.3)	-2.4 (6.9)	-17	-1.0	9	
		Week 8	CR845	25	22 (88.0)	-2.5 (5.2)	-12	-1.0	11	0.33 [-0.24, 0.91]
			Placebo	28	26 (92.9)	-4.6 (7.0)	-17	-4.5	10	
		Week 10	CR845	25	22 (88.0)	-3.6 (5.9)	-14	-3.5	12	0.41 [-0.18, 1.00]
			Placebo	28	23 (82.1)	-6.2 (6.7)	-17	-5.0	7	
		Week 12	CR845	25	23 (92.0)	-4.4 (6.3)	-15	-4.0	12	0.29 [-0.27, 0.86]
			Placebo	28	26 (92.9)	-6.3 (7.1)	-21	-5.0	7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SSC_ISHF: Change from baseline in Skindex-10 social functioning score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	Skindex-10 social functioning score	Baseline	CR845	117	114 (97.4)	11.2 (7.8)	0	11.0	24	
			Placebo	111	111 (100.0)	12.6 (8.0)	0	12.0	24	
		Week 4	CR845	117	106 (90.6)	7.4 (7.4)	0	4.5	24	
			Placebo	111	94 (84.7)	9.8 (8.0)	0	9.0	24	
		Week 8	CR845	117	101 (86.3)	6.4 (6.9)	0	4.0	24	
			Placebo	111	100 (90.1)	9.1 (8.0)	0	8.0	24	
		Week 10	CR845	117	99 (84.6)	6.3 (7.1)	0	4.0	24	
			Placebo	111	98 (88.3)	7.7 (7.8)	0	4.5	24	
		Week 12	CR845	117	100 (85.5)	5.8 (6.6)	0	3.0	24	
			Placebo	111	100 (90.1)	7.5 (7.4)	0	5.0	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	117	104 (88.9)	-3.9 (7.0)	-24	-3.0	9	-0.11 [-0.39, 0.17]
			Placebo	111	94 (84.7)	-3.1 (7.6)	-23	-1.5	20	
		Week 8	CR845	117	99 (84.6)	-4.8 (7.2)	-24	-4.0	11	-0.16 [-0.44, 0.12]
			Placebo	111	100 (90.1)	-3.6 (8.1)	-24	-3.0	20	
		Week 10	CR845	117	98 (83.8)	-4.8 (7.1)	-24	-4.0	12	0.00 [-0.28, 0.28]
			Placebo	111	98 (88.3)	-4.8 (8.3)	-24	-3.0	20	
		Week 12	CR845	117	99 (84.6)	-5.8 (8.0)	-24	-5.0	16	-0.11 [-0.39, 0.17]
			Placebo	111	100 (90.1)	-4.9 (7.9)	-24	-3.0	20	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2SSC_ISHF: Change from baseline in Skindex-10 social functioning score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	Skindex-10 social functioning score	Baseline	CR845	72	71 (98.6)	11.5 (7.6)	0	10.0	24	
			Placebo	78	76 (97.4)	12.6 (8.3)	0	13.0	24	
		Week 4	CR845	72	62 (86.1)	8.8 (7.3)	0	8.0	24	
			Placebo	78	71 (91.0)	10.2 (7.9)	0	10.0	24	
		Week 8	CR845	72	56 (77.8)	8.1 (7.5)	0	5.0	24	
			Placebo	78	69 (88.5)	9.5 (8.2)	0	9.0	24	
		Week 10	CR845	72	58 (80.6)	6.1 (7.0)	0	4.0	24	
			Placebo	78	68 (87.2)	9.1 (8.0)	0	7.0	24	
		Week 12	CR845	72	59 (81.9)	6.0 (6.9)	0	4.0	24	
			Placebo	78	66 (84.6)	8.7 (8.2)	0	7.0	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	72	61 (84.7)	-2.8 (5.8)	-24	-2.0	11	-0.00 [-0.35, 0.34]
			Placebo	78	69 (88.5)	-2.8 (6.0)	-20	-1.0	8	
		Week 8	CR845	72	55 (76.4)	-3.1 (5.6)	-24	-3.0	5	0.06 [-0.30, 0.41]
			Placebo	78	67 (85.9)	-3.5 (7.0)	-24	-3.0	19	
		Week 10	CR845	72	57 (79.2)	-4.7 (6.0)	-24	-4.0	10	-0.21 [-0.56, 0.15]
			Placebo	78	66 (84.6)	-3.3 (7.2)	-18	-3.0	17	
		Week 12	CR845	72	58 (80.6)	-4.9 (6.4)	-24	-5.0	12	-0.09 [-0.44, 0.27]
			Placebo	78	64 (82.1)	-4.3 (6.6)	-21	-4.0	10	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table AT2STC_ISCA: Change from baseline in Skindex-10 total score - MMRM results by age
ITT

Change from baseline in Skindex-10 total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
A: Age									0.349
< 65 years	Week 4	CR845	135	114 (84.4)	-9.1 (1.4)	(-11.7, -6.4)	-3.5 (1.6)	(-6.7, -0.4)	0.028 *
		Placebo	137	111 (81.0)	-5.6 (1.4)	(-8.3, -2.8)			
>= 65 years	Week 4	CR845	54	48 (88.9)	-10.7 (2.5)	(-15.7, -5.8)	-1.6 (2.9)	(-7.4, 4.1)	0.575
		Placebo	52	47 (90.4)	-9.1 (2.4)	(-13.7, -4.4)			
< 65 years	Week 8	CR845	135	104 (77.0)	-12.1 (1.5)	(-15.1, -9.1)	-4.5 (1.8)	(-8.1, -0.9)	0.014 *
		Placebo	137	115 (83.9)	-7.6 (1.5)	(-10.6, -4.6)			
>= 65 years	Week 8	CR845	54	47 (87.0)	-15.6 (2.4)	(-20.3, -10.8)	-2.6 (2.8)	(-8.1, 2.8)	0.341
		Placebo	52	47 (90.4)	-12.9 (2.3)	(-17.4, -8.5)			
< 65 years	Week 10	CR845	135	107 (79.3)	-15.4 (1.6)	(-18.5, -12.3)	-5.7 (1.9)	(-9.4, -1.9)	0.003 *
		Placebo	137	113 (82.5)	-9.7 (1.6)	(-12.8, -6.6)			
>= 65 years	Week 10	CR845	54	45 (83.3)	-16.1 (2.5)	(-21.2, -11.1)	0.0 (3.0)	(-5.9, 5.9)	0.993
		Placebo	52	48 (92.3)	-16.2 (2.4)	(-20.8, -11.5)			
< 65 years	Week 12	CR845	135	108 (80.0)	-17.1 (1.5)	(-20.1, -14.1)	-6.6 (1.9)	(-10.3, -2.9)	<0.001 *
		Placebo	137	113 (82.5)	-10.5 (1.5)	(-13.5, -7.4)			
>= 65 years	Week 12	CR845	54	46 (85.2)	-18.0 (2.5)	(-23.0, -13.0)	-1.6 (3.0)	(-7.5, 4.3)	0.601
		Placebo	52	45 (86.5)	-16.5 (2.4)	(-21.1, -11.8)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table AT2STC_ISCB: Change from baseline in Skindex-10 total score - MMRM results by sex
ITT

Change from baseline in Skindex-10 total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
B: Sex									0.637
Male	Week 4	CR845	112	95 (84.8)	-9.4 (1.6)	(-12.5, -6.3)	-3.4 (1.7)	(-6.7, -0.0)	0.048 *
		Placebo	119	94 (79.0)	-6.0 (1.5)	(-9.1, -3.0)			
Female	Week 4	CR845	77	67 (87.0)	-9.9 (1.9)	(-13.7, -6.2)	-2.5 (2.5)	(-7.4, 2.3)	0.301
		Placebo	70	64 (91.4)	-7.4 (2.0)	(-11.3, -3.5)			
Male	Week 8	CR845	112	87 (77.7)	-12.3 (1.7)	(-15.7, -8.9)	-4.8 (1.9)	(-8.6, -1.0)	0.013 *
		Placebo	119	101 (84.9)	-7.5 (1.6)	(-10.7, -4.3)			
Female	Week 8	CR845	77	64 (83.1)	-14.5 (1.9)	(-18.3, -10.7)	-2.9 (2.5)	(-7.9, 2.0)	0.242
		Placebo	70	61 (87.1)	-11.6 (2.0)	(-15.5, -7.7)			
Male	Week 10	CR845	112	90 (80.4)	-13.6 (1.8)	(-17.1, -10.1)	-3.8 (2.0)	(-7.8, 0.1)	0.055
		Placebo	119	102 (85.7)	-9.8 (1.7)	(-13.1, -6.5)			
Female	Week 10	CR845	77	62 (80.5)	-18.5 (2.0)	(-22.6, -14.5)	-4.1 (2.7)	(-9.4, 1.1)	0.122
		Placebo	70	59 (84.3)	-14.4 (2.1)	(-18.5, -10.2)			
Male	Week 12	CR845	112	89 (79.5)	-16.3 (1.8)	(-19.8, -12.8)	-5.7 (2.0)	(-9.6, -1.8)	0.005 *
		Placebo	119	101 (84.9)	-10.6 (1.7)	(-13.9, -7.2)			
Female	Week 12	CR845	77	65 (84.4)	-18.9 (2.0)	(-22.8, -15.0)	-4.2 (2.6)	(-9.3, 0.9)	0.104
		Placebo	70	57 (81.4)	-14.7 (2.1)	(-18.8, -10.6)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table AT2STC_ISCC: Change from baseline in Skindex-10 total score - MMRM results by race
ITT

Change from baseline in Skindex-10 total score					Repeated measures analysis					
					Change from Baseline		Treatment Difference			
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value	
C: Race									0.739	
Black/African American	Week 4	CR845	82	68 (82.9)	-10.5 (1.8)	(-14.1, -6.9)	-4.6 (2.2)	(-9.0, -0.3)	0.037	*
		Placebo	76	64 (84.2)	-5.9 (1.9)	(-9.6, -2.1)				
White	Week 4	CR845	91	79 (86.8)	-9.4 (1.7)	(-12.8, -6.0)	-2.7 (2.0)	(-6.6, 1.3)	0.186	
		Placebo	93	77 (82.8)	-6.7 (1.7)	(-10.1, -3.4)				
Other	Week 4	CR845	15	14 (93.3)	-9.5 (5.2)	(-20.1, 1.1)	-2.6 (5.1)	(-13.0, 7.8)	0.617	
		Placebo	18	16 (88.9)	-6.9 (4.7)	(-16.7, 2.8)				
Black/African American	Week 8	CR845	82	64 (78.0)	-14.3 (1.9)	(-18.1, -10.5)	-4.3 (2.4)	(-8.9, 0.4)	0.072	
		Placebo	76	66 (86.8)	-10.0 (2.0)	(-13.9, -6.1)				
White	Week 8	CR845	91	72 (79.1)	-12.6 (1.9)	(-16.3, -8.9)	-4.3 (2.2)	(-8.7, 0.0)	0.051	
		Placebo	93	79 (84.9)	-8.3 (1.8)	(-11.8, -4.8)				
Other	Week 8	CR845	15	14 (93.3)	-13.6 (5.5)	(-24.7, -2.4)	-6.2 (5.6)	(-17.7, 5.2)	0.272	
		Placebo	18	16 (88.9)	-7.3 (5.0)	(-17.5, 2.9)				
Black/African American	Week 10	CR845	82	63 (76.8)	-17.7 (2.0)	(-21.6, -13.8)	-5.9 (2.4)	(-10.8, -1.1)	0.017	*
		Placebo	76	64 (84.2)	-11.7 (2.0)	(-15.8, -7.7)				
White	Week 10	CR845	91	75 (82.4)	-14.9 (1.9)	(-18.7, -11.0)	-3.1 (2.3)	(-7.7, 1.5)	0.190	
		Placebo	93	79 (84.9)	-11.8 (1.9)	(-15.4, -8.1)				
Other	Week 10	CR845	15	13 (86.7)	-14.2 (5.2)	(-24.8, -3.5)	-7.1 (5.1)	(-17.5, 3.3)	0.172	
		Placebo	18	17 (94.4)	-7.0 (4.8)	(-16.8, 2.7)				
Black/African American	Week 12	CR845	82	63 (76.8)	-18.7 (2.0)	(-22.6, -14.8)	-7.3 (2.5)	(-12.2, -2.5)	0.003	*
		Placebo	76	64 (84.2)	-11.4 (2.0)	(-15.4, -7.3)				
White	Week 12	CR845	91	77 (84.6)	-17.3 (1.9)	(-20.9, -13.6)	-5.1 (2.2)	(-9.5, -0.7)	0.023	*
		Placebo	93	75 (80.6)	-12.2 (1.8)	(-15.7, -8.6)				

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table AT2STC_ISCC: Change from baseline in Skindex-10 total score - MMRM results by race
ITT

Change from baseline in Skindex-10 total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Other	Week 12	CR845	15	13 (86.7)	-15.4 (5.9)	(-27.3, -3.5)	-3.1 (6.2)	(-15.7, 9.5)	0.620
		Placebo	18	18 (100.0)	-12.3 (5.3)	(-23.0, -1.6)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table AT2STC_ISCD: Change from baseline in Skindex-10 total score - MMRM results by baseline WI-NRS
ITT

Change from baseline in Skindex-10 total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
D: Baseline worst itching NRS score (WI-NRS)									0.585
>= 4 to < 7	Week 4	CR845	83	70 (84.3)	-9.8 (1.8)	(-13.3, -6.3)	-4.2 (2.0)	(-8.2, -0.3)	0.037 *
		Placebo	80	66 (82.5)	-5.6 (1.7)	(-9.0, -2.1)			
>= 7	Week 4	CR845	106	92 (86.8)	-9.9 (1.6)	(-13.1, -6.7)	-2.5 (2.0)	(-6.4, 1.3)	0.201
		Placebo	109	92 (84.4)	-7.4 (1.6)	(-10.6, -4.2)			
>= 4 to < 7	Week 8	CR845	83	67 (80.7)	-13.1 (1.8)	(-16.6, -9.6)	-4.3 (2.0)	(-8.2, -0.3)	0.033 *
		Placebo	80	67 (83.8)	-8.9 (1.7)	(-12.2, -5.5)			
>= 7	Week 8	CR845	106	84 (79.2)	-13.5 (1.8)	(-17.0, -9.9)	-3.9 (2.2)	(-8.3, 0.4)	0.077
		Placebo	109	95 (87.2)	-9.5 (1.8)	(-13.0, -6.1)			
>= 4 to < 7	Week 10	CR845	83	68 (81.9)	-14.6 (1.9)	(-18.3, -10.9)	-4.7 (2.1)	(-8.9, -0.5)	0.030 *
		Placebo	80	69 (86.3)	-9.9 (1.8)	(-13.5, -6.4)			
>= 7	Week 10	CR845	106	84 (79.2)	-16.8 (1.9)	(-20.5, -13.2)	-3.8 (2.3)	(-8.4, 0.8)	0.102
		Placebo	109	92 (84.4)	-13.0 (1.8)	(-16.6, -9.4)			
>= 4 to < 7	Week 12	CR845	83	66 (79.5)	-16.1 (1.8)	(-19.6, -12.5)	-6.3 (2.0)	(-10.3, -2.4)	0.002 *
		Placebo	80	68 (85.0)	-9.7 (1.7)	(-13.1, -6.4)			
>= 7	Week 12	CR845	106	88 (83.0)	-18.7 (1.9)	(-22.4, -15.1)	-4.5 (2.3)	(-9.2, 0.1)	0.055
		Placebo	109	90 (82.6)	-14.2 (1.8)	(-17.9, -10.6)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table AT2STC_ISCE: Change from baseline in Skindex-10 total score - MMRM results by specific medical condition
ITT

Change from baseline in Skindex-10 total score					Repeated measures analysis					
					Change from Baseline		Treatment Difference			
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value	
E: Presence of specific medical conditions									0.390	
No	Week 4	CR845	164	139 (84.8)	-10.9 (1.1)	(-13.1, -8.8)	-3.5 (1.5)	(-6.5, -0.5)	0.022	*
		Placebo	161	136 (84.5)	-7.4 (1.1)	(-9.6, -5.3)				
Yes	Week 4	CR845	25	23 (92.0)	-6.9 (2.6)	(-12.0, -1.7)	-0.5 (3.7)	(-8.0, 7.0)	0.895	
		Placebo	28	22 (78.6)	-6.4 (2.6)	(-11.6, -1.1)				
No	Week 8	CR845	164	129 (78.7)	-14.2 (1.2)	(-16.6, -11.8)	-4.5 (1.7)	(-7.7, -1.2)	0.008	*
		Placebo	161	138 (85.7)	-9.8 (1.2)	(-12.1, -7.5)				
Yes	Week 8	CR845	25	22 (88.0)	-11.9 (2.6)	(-17.1, -6.6)	-1.2 (3.7)	(-8.6, 6.2)	0.741	
		Placebo	28	24 (85.7)	-10.6 (2.5)	(-15.7, -5.6)				
No	Week 10	CR845	164	130 (79.3)	-16.7 (1.2)	(-19.1, -14.2)	-5.0 (1.7)	(-8.4, -1.6)	0.004	*
		Placebo	161	139 (86.3)	-11.7 (1.2)	(-14.0, -9.3)				
Yes	Week 10	CR845	25	22 (88.0)	-14.6 (3.1)	(-20.9, -8.2)	2.2 (4.5)	(-6.8, 11.2)	0.629	
		Placebo	28	22 (78.6)	-16.7 (3.1)	(-23.0, -10.5)				
No	Week 12	CR845	164	131 (79.9)	-18.1 (1.2)	(-20.6, -15.7)	-5.7 (1.7)	(-9.1, -2.3)	<0.001	*
		Placebo	161	134 (83.2)	-12.4 (1.2)	(-14.8, -10.0)				
Yes	Week 12	CR845	25	23 (92.0)	-17.9 (2.8)	(-23.6, -12.1)	-1.5 (4.0)	(-9.6, 6.6)	0.712	
		Placebo	28	24 (85.7)	-16.4 (2.8)	(-21.9, -10.8)				

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor previous use of anti-itch medication is also included in the model.
Source Data: askin, created on: 17FEB2022

Table AT2STC_ISCF: Change from baseline in Skindex-10 total score - MMRM results by use of concomitant itch medication
ITT

Change from baseline in Skindex-10 total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
F: Use of concomitant itch medication									0.505
No	Week 4	CR845	117	101 (86.3)	-10.3 (1.6)	(-13.6, -7.1)	-4.2 (1.9)	(-7.8, -0.5)	0.026 *
		Placebo	111	91 (82.0)	-6.2 (1.6)	(-9.4, -2.9)			
Yes	Week 4	CR845	72	61 (84.7)	-9.0 (1.8)	(-12.5, -5.6)	-1.6 (2.2)	(-5.9, 2.6)	0.451
		Placebo	78	67 (85.9)	-7.4 (1.8)	(-10.9, -3.9)			
No	Week 8	CR845	117	97 (82.9)	-14.6 (1.7)	(-18.0, -11.2)	-5.9 (2.0)	(-9.8, -2.0)	0.003 *
		Placebo	111	97 (87.4)	-8.7 (1.7)	(-12.0, -5.4)			
Yes	Week 8	CR845	72	54 (75.0)	-11.2 (1.9)	(-15.0, -7.4)	-1.0 (2.4)	(-5.8, 3.7)	0.668
		Placebo	78	65 (83.3)	-10.1 (1.9)	(-13.8, -6.4)			
No	Week 10	CR845	117	96 (82.1)	-15.4 (1.8)	(-19.0, -11.9)	-3.4 (2.1)	(-7.5, 0.7)	0.106
		Placebo	111	97 (87.4)	-12.1 (1.8)	(-15.5, -8.6)			
Yes	Week 10	CR845	72	56 (77.8)	-16.5 (2.0)	(-20.4, -12.6)	-5.2 (2.5)	(-10.1, -0.3)	0.039 *
		Placebo	78	64 (82.1)	-11.3 (1.9)	(-15.1, -7.5)			
No	Week 12	CR845	117	97 (82.9)	-17.7 (1.7)	(-21.1, -14.2)	-4.7 (2.0)	(-8.7, -0.8)	0.018 *
		Placebo	111	97 (87.4)	-12.9 (1.7)	(-16.3, -9.6)			
Yes	Week 12	CR845	72	57 (79.2)	-17.4 (2.0)	(-21.4, -13.4)	-6.0 (2.6)	(-11.0, -0.9)	0.022 *
		Placebo	78	61 (78.2)	-11.5 (2.0)	(-15.4, -7.5)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor presence of medical condition is also included in the model.
Source Data: askin, created on: 17FEB2022

Table AT2SDC_ISCA: Change from baseline in Skindex-10 disease score - MMRM results by age
ITT

Change from baseline in Skindex-10 disease score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
A: Age									0.056
< 65 years	Week 4	CR845	135	116 (85.9)	-3.2 (0.4)	(-4.0, -2.4)	-1.7 (0.5)	(-2.6, -0.7)	<0.001 *
		Placebo	137	115 (83.9)	-1.5 (0.4)	(-2.4, -0.7)			
>= 65 years	Week 4	CR845	54	50 (92.6)	-3.6 (0.7)	(-5.0, -2.1)	0.0 (0.9)	(-1.8, 1.8)	0.980
		Placebo	52	48 (92.3)	-3.6 (0.7)	(-5.0, -2.2)			
< 65 years	Week 8	CR845	135	108 (80.0)	-4.2 (0.5)	(-5.2, -3.3)	-1.7 (0.6)	(-2.9, -0.5)	0.004 *
		Placebo	137	119 (86.9)	-2.5 (0.5)	(-3.5, -1.6)			
>= 65 years	Week 8	CR845	54	48 (88.9)	-5.2 (0.7)	(-6.7, -3.8)	-0.7 (0.9)	(-2.4, 1.0)	0.412
		Placebo	52	48 (92.3)	-4.5 (0.7)	(-5.9, -3.2)			
< 65 years	Week 10	CR845	135	108 (80.0)	-5.1 (0.5)	(-6.1, -4.1)	-1.9 (0.6)	(-3.1, -0.7)	0.002 *
		Placebo	137	116 (84.7)	-3.2 (0.5)	(-4.2, -2.2)			
>= 65 years	Week 10	CR845	54	46 (85.2)	-5.6 (0.8)	(-7.2, -4.0)	-0.2 (1.0)	(-2.2, 1.8)	0.840
		Placebo	52	48 (92.3)	-5.4 (0.8)	(-6.9, -3.9)			
< 65 years	Week 12	CR845	135	110 (81.5)	-6.0 (0.5)	(-7.0, -5.1)	-2.8 (0.6)	(-3.9, -1.6)	<0.001 *
		Placebo	137	115 (83.9)	-3.3 (0.5)	(-4.2, -2.3)			
>= 65 years	Week 12	CR845	54	47 (87.0)	-5.9 (0.8)	(-7.5, -4.3)	-0.1 (1.0)	(-2.0, 1.8)	0.912
		Placebo	52	46 (88.5)	-5.8 (0.8)	(-7.3, -4.3)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table AT2SDC_ISCB: Change from baseline in Skindex-10 disease score - MMRM results by sex
ITT

Change from baseline in Skindex-10 disease score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
B: Sex									0.683
Male	Week 4	CR845	112	96 (85.7)	-2.9 (0.5)	(-3.9, -1.9)	-1.3 (0.5)	(-2.4, -0.3)	0.015 *
		Placebo	119	99 (83.2)	-1.6 (0.5)	(-2.5, -0.7)			
Female	Week 4	CR845	77	70 (90.9)	-3.8 (0.6)	(-5.0, -2.7)	-1.0 (0.7)	(-2.4, 0.5)	0.198
		Placebo	70	64 (91.4)	-2.9 (0.6)	(-4.1, -1.7)			
Male	Week 8	CR845	112	89 (79.5)	-4.2 (0.5)	(-5.3, -3.2)	-1.7 (0.6)	(-2.9, -0.4)	0.008 *
		Placebo	119	106 (89.1)	-2.6 (0.5)	(-3.6, -1.6)			
Female	Week 8	CR845	77	67 (87.0)	-5.0 (0.6)	(-6.1, -3.8)	-1.0 (0.8)	(-2.5, 0.6)	0.208
		Placebo	70	61 (87.1)	-4.0 (0.6)	(-5.2, -2.7)			
Male	Week 10	CR845	112	90 (80.4)	-4.4 (0.6)	(-5.5, -3.3)	-1.1 (0.6)	(-2.4, 0.2)	0.088
		Placebo	119	105 (88.2)	-3.3 (0.5)	(-4.4, -2.3)			
Female	Week 10	CR845	77	64 (83.1)	-6.4 (0.7)	(-7.7, -5.1)	-1.8 (0.9)	(-3.5, -0.1)	0.039 *
		Placebo	70	59 (84.3)	-4.6 (0.7)	(-5.9, -3.2)			
Male	Week 12	CR845	112	90 (80.4)	-5.6 (0.6)	(-6.7, -4.5)	-2.1 (0.6)	(-3.3, -0.8)	0.001 *
		Placebo	119	104 (87.4)	-3.6 (0.5)	(-4.6, -2.6)			
Female	Week 12	CR845	77	67 (87.0)	-6.4 (0.6)	(-7.7, -5.2)	-1.8 (0.9)	(-3.5, -0.1)	0.037 *
		Placebo	70	57 (81.4)	-4.6 (0.7)	(-6.0, -3.3)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table AT2SDC_ISCC: Change from baseline in Skindex-10 disease score - MMRM results by race
ITT

Change from baseline in Skindex-10 disease score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
C: Race									0.583
Black/African American	Week 4	CR845	82	69 (84.1)	-3.4 (0.6)	(-4.5, -2.2)	-1.6 (0.7)	(-3.0, -0.2)	0.021 *
		Placebo	76	65 (85.5)	-1.7 (0.6)	(-2.9, -0.5)			
White	Week 4	CR845	91	82 (90.1)	-3.2 (0.5)	(-4.3, -2.2)	-0.9 (0.6)	(-2.1, 0.3)	0.142
		Placebo	93	80 (86.0)	-2.3 (0.5)	(-3.3, -1.4)			
Other	Week 4	CR845	15	14 (93.3)	-3.6 (1.6)	(-7.0, -0.3)	-0.8 (1.6)	(-4.2, 2.5)	0.622
		Placebo	18	16 (88.9)	-2.8 (1.5)	(-5.8, 0.2)			
Black/African American	Week 8	CR845	82	66 (80.5)	-4.7 (0.6)	(-5.9, -3.4)	-1.4 (0.8)	(-2.9, 0.1)	0.069
		Placebo	76	68 (89.5)	-3.3 (0.6)	(-4.5, -2.0)			
White	Week 8	CR845	91	75 (82.4)	-4.4 (0.6)	(-5.5, -3.3)	-1.5 (0.7)	(-2.8, -0.1)	0.037 *
		Placebo	93	81 (87.1)	-2.9 (0.5)	(-4.0, -1.9)			
Other	Week 8	CR845	15	14 (93.3)	-4.9 (1.7)	(-8.4, -1.4)	-1.3 (1.8)	(-5.0, 2.3)	0.463
		Placebo	18	16 (88.9)	-3.5 (1.6)	(-6.7, -0.3)			
Black/African American	Week 10	CR845	82	63 (76.8)	-5.3 (0.7)	(-6.7, -4.0)	-1.6 (0.8)	(-3.3, 0.0)	0.055
		Placebo	76	65 (85.5)	-3.7 (0.7)	(-5.0, -2.4)			
White	Week 10	CR845	91	77 (84.6)	-5.4 (0.6)	(-6.5, -4.2)	-1.4 (0.7)	(-2.9, -0.0)	0.048 *
		Placebo	93	80 (86.0)	-3.9 (0.6)	(-5.0, -2.8)			
Other	Week 10	CR845	15	13 (86.7)	-4.9 (1.7)	(-8.4, -1.4)	-1.1 (1.8)	(-4.8, 2.5)	0.536
		Placebo	18	17 (94.4)	-3.8 (1.6)	(-7.0, -0.6)			
Black/African American	Week 12	CR845	82	64 (78.0)	-6.0 (0.7)	(-7.3, -4.7)	-2.4 (0.9)	(-4.1, -0.7)	0.006 *
		Placebo	76	66 (86.8)	-3.6 (0.7)	(-5.0, -2.2)			
White	Week 12	CR845	91	79 (86.8)	-6.2 (0.6)	(-7.4, -5.1)	-2.3 (0.7)	(-3.6, -0.9)	0.001 *
		Placebo	93	76 (81.7)	-4.0 (0.5)	(-5.1, -2.9)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table AT2SDC_ISCC: Change from baseline in Skindex-10 disease score - MMRM results by race
ITT

Change from baseline in Skindex-10 disease score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Other	Week 12	CR845	15	13 (86.7)	-5.1 (1.8)	(-8.7, -1.4)	0.5 (1.9)	(-3.4, 4.4)	0.799
		Placebo	18	18 (100.0)	-5.5 (1.6)	(-8.8, -2.3)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table AT2SDC_ISCD: Change from baseline in Skindex-10 disease score - MMRM results by baseline WI-NRS
ITT

Change from baseline in Skindex-10 disease score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
D: Baseline worst itching NRS score (WI-NRS)									0.609
>= 4 to < 7	Week 4	CR845	83	72 (86.7)	-3.5 (0.6)	(-4.6, -2.3)	-1.5 (0.7)	(-2.8, -0.2)	0.021 *
		Placebo	80	68 (85.0)	-1.9 (0.6)	(-3.1, -0.8)			
>= 7	Week 4	CR845	106	94 (88.7)	-3.4 (0.5)	(-4.3, -2.4)	-1.0 (0.6)	(-2.2, 0.2)	0.091
		Placebo	109	95 (87.2)	-2.4 (0.5)	(-3.3, -1.4)			
>= 4 to < 7	Week 8	CR845	83	69 (83.1)	-4.8 (0.6)	(-6.0, -3.6)	-1.8 (0.7)	(-3.2, -0.5)	0.008 *
		Placebo	80	69 (86.3)	-3.0 (0.6)	(-4.1, -1.8)			
>= 7	Week 8	CR845	106	87 (82.1)	-4.5 (0.5)	(-5.5, -3.4)	-1.1 (0.7)	(-2.4, 0.2)	0.092
		Placebo	109	98 (89.9)	-3.4 (0.5)	(-4.4, -2.3)			
>= 4 to < 7	Week 10	CR845	83	69 (83.1)	-5.0 (0.6)	(-6.2, -3.8)	-1.3 (0.7)	(-2.7, 0.1)	0.069
		Placebo	80	69 (86.3)	-3.7 (0.6)	(-4.9, -2.5)			
>= 7	Week 10	CR845	106	85 (80.2)	-5.6 (0.6)	(-6.8, -4.5)	-1.6 (0.7)	(-3.0, -0.2)	0.031 *
		Placebo	109	95 (87.2)	-4.0 (0.6)	(-5.1, -3.0)			
>= 4 to < 7	Week 12	CR845	83	67 (80.7)	-5.6 (0.6)	(-6.8, -4.4)	-1.9 (0.7)	(-3.3, -0.6)	0.006 *
		Placebo	80	69 (86.3)	-3.7 (0.6)	(-4.8, -2.5)			
>= 7	Week 12	CR845	106	90 (84.9)	-6.5 (0.6)	(-7.6, -5.3)	-2.1 (0.7)	(-3.5, -0.6)	0.005 *
		Placebo	109	92 (84.4)	-4.4 (0.6)	(-5.5, -3.3)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table AT2SDC_ISCE: Change from baseline in Skindex-10 disease score - MMRM results by specific medical condition
ITT

Change from baseline in Skindex-10 disease score					Repeated measures analysis					
					Change from Baseline		Treatment Difference			
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value	
E: Presence of specific medical conditions									0.870	
No	Week 4	CR845	164	142 (86.6)	-3.8 (0.3)	(-4.4, -3.1)	-1.3 (0.5)	(-2.2, -0.3)	0.008	*
		Placebo	161	137 (85.1)	-2.5 (0.3)	(-3.2, -1.8)				
Yes	Week 4	CR845	25	24 (96.0)	-2.5 (0.7)	(-4.0, -1.1)	-0.4 (1.0)	(-2.4, 1.7)	0.731	
		Placebo	28	26 (92.9)	-2.2 (0.7)	(-3.6, -0.8)				
No	Week 8	CR845	164	133 (81.1)	-4.9 (0.4)	(-5.7, -4.1)	-1.4 (0.5)	(-2.5, -0.4)	0.008	*
		Placebo	161	140 (87.0)	-3.5 (0.4)	(-4.2, -2.7)				
Yes	Week 8	CR845	25	23 (92.0)	-4.3 (0.8)	(-5.9, -2.6)	-0.9 (1.1)	(-3.2, 1.4)	0.446	
		Placebo	28	27 (96.4)	-3.4 (0.8)	(-4.9, -1.9)				
No	Week 10	CR845	164	132 (80.5)	-5.7 (0.4)	(-6.4, -4.9)	-1.6 (0.6)	(-2.7, -0.5)	0.004	*
		Placebo	161	140 (87.0)	-4.0 (0.4)	(-4.8, -3.3)				
Yes	Week 10	CR845	25	22 (88.0)	-4.7 (1.1)	(-6.9, -2.5)	0.3 (1.5)	(-2.7, 3.3)	0.851	
		Placebo	28	24 (85.7)	-5.0 (1.0)	(-7.0, -2.9)				
No	Week 12	CR845	164	133 (81.1)	-6.2 (0.4)	(-7.0, -5.4)	-1.9 (0.6)	(-3.0, -0.8)	<0.001	*
		Placebo	161	135 (83.9)	-4.3 (0.4)	(-5.1, -3.5)				
Yes	Week 12	CR845	25	24 (96.0)	-6.6 (0.9)	(-8.5, -4.7)	-1.9 (1.3)	(-4.6, 0.7)	0.145	
		Placebo	28	26 (92.9)	-4.6 (0.9)	(-6.4, -2.9)				

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor previous use of anti-itch medication is also included in the model.
Source Data: askin, created on: 17FEB2022

Table AT2SDC_ISCF: Change from baseline in Skindex-10 disease score - MMRM results by use of concomitant itch medication
ITT

Change from baseline in Skindex-10 disease score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
F: Use of concomitant itch medication									0.567
No	Week 4	CR845	117	105 (89.7)	-3.3 (0.5)	(-4.2, -2.4)	-1.4 (0.6)	(-2.5, -0.2)	0.017 *
		Placebo	111	92 (82.9)	-1.9 (0.5)	(-2.9, -1.0)			
Yes	Week 4	CR845	72	61 (84.7)	-3.4 (0.6)	(-4.5, -2.3)	-1.0 (0.7)	(-2.4, 0.4)	0.147
		Placebo	78	71 (91.0)	-2.4 (0.5)	(-3.5, -1.3)			
No	Week 8	CR845	117	100 (85.5)	-4.9 (0.5)	(-5.9, -3.9)	-2.1 (0.6)	(-3.3, -0.9)	<0.001 *
		Placebo	111	98 (88.3)	-2.8 (0.5)	(-3.9, -1.8)			
Yes	Week 8	CR845	72	56 (77.8)	-3.9 (0.6)	(-5.2, -2.7)	-0.4 (0.8)	(-1.9, 1.2)	0.638
		Placebo	78	69 (88.5)	-3.5 (0.6)	(-4.7, -2.4)			
No	Week 10	CR845	117	98 (83.8)	-5.1 (0.5)	(-6.2, -4.0)	-1.4 (0.7)	(-2.7, -0.0)	0.042 *
		Placebo	111	97 (87.4)	-3.7 (0.5)	(-4.8, -2.7)			
Yes	Week 10	CR845	72	56 (77.8)	-5.7 (0.7)	(-7.0, -4.3)	-1.7 (0.8)	(-3.3, -0.0)	0.050 *
		Placebo	78	67 (85.9)	-4.0 (0.6)	(-5.2, -2.8)			
No	Week 12	CR845	117	100 (85.5)	-6.1 (0.5)	(-7.1, -5.0)	-1.8 (0.6)	(-3.0, -0.5)	0.005 *
		Placebo	111	97 (87.4)	-4.3 (0.5)	(-5.3, -3.2)			
Yes	Week 12	CR845	72	57 (79.2)	-6.0 (0.7)	(-7.3, -4.6)	-2.4 (0.9)	(-4.1, -0.6)	0.008 *
		Placebo	78	64 (82.1)	-3.6 (0.7)	(-4.9, -2.3)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor presence of medical condition is also included in the model.
Source Data: askin, created on: 17FEB2022

Table AT2SMC_ISCA: Change from baseline in Skindex-10 mood/emotional distress score - MMRM results by age
ITT

Change from baseline in Skindex-10 mood/emotional distress score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
A: Age									0.163
< 65 years	Week 4	CR845	135	115 (85.2)	-2.9 (0.5)	(-3.8, -1.9)	-1.2 (0.6)	(-2.3, -0.1)	0.034 *
		Placebo	137	114 (83.2)	-1.7 (0.5)	(-2.6, -0.7)			
>= 65 years	Week 4	CR845	54	50 (92.6)	-3.0 (0.8)	(-4.7, -1.4)	-0.0 (1.0)	(-2.0, 2.0)	0.990
		Placebo	52	47 (90.4)	-3.0 (0.8)	(-4.6, -1.4)			
< 65 years	Week 8	CR845	135	106 (78.5)	-4.4 (0.5)	(-5.4, -3.4)	-2.0 (0.6)	(-3.2, -0.7)	0.002 *
		Placebo	137	117 (85.4)	-2.4 (0.5)	(-3.4, -1.4)			
>= 65 years	Week 8	CR845	54	48 (88.9)	-4.9 (0.8)	(-6.5, -3.2)	-1.0 (1.0)	(-2.9, 0.9)	0.304
		Placebo	52	48 (92.3)	-3.9 (0.8)	(-5.4, -2.3)			
< 65 years	Week 10	CR845	135	108 (80.0)	-5.5 (0.5)	(-6.5, -4.5)	-2.5 (0.6)	(-3.7, -1.2)	<0.001 *
		Placebo	137	116 (84.7)	-3.0 (0.5)	(-4.0, -2.0)			
>= 65 years	Week 10	CR845	54	45 (83.3)	-5.1 (0.8)	(-6.8, -3.4)	-0.1 (1.0)	(-2.1, 1.8)	0.897
		Placebo	52	48 (92.3)	-5.0 (0.8)	(-6.6, -3.4)			
< 65 years	Week 12	CR845	135	109 (80.7)	-5.9 (0.5)	(-6.9, -4.9)	-2.6 (0.6)	(-3.8, -1.3)	<0.001 *
		Placebo	137	116 (84.7)	-3.3 (0.5)	(-4.4, -2.3)			
>= 65 years	Week 12	CR845	54	47 (87.0)	-5.8 (0.8)	(-7.4, -4.1)	-0.9 (1.0)	(-2.9, 1.0)	0.352
		Placebo	52	47 (90.4)	-4.9 (0.8)	(-6.4, -3.3)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table AT2SMC_ISCB: Change from baseline in Skindex-10 mood/emotional distress score - MMRM results by sex
ITT

Change from baseline in Skindex-10 mood/emotional distress score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
B: Sex									0.362
Male	Week 4	CR845	112	96 (85.7)	-3.2 (0.5)	(-4.3, -2.2)	-1.3 (0.6)	(-2.4, -0.1)	0.035 *
		Placebo	119	97 (81.5)	-2.0 (0.5)	(-3.0, -1.0)			
Female	Week 4	CR845	77	69 (89.6)	-2.5 (0.6)	(-3.8, -1.3)	-0.5 (0.8)	(-2.2, 1.2)	0.566
		Placebo	70	64 (91.4)	-2.0 (0.7)	(-3.4, -0.7)			
Male	Week 8	CR845	112	88 (78.6)	-4.3 (0.6)	(-5.5, -3.1)	-1.9 (0.7)	(-3.2, -0.6)	0.004 *
		Placebo	119	103 (86.6)	-2.4 (0.6)	(-3.5, -1.3)			
Female	Week 8	CR845	77	66 (85.7)	-4.9 (0.7)	(-6.2, -3.6)	-1.4 (0.9)	(-3.1, 0.3)	0.108
		Placebo	70	62 (88.6)	-3.5 (0.7)	(-4.9, -2.1)			
Male	Week 10	CR845	112	90 (80.4)	-5.0 (0.6)	(-6.2, -3.8)	-1.9 (0.7)	(-3.2, -0.5)	0.006 *
		Placebo	119	104 (87.4)	-3.1 (0.6)	(-4.2, -2.0)			
Female	Week 10	CR845	77	63 (81.8)	-6.0 (0.7)	(-7.4, -4.7)	-1.8 (0.9)	(-3.6, -0.0)	0.047 *
		Placebo	70	60 (85.7)	-4.2 (0.7)	(-5.6, -2.9)			
Male	Week 12	CR845	112	89 (79.5)	-5.8 (0.6)	(-7.0, -4.7)	-2.5 (0.7)	(-3.9, -1.2)	<0.001 *
		Placebo	119	103 (86.6)	-3.3 (0.6)	(-4.4, -2.2)			
Female	Week 12	CR845	77	67 (87.0)	-6.0 (0.7)	(-7.3, -4.7)	-1.5 (0.9)	(-3.3, 0.2)	0.087
		Placebo	70	60 (85.7)	-4.5 (0.7)	(-5.9, -3.1)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table AT2SMC_ISCC: Change from baseline in Skindex-10 mood/emotional distress score - MMRM results by race
ITT

Change from baseline in Skindex-10 mood/emotional distress score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
C: Race									0.451
Black/African American	Week 4	CR845	82	69 (84.1)	-3.1 (0.6)	(-4.4, -1.9)	-1.6 (0.8)	(-3.2, 0.0)	0.054
		Placebo	76	66 (86.8)	-1.6 (0.7)	(-2.9, -0.2)			
White	Week 4	CR845	91	81 (89.0)	-2.9 (0.6)	(-4.0, -1.7)	-0.6 (0.7)	(-1.9, 0.7)	0.379
		Placebo	93	77 (82.8)	-2.3 (0.6)	(-3.4, -1.2)			
Other	Week 4	CR845	15	14 (93.3)	-2.8 (1.7)	(-6.2, 0.6)	-1.0 (1.6)	(-4.4, 2.3)	0.543
		Placebo	18	16 (88.9)	-1.8 (1.5)	(-4.9, 1.3)			
Black/African American	Week 8	CR845	82	66 (80.5)	-5.1 (0.7)	(-6.5, -3.8)	-2.1 (0.9)	(-3.8, -0.4)	0.014 *
		Placebo	76	67 (88.2)	-3.0 (0.7)	(-4.4, -1.6)			
White	Week 8	CR845	91	73 (80.2)	-4.3 (0.6)	(-5.5, -3.1)	-1.7 (0.7)	(-3.1, -0.2)	0.026 *
		Placebo	93	79 (84.9)	-2.7 (0.6)	(-3.8, -1.5)			
Other	Week 8	CR845	15	14 (93.3)	-3.1 (1.8)	(-6.8, 0.6)	-1.5 (1.9)	(-5.4, 2.3)	0.421
		Placebo	18	17 (94.4)	-1.5 (1.7)	(-4.9, 1.8)			
Black/African American	Week 10	CR845	82	64 (78.0)	-6.3 (0.7)	(-7.6, -4.9)	-2.9 (0.9)	(-4.6, -1.2)	0.001 *
		Placebo	76	66 (86.8)	-3.4 (0.7)	(-4.8, -2.0)			
White	Week 10	CR845	91	75 (82.4)	-5.0 (0.6)	(-6.2, -3.8)	-1.1 (0.8)	(-2.6, 0.4)	0.158
		Placebo	93	79 (84.9)	-3.9 (0.6)	(-5.1, -2.7)			
Other	Week 10	CR845	15	13 (86.7)	-4.0 (1.6)	(-7.3, -0.7)	-2.8 (1.5)	(-5.9, 0.3)	0.076
		Placebo	18	17 (94.4)	-1.2 (1.5)	(-4.3, 1.8)			
Black/African American	Week 12	CR845	82	65 (79.3)	-6.6 (0.7)	(-7.9, -5.3)	-3.1 (0.8)	(-4.8, -1.5)	<0.001 *
		Placebo	76	65 (85.5)	-3.5 (0.7)	(-4.9, -2.1)			
White	Week 12	CR845	91	77 (84.6)	-5.5 (0.6)	(-6.8, -4.3)	-1.9 (0.7)	(-3.3, -0.4)	0.013 *
		Placebo	93	78 (83.9)	-3.7 (0.6)	(-4.9, -2.5)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table AT2SMC_ISCC: Change from baseline in Skindex-10 mood/emotional distress score - MMRM results by race
ITT

Change from baseline in Skindex-10 mood/emotional distress score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Other	Week 12	CR845	15	13 (86.7)	-4.9 (2.0)	(-8.9, -0.9)	-1.8 (2.1)	(-6.1, 2.6)	0.412
		Placebo	18	18 (100.0)	-3.1 (1.8)	(-6.7, 0.4)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table AT2SMC_ISCD: Change from baseline in Skindex-10 mood/emotional distress score - MMRM results by baseline WI-NRS
ITT

Change from baseline in Skindex-10 mood/emotional distress score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
D: Baseline worst itching NRS score (WI-NRS)									0.831
>= 4 to < 7	Week 4	CR845	83	72 (86.7)	-3.3 (0.6)	(-4.6, -2.1)	-1.4 (0.7)	(-2.7, 0.0)	0.056
		Placebo	80	67 (83.8)	-2.0 (0.6)	(-3.2, -0.8)			
>= 7	Week 4	CR845	106	93 (87.7)	-2.8 (0.5)	(-3.9, -1.7)	-0.7 (0.7)	(-2.0, 0.6)	0.300
		Placebo	109	94 (86.2)	-2.1 (0.5)	(-3.2, -1.0)			
>= 4 to < 7	Week 8	CR845	83	68 (81.9)	-4.8 (0.6)	(-6.1, -3.6)	-1.3 (0.7)	(-2.8, 0.1)	0.070
		Placebo	80	68 (85.0)	-3.5 (0.6)	(-4.7, -2.3)			
>= 7	Week 8	CR845	106	86 (81.1)	-4.5 (0.6)	(-5.7, -3.3)	-2.1 (0.7)	(-3.6, -0.7)	0.005 *
		Placebo	109	97 (89.0)	-2.4 (0.6)	(-3.5, -1.3)			
>= 4 to < 7	Week 10	CR845	83	68 (81.9)	-5.3 (0.6)	(-6.6, -4.1)	-1.7 (0.7)	(-3.2, -0.3)	0.017 *
		Placebo	80	69 (86.3)	-3.6 (0.6)	(-4.8, -2.4)			
>= 7	Week 10	CR845	106	85 (80.2)	-5.6 (0.6)	(-6.8, -4.4)	-2.0 (0.8)	(-3.5, -0.5)	0.009 *
		Placebo	109	95 (87.2)	-3.6 (0.6)	(-4.8, -2.4)			
>= 4 to < 7	Week 12	CR845	83	66 (79.5)	-5.7 (0.6)	(-6.9, -4.4)	-2.5 (0.7)	(-3.9, -1.0)	<0.001 *
		Placebo	80	70 (87.5)	-3.2 (0.6)	(-4.4, -2.0)			
>= 7	Week 12	CR845	106	90 (84.9)	-6.2 (0.6)	(-7.4, -5.0)	-2.0 (0.8)	(-3.5, -0.5)	0.010 *
		Placebo	109	93 (85.3)	-4.2 (0.6)	(-5.4, -3.0)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table AT2SMC_ISCE: Change from baseline in Skindex-10 mood/emotional distress score - MMRM results by specific medical condition
ITT

Change from baseline in Skindex-10 mood/emotional distress score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
E: Presence of specific medical conditions									0.284
No	Week 4	CR845	164	141 (86.0)	-3.4 (0.4)	(-4.2, -2.7)	-1.1 (0.5)	(-2.2, -0.1)	0.033 *
		Placebo	161	138 (85.7)	-2.3 (0.4)	(-3.0, -1.5)			
Yes	Week 4	CR845	25	24 (96.0)	-1.8 (0.9)	(-3.8, 0.1)	0.3 (1.4)	(-2.4, 3.1)	0.801
		Placebo	28	23 (82.1)	-2.2 (1.0)	(-4.1, -0.3)			
No	Week 8	CR845	164	131 (79.9)	-4.9 (0.4)	(-5.7, -4.0)	-1.8 (0.6)	(-3.0, -0.7)	0.002 *
		Placebo	161	140 (87.0)	-3.1 (0.4)	(-3.9, -2.2)			
Yes	Week 8	CR845	25	23 (92.0)	-4.2 (0.9)	(-6.0, -2.5)	-0.9 (1.2)	(-3.4, 1.6)	0.455
		Placebo	28	25 (89.3)	-3.3 (0.8)	(-5.0, -1.6)			
No	Week 10	CR845	164	131 (79.9)	-5.8 (0.4)	(-6.6, -5.0)	-2.1 (0.6)	(-3.2, -0.9)	<0.001 *
		Placebo	161	141 (87.6)	-3.7 (0.4)	(-4.5, -2.9)			
Yes	Week 10	CR845	25	22 (88.0)	-4.8 (1.1)	(-7.1, -2.6)	-0.1 (1.6)	(-3.3, 3.0)	0.932
		Placebo	28	23 (82.1)	-4.7 (1.1)	(-6.9, -2.5)			
No	Week 12	CR845	164	132 (80.5)	-6.3 (0.4)	(-7.1, -5.4)	-2.4 (0.6)	(-3.5, -1.3)	<0.001 *
		Placebo	161	137 (85.1)	-3.9 (0.4)	(-4.7, -3.1)			
Yes	Week 12	CR845	25	24 (96.0)	-5.5 (1.0)	(-7.7, -3.4)	-0.4 (1.5)	(-3.4, 2.5)	0.771
		Placebo	28	26 (92.9)	-5.1 (1.0)	(-7.1, -3.1)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor previous use of anti-itch medication is also included in the model.
Source Data: askin, created on: 17FEB2022

Table AT2SMC_ISCF: Change from baseline in Skindex-10 mood/emotional distress score - MMRM results by use of concomitant itch medication
ITT

Change from baseline in Skindex-10 mood/emotional distress score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
F: Use of concomitant itch medication									0.905
No	Week 4	CR845	117	104 (88.9)	-3.2 (0.5)	(-4.2, -2.1)	-1.1 (0.6)	(-2.3, 0.1)	0.078
		Placebo	111	92 (82.9)	-2.1 (0.5)	(-3.1, -1.0)			
Yes	Week 4	CR845	72	61 (84.7)	-2.6 (0.7)	(-3.9, -1.3)	-0.7 (0.8)	(-2.3, 0.9)	0.407
		Placebo	78	69 (88.5)	-1.9 (0.6)	(-3.2, -0.6)			
No	Week 8	CR845	117	98 (83.8)	-4.9 (0.6)	(-6.0, -3.8)	-2.1 (0.7)	(-3.4, -0.8)	0.001 *
		Placebo	111	98 (88.3)	-2.8 (0.6)	(-3.9, -1.7)			
Yes	Week 8	CR845	72	56 (77.8)	-3.9 (0.7)	(-5.4, -2.5)	-1.2 (0.9)	(-3.0, 0.6)	0.184
		Placebo	78	67 (85.9)	-2.7 (0.7)	(-4.1, -1.4)			
No	Week 10	CR845	117	96 (82.1)	-5.3 (0.6)	(-6.5, -4.2)	-1.4 (0.7)	(-2.8, -0.1)	0.036 *
		Placebo	111	97 (87.4)	-3.9 (0.6)	(-5.0, -2.8)			
Yes	Week 10	CR845	72	57 (79.2)	-5.6 (0.7)	(-7.0, -4.1)	-2.5 (0.9)	(-4.3, -0.7)	0.006 *
		Placebo	78	67 (85.9)	-3.1 (0.7)	(-4.4, -1.7)			
No	Week 12	CR845	117	98 (83.8)	-5.8 (0.6)	(-6.9, -4.7)	-1.8 (0.7)	(-3.1, -0.5)	0.006 *
		Placebo	111	99 (89.2)	-4.0 (0.5)	(-5.1, -2.9)			
Yes	Week 12	CR845	72	58 (80.6)	-6.0 (0.7)	(-7.5, -4.6)	-2.7 (0.9)	(-4.5, -0.8)	0.005 *
		Placebo	78	64 (82.1)	-3.4 (0.7)	(-4.8, -2.0)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor presence of medical condition is also included in the model.
Source Data: askin, created on: 17FEB2022

Table AT2SSC_ISCA: Change from baseline in Skindex-10 social functioning score - MMRM results by age
ITT

Change from baseline in Skindex-10 social functioning score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
A: Age									0.555
< 65 years	Week 4	CR845	135	117 (86.7)	-3.0 (0.6)	(-4.2, -1.8)	-1.2 (0.7)	(-2.6, 0.3)	0.117
		Placebo	137	115 (83.9)	-1.8 (0.6)	(-3.1, -0.6)			
>= 65 years	Week 4	CR845	54	48 (88.9)	-4.3 (1.1)	(-6.5, -2.0)	-1.5 (1.4)	(-4.2, 1.2)	0.261
		Placebo	52	48 (92.3)	-2.7 (1.1)	(-4.9, -0.6)			
< 65 years	Week 8	CR845	135	107 (79.3)	-3.6 (0.7)	(-4.9, -2.3)	-1.5 (0.8)	(-3.1, 0.1)	0.070
		Placebo	137	118 (86.1)	-2.1 (0.7)	(-3.5, -0.8)			
>= 65 years	Week 8	CR845	54	47 (87.0)	-5.6 (1.1)	(-7.7, -3.5)	-1.0 (1.3)	(-3.5, 1.5)	0.415
		Placebo	52	49 (94.2)	-4.6 (1.0)	(-6.6, -2.6)			
< 65 years	Week 10	CR845	135	109 (80.7)	-4.7 (0.7)	(-6.1, -3.4)	-1.8 (0.8)	(-3.5, -0.2)	0.028 *
		Placebo	137	116 (84.7)	-2.9 (0.7)	(-4.3, -1.5)			
>= 65 years	Week 10	CR845	54	46 (85.2)	-5.5 (1.1)	(-7.6, -3.4)	0.5 (1.2)	(-1.9, 3.0)	0.671
		Placebo	52	48 (92.3)	-6.0 (1.0)	(-8.0, -4.1)			
< 65 years	Week 12	CR845	135	111 (82.2)	-5.1 (0.7)	(-6.4, -3.8)	-1.7 (0.8)	(-3.3, -0.1)	0.038 *
		Placebo	137	116 (84.7)	-3.4 (0.7)	(-4.7, -2.1)			
>= 65 years	Week 12	CR845	54	46 (85.2)	-6.3 (1.1)	(-8.5, -4.2)	-0.7 (1.3)	(-3.3, 1.8)	0.562
		Placebo	52	48 (92.3)	-5.6 (1.0)	(-7.6, -3.6)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table AT2SSC_ISCB: Change from baseline in Skindex-10 social functioning score - MMRM results by sex
ITT

Change from baseline in Skindex-10 social functioning score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
B: Sex									0.745
Male	Week 4	CR845	112	97 (86.6)	-3.2 (0.7)	(-4.6, -1.8)	-1.2 (0.8)	(-2.8, 0.3)	0.110
		Placebo	119	98 (82.4)	-1.9 (0.7)	(-3.3, -0.6)			
Female	Week 4	CR845	77	68 (88.3)	-3.5 (0.9)	(-5.2, -1.8)	-1.3 (1.1)	(-3.6, 1.0)	0.261
		Placebo	70	65 (92.9)	-2.2 (0.9)	(-4.0, -0.4)			
Male	Week 8	CR845	112	89 (79.5)	-3.8 (0.8)	(-5.3, -2.2)	-1.5 (0.9)	(-3.3, 0.2)	0.081
		Placebo	119	104 (87.4)	-2.2 (0.7)	(-3.7, -0.8)			
Female	Week 8	CR845	77	65 (84.4)	-4.7 (0.9)	(-6.4, -3.0)	-1.0 (1.1)	(-3.2, 1.2)	0.352
		Placebo	70	63 (90.0)	-3.6 (0.9)	(-5.4, -1.9)			
Male	Week 10	CR845	112	90 (80.4)	-4.2 (0.8)	(-5.7, -2.6)	-1.3 (0.9)	(-3.1, 0.5)	0.150
		Placebo	119	103 (86.6)	-2.9 (0.7)	(-4.4, -1.4)			
Female	Week 10	CR845	77	65 (84.4)	-5.8 (0.8)	(-7.5, -4.1)	-0.8 (1.1)	(-2.9, 1.4)	0.489
		Placebo	70	61 (87.1)	-5.1 (0.9)	(-6.8, -3.3)			
Male	Week 12	CR845	112	90 (80.4)	-4.8 (0.8)	(-6.3, -3.2)	-1.5 (0.9)	(-3.3, 0.2)	0.087
		Placebo	119	103 (86.6)	-3.3 (0.7)	(-4.7, -1.8)			
Female	Week 12	CR845	77	67 (87.0)	-6.2 (0.8)	(-7.8, -4.5)	-1.1 (1.1)	(-3.2, 1.0)	0.303
		Placebo	70	61 (87.1)	-5.1 (0.9)	(-6.8, -3.4)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table AT2SSC_ISCC: Change from baseline in Skindex-10 social functioning score - MMRM results by race
ITT

Change from baseline in Skindex-10 social functioning score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
C: Race									0.978
Black/African American	Week 4	CR845	82	68 (82.9)	-3.7 (0.8)	(-5.3, -2.1)	-1.5 (1.0)	(-3.5, 0.5)	0.132
		Placebo	76	65 (85.5)	-2.2 (0.8)	(-3.9, -0.5)			
White	Week 4	CR845	91	82 (90.1)	-3.3 (0.8)	(-4.9, -1.8)	-1.5 (0.9)	(-3.3, 0.4)	0.117
		Placebo	93	81 (87.1)	-1.9 (0.8)	(-3.4, -0.4)			
Other	Week 4	CR845	15	14 (93.3)	-2.9 (2.3)	(-7.7, 1.8)	-0.9 (2.3)	(-5.6, 3.8)	0.699
		Placebo	18	16 (88.9)	-2.0 (2.1)	(-6.3, 2.3)			
Black/African American	Week 8	CR845	82	64 (78.0)	-4.3 (0.8)	(-5.9, -2.6)	-1.1 (1.0)	(-3.1, 1.0)	0.301
		Placebo	76	67 (88.2)	-3.2 (0.9)	(-4.9, -1.5)			
White	Week 8	CR845	91	75 (82.4)	-4.1 (0.9)	(-5.8, -2.4)	-1.4 (1.0)	(-3.4, 0.6)	0.161
		Placebo	93	82 (88.2)	-2.6 (0.8)	(-4.2, -1.1)			
Other	Week 8	CR845	15	14 (93.3)	-5.5 (2.4)	(-10.4, -0.5)	-4.3 (2.5)	(-9.5, 0.8)	0.092
		Placebo	18	17 (94.4)	-1.1 (2.2)	(-5.6, 3.4)			
Black/African American	Week 10	CR845	82	64 (78.0)	-5.7 (0.8)	(-7.3, -4.1)	-1.7 (1.0)	(-3.7, 0.2)	0.082
		Placebo	76	65 (85.5)	-3.9 (0.8)	(-5.6, -2.3)			
White	Week 10	CR845	91	77 (84.6)	-4.5 (0.9)	(-6.2, -2.8)	-0.7 (1.0)	(-2.8, 1.3)	0.483
		Placebo	93	81 (87.1)	-3.8 (0.8)	(-5.4, -2.2)			
Other	Week 10	CR845	15	13 (86.7)	-5.0 (2.3)	(-9.6, -0.3)	-3.4 (2.2)	(-7.9, 1.0)	0.125
		Placebo	18	17 (94.4)	-1.6 (2.1)	(-5.8, 2.7)			
Black/African American	Week 12	CR845	82	64 (78.0)	-5.6 (0.8)	(-7.2, -4.0)	-1.9 (1.0)	(-3.8, 0.1)	0.061
		Placebo	76	65 (85.5)	-3.7 (0.8)	(-5.4, -2.1)			
White	Week 12	CR845	91	79 (86.8)	-5.5 (0.9)	(-7.2, -3.8)	-1.4 (1.0)	(-3.4, 0.6)	0.160
		Placebo	93	80 (86.0)	-4.1 (0.8)	(-5.7, -2.5)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table AT2SSC_ISCC: Change from baseline in Skindex-10 social functioning score - MMRM results by race
ITT

Change from baseline in Skindex-10 social functioning score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Other	Week 12	CR845	15	13 (86.7)	-5.3 (2.5)	(-10.5, -0.2)	-2.1 (2.6)	(-7.5, 3.3)	0.429
		Placebo	18	18 (100.0)	-3.2 (2.3)	(-7.8, 1.4)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table AT2SSC_ISCD: Change from baseline in Skindex-10 social functioning score - MMRM results by baseline WI-NRS
ITT

Change from baseline in Skindex-10 social functioning score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
D: Baseline worst itching NRS score (WI-NRS)									0.868
>= 4 to < 7	Week 4	CR845	83	72 (86.7)	-3.1 (0.8)	(-4.7, -1.6)	-1.3 (0.9)	(-3.0, 0.4)	0.134
		Placebo	80	70 (87.5)	-1.8 (0.8)	(-3.3, -0.3)			
>= 7	Week 4	CR845	106	93 (87.7)	-3.7 (0.8)	(-5.2, -2.2)	-1.3 (0.9)	(-3.2, 0.5)	0.156
		Placebo	109	93 (85.3)	-2.4 (0.8)	(-3.9, -0.9)			
>= 4 to < 7	Week 8	CR845	83	68 (81.9)	-3.9 (0.8)	(-5.5, -2.4)	-1.4 (0.9)	(-3.1, 0.3)	0.117
		Placebo	80	71 (88.8)	-2.5 (0.8)	(-4.0, -1.1)			
>= 7	Week 8	CR845	106	86 (81.1)	-4.6 (0.8)	(-6.2, -3.0)	-1.4 (1.0)	(-3.4, 0.6)	0.167
		Placebo	109	96 (88.1)	-3.2 (0.8)	(-4.8, -1.6)			
>= 4 to < 7	Week 10	CR845	83	69 (83.1)	-4.5 (0.8)	(-6.1, -2.8)	-1.7 (0.9)	(-3.5, 0.2)	0.075
		Placebo	80	70 (87.5)	-2.8 (0.8)	(-4.4, -1.2)			
>= 7	Week 10	CR845	106	86 (81.1)	-5.5 (0.8)	(-7.1, -3.9)	-0.8 (1.0)	(-2.8, 1.1)	0.402
		Placebo	109	94 (86.2)	-4.7 (0.8)	(-6.2, -3.1)			
>= 4 to < 7	Week 12	CR845	83	67 (80.7)	-5.0 (0.8)	(-6.5, -3.4)	-1.8 (0.9)	(-3.5, -0.1)	0.040 *
		Placebo	80	72 (90.0)	-3.2 (0.7)	(-4.6, -1.7)			
>= 7	Week 12	CR845	106	90 (84.9)	-6.0 (0.8)	(-7.6, -4.4)	-1.2 (1.0)	(-3.2, 0.8)	0.255
		Placebo	109	92 (84.4)	-4.8 (0.8)	(-6.4, -3.3)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table AT2SSC_ISCE: Change from baseline in Skindex-10 social functioning score - MMRM results by specific medical condition
ITT

Change from baseline in Skindex-10 social functioning score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
E: Presence of specific medical conditions									0.373
No	Week 4	CR845	164	142 (86.6)	-3.8 (0.5)	(-4.8, -2.8)	-1.3 (0.7)	(-2.7, 0.1)	0.065
		Placebo	161	138 (85.7)	-2.5 (0.5)	(-3.5, -1.5)			
Yes	Week 4	CR845	25	23 (92.0)	-2.4 (1.2)	(-4.9, 0.0)	-1.0 (1.7)	(-4.5, 2.5)	0.564
		Placebo	28	25 (89.3)	-1.4 (1.2)	(-3.8, 0.9)			
No	Week 8	CR845	164	132 (80.5)	-4.7 (0.5)	(-5.8, -3.6)	-1.7 (0.7)	(-3.2, -0.2)	0.025 *
		Placebo	161	141 (87.6)	-3.0 (0.5)	(-4.0, -2.0)			
Yes	Week 8	CR845	25	22 (88.0)	-3.2 (1.2)	(-5.6, -0.8)	0.6 (1.7)	(-2.8, 3.9)	0.731
		Placebo	28	26 (92.9)	-3.8 (1.1)	(-6.0, -1.5)			
No	Week 10	CR845	164	133 (81.1)	-5.3 (0.5)	(-6.4, -4.2)	-1.6 (0.7)	(-3.0, -0.1)	0.037 *
		Placebo	161	141 (87.6)	-3.7 (0.5)	(-4.8, -2.7)			
Yes	Week 10	CR845	25	22 (88.0)	-4.6 (1.2)	(-7.1, -2.1)	1.6 (1.7)	(-1.8, 5.1)	0.347
		Placebo	28	23 (82.1)	-6.2 (1.2)	(-8.6, -3.9)			
No	Week 12	CR845	164	134 (81.7)	-5.8 (0.5)	(-6.8, -4.7)	-1.7 (0.7)	(-3.1, -0.2)	0.026 *
		Placebo	161	138 (85.7)	-4.1 (0.5)	(-5.1, -3.1)			
Yes	Week 12	CR845	25	23 (92.0)	-5.2 (1.2)	(-7.6, -2.9)	0.3 (1.6)	(-2.9, 3.6)	0.841
		Placebo	28	26 (92.9)	-5.5 (1.1)	(-7.7, -3.3)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor previous use of anti-itch medication is also included in the model.
Source Data: askin, created on: 17FEB2022

Table AT2SSC_ISCF: Change from baseline in Skindex-10 social functioning score - MMRM results by use of concomitant itch medication
ITT

Change from baseline in Skindex-10 social functioning score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
F: Use of concomitant itch medication									0.773
No	Week 4	CR845	117	104 (88.9)	-3.7 (0.8)	(-5.3, -2.2)	-1.8 (0.9)	(-3.6, -0.0)	0.045 *
		Placebo	111	94 (84.7)	-1.9 (0.8)	(-3.4, -0.4)			
Yes	Week 4	CR845	72	61 (84.7)	-2.8 (0.7)	(-4.3, -1.4)	-0.5 (0.9)	(-2.3, 1.3)	0.571
		Placebo	78	69 (88.5)	-2.3 (0.7)	(-3.7, -0.9)			
No	Week 8	CR845	117	99 (84.6)	-4.7 (0.8)	(-6.3, -3.1)	-2.0 (0.9)	(-3.8, -0.3)	0.025 *
		Placebo	111	100 (90.1)	-2.7 (0.8)	(-4.2, -1.1)			
Yes	Week 8	CR845	72	55 (76.4)	-3.4 (0.8)	(-5.0, -1.8)	-0.3 (1.0)	(-2.3, 1.8)	0.807
		Placebo	78	67 (85.9)	-3.2 (0.8)	(-4.7, -1.6)			
No	Week 10	CR845	117	98 (83.8)	-4.8 (0.8)	(-6.4, -3.3)	-0.7 (0.9)	(-2.4, 1.1)	0.466
		Placebo	111	98 (88.3)	-4.2 (0.8)	(-5.7, -2.6)			
Yes	Week 10	CR845	72	57 (79.2)	-5.2 (0.8)	(-6.8, -3.5)	-1.9 (1.1)	(-4.0, 0.2)	0.074
		Placebo	78	66 (84.6)	-3.3 (0.8)	(-4.9, -1.7)			
No	Week 12	CR845	117	99 (84.6)	-5.6 (0.8)	(-7.1, -4.0)	-1.3 (0.9)	(-3.0, 0.5)	0.146
		Placebo	111	100 (90.1)	-4.3 (0.8)	(-5.8, -2.8)			
Yes	Week 12	CR845	72	58 (80.6)	-5.3 (0.8)	(-6.9, -3.7)	-1.5 (1.0)	(-3.6, 0.5)	0.142
		Placebo	78	64 (82.1)	-3.7 (0.8)	(-5.3, -2.2)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor presence of medical condition is also included in the model.
Source Data: askin, created on: 17FEB2022

Table AT2STCD15_ISPA: Decrease of Skindex-10 total score of at least 15 points by age
ITT

Decrease of Skindex-10 total score of at least 15 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	A: Age										0.135	
	< 65 years	135	108 (80.0)	61 (45.2) [36.6, 54.0]	137	113 (82.5)	45 (32.8) [25.1, 41.4]	1.376 [1.016, 1.863]	1.685 [1.030, 2.756]	12.3 [0.1, 24.6]	0.037	*
	>= 65 years	54	46 (85.2)	23 (42.6) [29.2, 56.8]	52	45 (86.5)	24 (46.2) [32.2, 60.5]	0.923 [0.602, 1.414]	0.866 [0.402, 1.864]	-3.6 [-24.4, 17.2]	0.713	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table AT2STCD15_ISPB: Decrease of Skindex-10 total score of at least 15 points by sex
ITT

Decrease of Skindex-10 total score of at least 15 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	B: Sex										0.596
	Male	112	89 (79.5)	47 (42.0) [32.7, 51.7]	119	101 (84.9)	39 (32.8) [24.4, 42.0]	1.280 [0.914, 1.794]	1.483 [0.868, 2.535]	9.2 [-4.1, 22.5]	0.150
	Female	77	65 (84.4)	37 (48.1) [36.5, 59.7]	70	57 (81.4)	30 (42.9) [31.1, 55.3]	1.121 [0.785, 1.601]	1.233 [0.643, 2.365]	5.2 [-12.3, 22.6]	0.529

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table AT2STCD15_ISPC: Decrease of Skindex-10 total score of at least 15 points by race
ITT

Decrease of Skindex-10 total score of at least 15 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	C: Race										0.500
	Black/African American	82	63 (76.8)	39 (47.6) [36.4, 58.9]	76	64 (84.2)	27 (35.5) [24.9, 47.3]	1.339 [0.917, 1.955]	1.646 [0.869, 3.119]	12.0 [-4.5, 28.6]	0.127
	White	91	77 (84.6)	39 (42.9) [32.5, 53.7]	93	75 (80.6)	32 (34.4) [24.9, 45.0]	1.246 [0.863, 1.799]	1.430 [0.788, 2.595]	8.4 [-6.7, 23.6]	0.240
	Other	15	13 (86.7)	6 (40.0) [16.3, 67.7]	18	18 (100.0)	9 (50.0) [26.0, 74.0]	0.800 [0.369, 1.733]	0.667 [0.167, 2.666]	-10.0 [-50.0, 30.0]	0.572

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table AT2STCD15_ISPD: Decrease of Skindex-10 total score of at least 15 points by baseline WI-NRS
ITT

Decrease of Skindex-10 total score of at least 15 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.698
	>= 4 to < 7	83	66 (79.5)	30 (36.1) [25.9, 47.4]	80	68 (85.0)	22 (27.5) [18.1, 38.6]	1.314 [0.833, 2.075]	1.492 [0.768, 2.900]	8.6 [-6.8, 24.1]	0.238
	>= 7	106	88 (83.0)	54 (50.9) [41.0, 60.8]	109	90 (82.6)	47 (43.1) [33.7, 53.0]	1.181 [0.888, 1.572]	1.370 [0.800, 2.344]	7.8 [-6.4, 22.1]	0.252

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table AT2STCD15_ISPE: Decrease of Skindex-10 total score of at least 15 points by specific medical condition
ITT

Decrease of Skindex-10 total score of at least 15 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	E: Presence of specific medical conditions										0.353
	No	164	131 (79.9)	72 (43.9) [36.2, 51.9]	161	134 (83.2)	55 (34.2) [26.9, 42.0]	1.285 [0.976, 1.693]	1.508 [0.963, 2.362]	9.7 [-1.4, 20.9]	0.072
	Yes	25	23 (92.0)	12 (48.0) [27.8, 68.7]	28	24 (85.7)	14 (50.0) [30.6, 69.4]	0.960 [0.553, 1.666]	0.923 [0.314, 2.716]	-2.0 [-32.7, 28.7]	0.885

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table AT2STCD15_ISPF: Decrease of Skindex-10 total score of at least 15 points by use of concomitant itch medication
ITT

Decrease of Skindex-10 total score of at least 15 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	F: Use of concomitant itch medication										0.589
	No	117	97 (82.9)	51 (43.6) [34.4, 53.1]	111	97 (87.4)	42 (37.8) [28.8, 47.5]	1.152 [0.841, 1.579]	1.269 [0.747, 2.156]	5.8 [-7.9, 19.4]	0.378
	Yes	72	57 (79.2)	33 (45.8) [34.0, 58.0]	78	61 (78.2)	27 (34.6) [24.2, 46.2]	1.324 [0.892, 1.966]	1.598 [0.828, 3.085]	11.2 [-5.7, 28.2]	0.163

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table AT2SDCD3_ISPA: Decrease of Skindex-10 disease score of at least 3 points by age
ITT

Decrease of Skindex-10 disease score of at least 3 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	A: Age										0.008	i
	< 65 years	135	110 (81.5)	83 (61.5) [52.7, 69.7]	137	115 (83.9)	64 (46.7) [38.1, 55.4]	1.316 [1.053, 1.645]	1.821 [1.124, 2.950]	14.8 [2.3, 27.2]	0.015	*
	>= 65 years	54	47 (87.0)	31 (57.4) [43.2, 70.8]	52	46 (88.5)	37 (71.2) [56.9, 82.9]	0.807 [0.605, 1.076]	0.546 [0.244, 1.224]	-13.7 [-33.7, 6.2]	0.142	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table AT2SDCD3_ISPB: Decrease of Skindex-10 disease score of at least 3 points by sex
ITT

Decrease of Skindex-10 disease score of at least 3 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	B: Sex										0.160	
	Male	112	90 (80.4)	62 (55.4) [45.7, 64.8]	119	104 (87.4)	65 (54.6) [45.2, 63.8]	1.013 [0.802, 1.280]	1.030 [0.613, 1.730]	0.7 [-13.0, 14.4]	0.911	
	Female	77	67 (87.0)	52 (67.5) [55.9, 77.8]	70	57 (81.4)	36 (51.4) [39.2, 63.6]	1.313 [0.997, 1.729]	1.964 [1.006, 3.834]	16.1 [-1.0, 33.2]	0.047	*

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table AT2SDCD3_ISPC: Decrease of Skindex-10 disease score of at least 3 points by race
ITT

Decrease of Skindex-10 disease score of at least 3 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	C: Race										0.042	i
	Black/African American	82	64 (78.0)	45 (54.9) [43.5, 65.9]	76	66 (86.8)	41 (53.9) [42.1, 65.5]	1.017 [0.764, 1.354]	1.038 [0.555, 1.943]	0.9 [-15.9, 17.7]	0.907	
	White	91	79 (86.8)	61 (67.0) [56.4, 76.5]	93	76 (81.7)	45 (48.4) [37.9, 59.0]	1.385 [1.074, 1.787]	2.169 [1.194, 3.940]	18.6 [3.5, 33.7]	0.011	*
	Other	15	13 (86.7)	8 (53.3) [26.6, 78.7]	18	18 (100.0)	14 (77.8) [52.4, 93.6]	0.686 [0.402, 1.170]	0.327 [0.073, 1.470]	-24.4 [-62.3, 13.4]	0.144	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table AT2SDCD3_ISPD: Decrease of Skindex-10 disease score of at least 3 points by baseline WI-NRS
ITT

Decrease of Skindex-10 disease score of at least 3 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.685
	>= 4 to < 7	83	67 (80.7)	49 (59.0) [47.7, 69.7]	80	69 (86.3)	40 (50.0) [38.6, 61.4]	1.181 [0.890, 1.567]	1.441 [0.776, 2.677]	9.0 [-7.4, 25.5]	0.248
	>= 7	106	90 (84.9)	65 (61.3) [51.4, 70.6]	109	92 (84.4)	61 (56.0) [46.1, 65.5]	1.096 [0.875, 1.372]	1.248 [0.724, 2.149]	5.4 [-8.7, 19.4]	0.426

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table AT2SDCD3_ISPE: Decrease of Skindex-10 disease score of at least 3 points by specific medical condition
ITT

Decrease of Skindex-10 disease score of at least 3 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	E: Presence of specific medical conditions										0.806
	No	164	133 (81.1)	95 (57.9) [50.0, 65.6]	161	135 (83.9)	83 (51.6) [43.6, 59.5]	1.124 [0.921, 1.370]	1.294 [0.835, 2.005]	6.4 [-5.0, 17.8]	0.249
	Yes	25	24 (96.0)	19 (76.0) [54.9, 90.6]	28	26 (92.9)	18 (64.3) [44.1, 81.4]	1.182 [0.830, 1.683]	1.759 [0.530, 5.841]	11.7 [-16.5, 39.9]	0.358

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table AT2SDCD3_ISPF: Decrease of Skindex-10 disease score of at least 3 points by use of concomitant itch medication
ITT

		CR845			Placebo						
Decrease of Skindex-10 disease score of at least 3 points		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	F: Use of concomitant itch medication										0.446
	No	117	100 (85.5)	73 (62.4) [53.0, 71.2]	111	97 (87.4)	65 (58.6) [48.8, 67.8]	1.065 [0.863, 1.315]	1.174 [0.690, 1.998]	3.8 [-9.7, 17.4]	0.555
	Yes	72	57 (79.2)	41 (56.9) [44.7, 68.6]	78	64 (82.1)	36 (46.2) [34.8, 57.8]	1.234 [0.902, 1.687]	1.543 [0.810, 2.940]	10.8 [-6.5, 28.0]	0.188

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table AT2SMCD3_ISPA: Decrease of Skindex-10 mood/emotional distress score of at least 3 points by age
ITT

Decrease of Skindex-10 mood/emotional distress score of at least 3 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	A: Age										0.033	i
	< 65 years	135	109 (80.7)	83 (61.5) [52.7, 69.7]	137	116 (84.7)	68 (49.6) [41.0, 58.3]	1.239 [0.999, 1.536]	1.620 [1.000, 2.623]	11.8 [-0.6, 24.3]	0.050	*
	>= 65 years	54	47 (87.0)	30 (55.6) [41.4, 69.1]	52	47 (90.4)	35 (67.3) [52.9, 79.7]	0.825 [0.609, 1.119]	0.607 [0.276, 1.338]	-11.8 [-32.0, 8.5]	0.216	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table AT2SMCD3_ISPB: Decrease of Skindex-10 mood/emotional distress score of at least 3 points by sex
ITT

Decrease of Skindex-10 mood/emotional distress score of at least 3 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	B: Sex										0.336
	Male	112	89 (79.5)	64 (57.1) [47.4, 66.5]	119	103 (86.6)	58 (48.7) [39.5, 58.1]	1.172 [0.918, 1.497]	1.402 [0.835, 2.356]	8.4 [-5.3, 22.1]	0.202
	Female	77	67 (87.0)	49 (63.6) [51.9, 74.3]	70	60 (85.7)	45 (64.3) [51.9, 75.4]	0.990 [0.776, 1.262]	0.972 [0.495, 1.908]	-0.6 [-17.6, 16.3]	0.935

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table AT2SMCD3_ISPC: Decrease of Skindex-10 mood/emotional distress score of at least 3 points by race
ITT

Decrease of Skindex-10 mood/emotional distress score of at least 3 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	C: Race										0.865
	Black/African American	82	65 (79.3)	50 (61.0) [49.6, 71.6]	76	65 (85.5)	44 (57.9) [46.0, 69.1]	1.053 [0.813, 1.364]	1.136 [0.602, 2.146]	3.1 [-13.5, 19.7]	0.694
	White	91	77 (84.6)	54 (59.3) [48.5, 69.5]	93	78 (83.9)	48 (51.6) [41.0, 62.1]	1.150 [0.886, 1.491]	1.368 [0.763, 2.452]	7.7 [-7.7, 23.1]	0.293
	Other	15	13 (86.7)	9 (60.0) [32.3, 83.7]	18	18 (100.0)	9 (50.0) [26.0, 74.0]	1.200 [0.646, 2.230]	1.500 [0.375, 5.998]	10.0 [-30.0, 50.0]	0.572

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table AT2SMCD3_ISPD: Decrease of Skindex-10 mood/emotional distress score of at least 3 points by baseline WI-NRS
ITT

Decrease of Skindex-10 mood/emotional distress score of at least 3 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.639
	>= 4 to < 7	83	66 (79.5)	48 (57.8) [46.5, 68.6]	80	70 (87.5)	40 (50.0) [38.6, 61.4]	1.157 [0.869, 1.539]	1.371 [0.739, 2.544]	7.8 [-8.7, 24.3]	0.317
	>= 7	106	90 (84.9)	65 (61.3) [51.4, 70.6]	109	93 (85.3)	63 (57.8) [48.0, 67.2]	1.061 [0.851, 1.323]	1.158 [0.671, 1.997]	3.5 [-10.5, 17.6]	0.600

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table AT2SMCD3_ISPE: Decrease of Skindex-10 mood/emotional distress score of at least 3 points by specific medical condition
ITT

Decrease of Skindex-10 mood/emotional distress score of at least 3 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	E: Presence of specific medical conditions										0.597
	No	164	132 (80.5)	96 (58.5) [50.6, 66.2]	161	137 (85.1)	84 (52.2) [44.2, 60.1]	1.122 [0.922, 1.365]	1.294 [0.835, 2.006]	6.4 [-5.0, 17.8]	0.249
	Yes	25	24 (96.0)	17 (68.0) [46.5, 85.1]	28	26 (92.9)	19 (67.9) [47.6, 84.1]	1.002 [0.692, 1.452]	1.007 [0.317, 3.196]	0.1 [-28.8, 29.1]	0.991

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table AT2SMCD3_ISPF: Decrease of Skindex-10 mood/emotional distress score of at least 3 points by use of concomitant itch medication
ITT

Decrease of Skindex-10 mood/emotional distress score of at least 3 points		CR845			Placebo			RR	OR	RD	p-value
		N	nval	n (%) [95 % CI]	N	nval	n (%) [95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	
Week 12	F: Use of concomitant itch medication										0.442
	No	117	98 (83.8)	71 (60.7) [51.2, 69.6]	111	99 (89.2)	65 (58.6) [48.8, 67.8]	1.036 [0.837, 1.283]	1.092 [0.643, 1.855]	2.1 [-11.5, 15.7]	0.744
	Yes	72	58 (80.6)	42 (58.3) [46.1, 69.8]	78	64 (82.1)	38 (48.7) [37.2, 60.3]	1.197 [0.887, 1.616]	1.474 [0.773, 2.810]	9.6 [-7.6, 26.8]	0.240

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table AT2SSCD4_ISPA: Decrease of Skindex-10 social functioning score of at least 4 points by age
ITT

Decrease of Skindex-10 social functioning score of at least 4 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	A: Age										0.254
	< 65 years	135	111 (82.2)	67 (49.6) [40.9, 58.4]	137	116 (84.7)	56 (40.9) [32.6, 49.6]	1.214 [0.933, 1.580]	1.425 [0.882, 2.302]	8.8 [-3.8, 21.3]	0.148
	>= 65 years	54	46 (85.2)	26 (48.1) [34.3, 62.2]	52	48 (92.3)	27 (51.9) [37.6, 66.0]	0.927 [0.634, 1.357]	0.860 [0.401, 1.842]	-3.8 [-24.7, 17.1]	0.699

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table AT2SSCD4_ISPB: Decrease of Skindex-10 social functioning score of at least 4 points by sex
ITT

Decrease of Skindex-10 social functioning score of at least 4 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	B: Sex										0.421
	Male	112	90 (80.4)	52 (46.4) [37.0, 56.1]	119	103 (86.6)	46 (38.7) [29.9, 48.0]	1.201 [0.889, 1.623]	1.375 [0.815, 2.321]	7.8 [-5.8, 21.4]	0.233
	Female	77	67 (87.0)	41 (53.2) [41.5, 64.7]	70	61 (87.1)	37 (52.9) [40.6, 64.9]	1.007 [0.743, 1.366]	1.016 [0.531, 1.943]	0.4 [-17.1, 17.9]	0.962

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table AT2SSCD4_ISPC: Decrease of Skindex-10 social functioning score of at least 4 points by race
ITT

Decrease of Skindex-10 social functioning score of at least 4 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	C: Race										0.831
	Black/African American	82	64 (78.0)	41 (50.0) [38.7, 61.3]	76	65 (85.5)	34 (44.7) [33.3, 56.6]	1.118 [0.803, 1.556]	1.235 [0.661, 2.310]	5.3 [-11.6, 22.1]	0.509
	White	91	79 (86.8)	46 (50.5) [39.9, 61.2]	93	80 (86.0)	40 (43.0) [32.8, 53.7]	1.175 [0.862, 1.602]	1.354 [0.758, 2.421]	7.5 [-7.9, 23.0]	0.307
	Other	15	13 (86.7)	6 (40.0) [16.3, 67.7]	18	18 (100.0)	8 (44.4) [21.5, 69.2]	0.900 [0.402, 2.017]	0.833 [0.208, 3.345]	-4.4 [-44.3, 35.5]	0.800

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table AT2SSCD4_ISPD: Decrease of Skindex-10 social functioning score of at least 4 points by baseline WI-NRS
ITT

Decrease of Skindex-10 social functioning score of at least 4 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.801
	>= 4 to < 7	83	67 (80.7)	36 (43.4) [32.5, 54.7]	80	72 (90.0)	32 (40.0) [29.2, 51.6]	1.084 [0.754, 1.560]	1.149 [0.616, 2.143]	3.4 [-13.0, 19.7]	0.663
	>= 7	106	90 (84.9)	57 (53.8) [43.8, 63.5]	109	92 (84.4)	51 (46.8) [37.2, 56.6]	1.149 [0.880, 1.501]	1.323 [0.774, 2.261]	7.0 [-7.3, 21.3]	0.307

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table AT2SSCD4_ISPE: Decrease of Skindex-10 social functioning score of at least 4 points by specific medical condition
ITT

Decrease of Skindex-10 social functioning score of at least 4 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	E: Presence of specific medical conditions										0.760
	No	164	134 (81.7)	80 (48.8) [40.9, 56.7]	161	138 (85.7)	69 (42.9) [35.1, 50.9]	1.138 [0.898, 1.443]	1.270 [0.820, 1.966]	5.9 [-5.5, 17.4]	0.285
	Yes	25	23 (92.0)	13 (52.0) [31.3, 72.2]	28	26 (92.9)	14 (50.0) [30.6, 69.4]	1.040 [0.613, 1.764]	1.083 [0.368, 3.187]	2.0 [-28.7, 32.7]	0.885

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table AT2SSCD4_ISPF: Decrease of Skindex-10 social functioning score of at least 4 points by use of concomitant itch medication
ITT

Decrease of Skindex-10 social functioning score of at least 4 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	F: Use of concomitant itch medication										0.664
	No	117	99 (84.6)	60 (51.3) [41.9, 60.6]	111	100 (90.1)	49 (44.1) [34.7, 53.9]	1.162 [0.883, 1.528]	1.332 [0.791, 2.243]	7.1 [-6.7, 21.0]	0.282
	Yes	72	58 (80.6)	33 (45.8) [34.0, 58.0]	78	64 (82.1)	34 (43.6) [32.4, 55.3]	1.051 [0.736, 1.501]	1.095 [0.575, 2.086]	2.2 [-15.0, 19.5]	0.783

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table AT2A_SSIA: Incidence of TEAEs by age
SAF-S

	CR845		Placebo					
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
A: Age								0.840
< 65 years	135	89 (65.9) [57.3, 73.9]	136	82 (60.3) [51.6, 68.6]	1.093 [0.911, 1.312]	1.274 [0.777, 2.089]	5.6 [-6.6, 17.8]	0.338
>= 65 years	54	41 (75.9) [62.4, 86.5]	52	35 (67.3) [52.9, 79.7]	1.128 [0.886, 1.437]	1.532 [0.654, 3.589]	8.6 [-10.4, 27.6]	0.327

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSIB: Incidence of TEAEs by sex
SAF-S

	CR845		Placebo					
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
B: Sex								0.348
Male	112	73 (65.2) [55.6, 73.9]	118	66 (55.9) [46.5, 65.1]	1.165 [0.945, 1.437]	1.475 [0.866, 2.511]	9.2 [-4.2, 22.7]	0.153
Female	77	57 (74.0) [62.8, 83.4]	70	51 (72.9) [60.9, 82.8]	1.016 [0.836, 1.235]	1.062 [0.510, 2.209]	1.2 [-14.5, 16.8]	0.873

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSIC: Incidence of TEAEs by race
SAF-S

	CR845		Placebo					
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
C: Race								0.111
Black/African American	82	62 (75.6) [64.9, 84.4]	75	43 (57.3) [45.4, 68.7]	1.319 [1.047, 1.661]	2.307 [1.168, 4.557]	18.3 [2.5, 34.1]	0.015 *
White	91	56 (61.5) [50.8, 71.6]	93	61 (65.6) [55.0, 75.1]	0.938 [0.754, 1.168]	0.839 [0.460, 1.531]	-4.1 [-19.0, 10.9]	0.569
Other	15	11 (73.3) [44.9, 92.2]	18	12 (66.7) [41.0, 86.7]	1.100 [0.703, 1.720]	1.375 [0.305, 6.203]	6.7 [-30.7, 44.0]	0.722 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSID: Incidence of TEAEs by baseline WI-NRS
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)								0.361
>= 4 to < 7	83	58 (69.9) [58.8, 79.5]	79	46 (58.2) [46.6, 69.2]	1.200 [0.950, 1.517]	1.664 [0.871, 3.182]	11.7 [-4.3, 27.6]	0.123
>= 7	106	72 (67.9) [58.2, 76.7]	109	71 (65.1) [55.4, 74.0]	1.043 [0.863, 1.261]	1.133 [0.643, 1.998]	2.8 [-10.8, 16.3]	0.666

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSIE: Incidence of TEAEs by specific medical condition
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
E: Presence of specific medical conditions								0.359
No	164	112 (68.3) [60.6, 75.3]	160	96 (60.0) [52.0, 67.7]	1.138 [0.966, 1.341]	1.436 [0.910, 2.266]	8.3 [-2.7, 19.3]	0.120
Yes	25	18 (72.0) [50.6, 87.9]	28	21 (75.0) [55.1, 89.3]	0.960 [0.694, 1.328]	0.857 [0.252, 2.910]	-3.0 [-30.6, 24.6]	0.806

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSIF: Incidence of TEAEs by use of concomitant itch medication
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
F: Use of concomitant itch medication								0.891
No	117	75 (64.1) [54.7, 72.8]	110	64 (58.2) [48.4, 67.5]	1.102 [0.894, 1.357]	1.283 [0.752, 2.191]	5.9 [-7.6, 19.5]	0.361
Yes	72	55 (76.4) [64.9, 85.6]	78	53 (67.9) [56.4, 78.1]	1.124 [0.921, 1.372]	1.526 [0.741, 3.143]	8.4 [-7.2, 24.0]	0.252

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AS_SSIA: Incidence of serious TEAEs by age
SAF-S

	CR845		Placebo					
Serious TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
A: Age								0.138
< 65 years	135	29 (21.5) [14.9, 29.4]	136	30 (22.1) [15.4, 30.0]	0.974 [0.620, 1.529]	0.967 [0.543, 1.721]	-0.6 [-11.1, 10.0]	0.908
>= 65 years	54	20 (37.0) [24.3, 51.3]	52	11 (21.2) [11.1, 34.7]	1.751 [0.933, 3.286]	2.193 [0.923, 5.206]	15.9 [-3.0, 34.8]	0.074

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AS_SSIB: Incidence of serious TEAEs by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Serious TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
B: Sex								0.772
Male	112	27 (24.1) [16.5, 33.1]	118	23 (19.5) [12.8, 27.8]	1.237 [0.756, 2.024]	1.312 [0.700, 2.460]	4.6 [-6.9, 16.2]	0.397
Female	77	22 (28.6) [18.8, 40.0]	70	18 (25.7) [16.0, 37.6]	1.111 [0.653, 1.892]	1.156 [0.557, 2.396]	2.9 [-12.9, 18.6]	0.698

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AS_SSIC: Incidence of serious TEAEs by race
SAF-S

	CR845		Placebo					
Serious TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
C: Race								0.449
Black/African American	82	25 (30.5) [20.8, 41.6]	75	15 (20.0) [11.6, 30.8]	1.524 [0.872, 2.664]	1.754 [0.841, 3.661]	10.5 [-4.3, 25.2]	0.133
White	91	21 (23.1) [14.9, 33.1]	93	23 (24.7) [16.4, 34.8]	0.933 [0.557, 1.564]	0.913 [0.463, 1.799]	-1.7 [-15.1, 11.8]	0.793
Other	15	3 (20.0) [4.3, 48.1]	18	3 (16.7) [3.6, 41.4]	1.200 [0.283, 5.096]	1.250 [0.213, 7.347]	3.3 [-29.4, 36.0]	1.000 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AS_SSID: Incidence of serious TEAEs by baseline WI-NRS
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Serious TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)								0.886
>= 4 to < 7	83	17 (20.5) [12.4, 30.8]	79	13 (16.5) [9.1, 26.5]	1.245 [0.648, 2.392]	1.308 [0.588, 2.906]	4.0 [-9.1, 17.2]	0.511
>= 7	106	32 (30.2) [21.7, 39.9]	109	28 (25.7) [17.8, 34.9]	1.175 [0.764, 1.808]	1.251 [0.689, 2.273]	4.5 [-8.4, 17.4]	0.463

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AS_SSIE: Incidence of serious TEAEs by specific medical condition
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Serious TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
E: Presence of specific medical conditions								0.614
No	164	41 (25.0) [18.6, 32.3]	160	32 (20.0) [14.1, 27.0]	1.250 [0.831, 1.879]	1.333 [0.789, 2.253]	5.0 [-4.7, 14.7]	0.282
Yes	25	8 (32.0) [14.9, 53.5]	28	9 (32.1) [15.9, 52.4]	0.996 [0.454, 2.183]	0.993 [0.313, 3.155]	-0.1 [-29.1, 28.8]	0.991

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AS_SSIF: Incidence of serious TEAEs by use of concomitant itch medication
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Serious TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
F: Use of concomitant itch medication								0.347
No	117	31 (26.5) [18.8, 35.5]	110	21 (19.1) [12.2, 27.7]	1.388 [0.851, 2.263]	1.528 [0.815, 2.863]	7.4 [-4.3, 19.1]	0.186
Yes	72	18 (25.0) [15.5, 36.6]	78	20 (25.6) [16.4, 36.8]	0.975 [0.562, 1.691]	0.967 [0.463, 2.020]	-0.6 [-15.9, 14.6]	0.928

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AC_SSIA: Incidence of severe TEAEs by age
SAF-S

	CR845		Placebo					
Severe TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
A: Age								0.809
< 65 years	135	12 (8.9) [4.7, 15.0]	136	11 (8.1) [4.1, 14.0]	1.099 [0.502, 2.404]	1.109 [0.471, 2.607]	0.8 [-6.6, 8.2]	0.813
>= 65 years	54	8 (14.8) [6.6, 27.1]	52	6 (11.5) [4.4, 23.4]	1.284 [0.478, 3.447]	1.333 [0.429, 4.147]	3.3 [-11.5, 18.0]	0.620

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AC_SSIB: Incidence of severe TEAEs by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Severe TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
B: Sex								0.517
Male	112	9 (8.0) [3.7, 14.7]	118	10 (8.5) [4.1, 15.0]	0.948 [0.400, 2.247]	0.944 [0.369, 2.416]	-0.4 [-8.4, 7.5]	0.904
Female	77	11 (14.3) [7.4, 24.1]	70	7 (10.0) [4.1, 19.5]	1.429 [0.586, 3.481]	1.500 [0.547, 4.112]	4.3 [-7.6, 16.2]	0.430

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AC_SSIC: Incidence of severe TEAEs by race
SAF-S

	CR845		Placebo					
Severe TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
C: Race								0.756
Black/African American	82	9 (11.0) [5.1, 19.8]	75	8 (10.7) [4.7, 19.9]	1.029 [0.419, 2.529]	1.033 [0.377, 2.831]	0.3 [-10.7, 11.3]	0.951
White	91	11 (12.1) [6.2, 20.6]	93	9 (9.7) [4.5, 17.6]	1.249 [0.543, 2.871]	1.283 [0.505, 3.261]	2.4 [-7.7, 12.5]	0.600
Other	15	0 (0.0) [0.0, 21.8]	18	0 (0.0) [0.0, 18.5]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AC_SSID: Incidence of severe TEAEs by baseline WI-NRS
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Severe TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)								0.997
>= 4 to < 7	83	5 (6.0) [2.0, 13.5]	79	4 (5.1) [1.4, 12.5]	1.190 [0.331, 4.271]	1.202 [0.311, 4.648]	1.0 [-7.3, 9.2]	1.000 #
>= 7	106	15 (14.2) [8.1, 22.3]	109	13 (11.9) [6.5, 19.5]	1.187 [0.593, 2.372]	1.217 [0.549, 2.699]	2.2 [-7.7, 12.2]	0.629

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AC_SSIE: Incidence of severe TEAEs by specific medical condition
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Severe TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
E: Presence of specific medical conditions								0.759
No	164	15 (9.1) [5.2, 14.6]	160	13 (8.1) [4.4, 13.5]	1.126 [0.553, 2.290]	1.138 [0.523, 2.476]	1.0 [-5.7, 7.8]	0.744
Yes	25	5 (20.0) [6.8, 40.7]	28	4 (14.3) [4.0, 32.7]	1.400 [0.422, 4.644]	1.500 [0.355, 6.347]	5.7 [-18.4, 29.8]	0.719 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AC_SSIF: Incidence of severe TEAEs by use of concomitant itch medication
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Severe TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
F: Use of concomitant itch medication								0.682
No	117	9 (7.7) [3.6, 14.1]	110	6 (5.5) [2.0, 11.5]	1.410 [0.519, 3.832]	1.444 [0.497, 4.201]	2.2 [-5.1, 9.5]	0.499
Yes	72	11 (15.3) [7.9, 25.7]	78	11 (14.1) [7.3, 23.8]	1.083 [0.501, 2.344]	1.098 [0.444, 2.715]	1.2 [-11.5, 13.9]	0.839

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AN_SSIA: Incidence of non-severe TEAEs by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Non-severe TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
A: Age								0.750
< 65 years	135	88 (65.2) [56.5, 73.2]	136	80 (58.8) [50.1, 67.2]	1.108 [0.919, 1.336]	1.311 [0.801, 2.144]	6.4 [-5.9, 18.6]	0.282
>= 65 years	54	40 (74.1) [60.3, 85.0]	52	33 (63.5) [49.0, 76.4]	1.167 [0.900, 1.513]	1.645 [0.717, 3.773]	10.6 [-8.8, 30.0]	0.240

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AN_SSIB: Incidence of non-severe TEAEs by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Non-severe TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
B: Sex								0.386
Male	112	72 (64.3) [54.7, 73.1]	118	64 (54.2) [44.8, 63.4]	1.185 [0.955, 1.471]	1.519 [0.894, 2.579]	10.0 [-3.5, 23.5]	0.122
Female	77	56 (72.7) [61.4, 82.3]	70	49 (70.0) [57.9, 80.4]	1.039 [0.846, 1.276]	1.143 [0.558, 2.339]	2.7 [-13.3, 18.7]	0.716

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AN_SSIC: Incidence of non-severe TEAEs by race
SAF-S

	CR845		Placebo						
Non-severe TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
C: Race								0.172	
Black/African American	82	61 (74.4) [63.6, 83.4]	75	42 (56.0) [44.1, 67.5]	1.328 [1.048, 1.684]	2.282 [1.164, 4.476]	18.4 [2.4, 34.3]	0.016	*
White	91	55 (60.4) [49.6, 70.5]	93	58 (62.4) [51.7, 72.2]	0.969 [0.771, 1.219]	0.922 [0.509, 1.669]	-1.9 [-17.1, 13.2]	0.789	
Other	15	11 (73.3) [44.9, 92.2]	18	12 (66.7) [41.0, 86.7]	1.100 [0.703, 1.720]	1.375 [0.305, 6.203]	6.7 [-30.7, 44.0]	0.722	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AN_SSID: Incidence of non-severe TEAEs by baseline WI-NRS
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Non-severe TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)								0.483
>= 4 to < 7	83	58 (69.9) [58.8, 79.5]	79	46 (58.2) [46.6, 69.2]	1.200 [0.950, 1.517]	1.664 [0.871, 3.182]	11.7 [-4.3, 27.6]	0.123
>= 7	106	70 (66.0) [56.2, 75.0]	109	67 (61.5) [51.7, 70.6]	1.074 [0.878, 1.315]	1.219 [0.698, 2.128]	4.6 [-9.2, 18.3]	0.487

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AN_SSIE: Incidence of non-severe TEAEs by specific medical condition
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Non-severe TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
E: Presence of specific medical conditions								0.484
No	164	110 (67.1) [59.3, 74.2]	160	93 (58.1) [50.1, 65.9]	1.154 [0.974, 1.367]	1.468 [0.933, 2.307]	8.9 [-2.2, 20.1]	0.096
Yes	25	18 (72.0) [50.6, 87.9]	28	20 (71.4) [51.3, 86.8]	1.008 [0.718, 1.414]	1.029 [0.311, 3.407]	0.6 [-27.5, 28.6]	0.964

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AN_SSIF: Incidence of non-severe TEAEs by use of concomitant itch medication
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Non-severe TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
F: Use of concomitant itch medication								0.886
No	117	74 (63.2) [53.8, 72.0]	110	62 (56.4) [46.6, 65.8]	1.122 [0.905, 1.391]	1.332 [0.782, 2.269]	6.9 [-6.7, 20.5]	0.291
Yes	72	54 (75.0) [63.4, 84.5]	78	51 (65.4) [53.8, 75.8]	1.147 [0.930, 1.414]	1.588 [0.782, 3.226]	9.6 [-6.3, 25.5]	0.201

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AT_SSIA: Incidence of TEAEs leading to study drug discontinuation by age
SAF-S

TEAEs leading to study drug discontinuation	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
A: Age								0.586	
< 65 years	135	10 (7.4) [3.6, 13.2]	136	7 (5.1) [2.1, 10.3]	1.439 [0.564, 3.670]	1.474 [0.544, 3.994]	2.3 [-4.2, 8.8]	0.444	
>= 65 years	54	5 (9.3) [3.1, 20.3]	52	2 (3.8) [0.5, 13.2]	2.407 [0.488, 11.864]	2.551 [0.472, 13.777]	5.4 [-5.8, 16.6]	0.438	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AT_SSIB: Incidence of TEAEs leading to study drug discontinuation by sex
SAF-S

TEAEs leading to study drug discontinuation	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
B: Sex								0.664	
Male	112	10 (8.9) [4.4, 15.8]	118	7 (5.9) [2.4, 11.8]	1.505 [0.593, 3.817]	1.555 [0.570, 4.237]	3.0 [-4.7, 10.7]	0.386	
Female	77	5 (6.5) [2.1, 14.5]	70	2 (2.9) [0.3, 9.9]	2.273 [0.455, 11.342]	2.361 [0.443, 12.580]	3.6 [-4.5, 11.7]	0.446	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AT_SSIC: Incidence of TEAEs leading to study drug discontinuation by race
SAF-S

TEAEs leading to study drug discontinuation	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
C: Race								0.139	
Black/African American	82	12 (14.6) [7.8, 24.2]	75	4 (5.3) [1.5, 13.1]	2.744 [0.925, 8.140]	3.043 [0.936, 9.890]	9.3 [-1.2, 19.8]	0.055	
White	91	2 (2.2) [0.3, 7.7]	93	5 (5.4) [1.8, 12.1]	0.409 [0.081, 2.054]	0.396 [0.075, 2.093]	-3.2 [-9.8, 3.4]	0.444	#
Other	15	1 (6.7) [0.2, 31.9]	18	0 (0.0) [0.0, 18.5]	3.563 + [0.156, 81.550]	3.828 + [0.145, 101.072]	6.7 [-12.1, 25.4]	0.455	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AT_SSID: Incidence of TEAEs leading to study drug discontinuation by baseline WI-NRS
SAF-S

TEAEs leading to study drug discontinuation	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
D: Baseline worst itching NRS score (WI-NRS)								0.022	i
>= 4 to < 7	83	10 (12.0) [5.9, 21.0]	79	1 (1.3) [0.0, 6.9]	9.518 [1.247, 72.646]	10.685 [1.335, 85.549]	10.8 [2.1, 19.4]	0.007	*
>= 7	106	5 (4.7) [1.5, 10.7]	109	8 (7.3) [3.2, 14.0]	0.643 [0.217, 1.902]	0.625 [0.198, 1.976]	-2.6 [-9.9, 4.7]	0.421	

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AT_SSIE: Incidence of TEAEs leading to study drug discontinuation by specific medical condition
SAF-S

TEAEs leading to study drug discontinuation	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
E: Presence of specific medical conditions								0.772	
No	164	14 (8.5) [4.7, 13.9]	160	8 (5.0) [2.2, 9.6]	1.707 [0.736, 3.958]	1.773 [0.723, 4.351]	3.5 [-2.5, 9.6]	0.207	
Yes	25	1 (4.0) [0.1, 20.4]	28	1 (3.6) [0.1, 18.3]	1.120 [0.074, 16.982]	1.125 [0.067, 18.984]	0.4 [-13.7, 14.5]	1.000	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AT_SSIF: Incidence of TEAEs leading to study drug discontinuation by use of concomitant itch medication
SAF-S

TEAEs leading to study drug discontinuation	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
F: Use of concomitant itch medication								0.356	
No	117	10 (8.5) [4.2, 15.2]	110	4 (3.6) [1.0, 9.0]	2.350 [0.759, 7.276]	2.477 [0.753, 8.143]	4.9 [-2.1, 11.9]	0.125	
Yes	72	5 (6.9) [2.3, 15.5]	78	5 (6.4) [2.1, 14.3]	1.083 [0.327, 3.588]	1.090 [0.302, 3.931]	0.5 [-8.8, 9.9]	1.000	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSSA: TEAEs - significant SOC and PT by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Gastrointestinal disorders								
A: Age								0.836
< 65 years	135	36 (26.7) [19.4, 35.0]	136	28 (20.6) [14.1, 28.4]	1.295 [0.840, 1.996]	1.403 [0.798, 2.466]	6.1 [-4.8, 16.9]	0.240
>= 65 years	54	11 (20.4) [10.6, 33.5]	52	9 (17.3) [8.2, 30.3]	1.177 [0.532, 2.605]	1.222 [0.460, 3.247]	3.1 [-13.7, 19.8]	0.688

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSSA: TEAEs - significant SOC and PT by age
SAF-S

	CR845		Placebo						
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
PT: Diarrhoea									
A: Age								0.698	
< 65 years	135	14 (10.4) [5.8, 16.8]	136	5 (3.7) [1.2, 8.4]	2.821 [1.045, 7.614]	3.031 [1.060, 8.668]	6.7 [-0.1, 13.5]	0.031	*
>= 65 years	54	4 (7.4) [2.1, 17.9]	52	2 (3.8) [0.5, 13.2]	1.926 [0.368, 10.070]	2.000 [0.350, 11.418]	3.6 [-7.1, 14.2]	0.679	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSSA: TEAEs - significant SOC and PT by age
SAF-S

	CR845		Placebo						
		n (%)		n (%)	RR	OR	RD		
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value	
SOC: Injury, poisoning and procedural complications									
A: Age								0.315	
< 65 years	135	7 (5.2) [2.1, 10.4]	136	21 (15.4) [9.8, 22.6]	0.336 [0.148, 0.764]	0.299 [0.123, 0.731]	-10.3 [-18.1, -2.4]	0.006	*
>= 65 years	54	6 (11.1) [4.2, 22.6]	52	9 (17.3) [8.2, 30.3]	0.642 [0.246, 1.677]	0.597 [0.196, 1.816]	-6.2 [-21.4, 9.0]	0.362	

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSSA: TEAEs - significant SOC and PT by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Nervous system disorders								
A: Age								0.946
< 65 years	135	21 (15.6) [9.9, 22.8]	136	14 (10.3) [5.7, 16.7]	1.511 [0.802, 2.846]	1.605 [0.779, 3.307]	5.3 [-3.4, 14.0]	0.197
>= 65 years	54	13 (24.1) [13.5, 37.6]	52	8 (15.4) [6.9, 28.1]	1.565 [0.707, 3.462]	1.744 [0.656, 4.638]	8.7 [-8.2, 25.6]	0.264

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSSA: TEAEs - significant SOC and PT by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
PT: Dizziness								
A: Age								0.573
< 65 years	135	9 (6.7) [3.1, 12.3]	136	1 (0.7) [0.0, 4.0]	9.067 [1.165, 70.585]	9.643 [1.204, 77.201]	5.9 [0.7, 11.1]	0.010 *
>= 65 years	54	4 (7.4) [2.1, 17.9]	52	1 (1.9) [0.0, 10.3]	3.852 [0.445, 33.332]	4.080 [0.441, 37.783]	5.5 [-4.3, 15.3]	0.363 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSSA: TEAEs - significant SOC and PT by age
SAF-S

	CR845		Placebo						
		n (%)		n (%)	RR	OR	RD		
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value	
SOC: Skin and subcutaneous tissue disorders									
A: Age								0.861	
< 65 years	135	2 (1.5) [0.2, 5.2]	136	8 (5.9) [2.6, 11.3]	0.252 [0.054, 1.164]	0.241 [0.050, 1.155]	-4.4 [-9.6, 0.8]	0.103	#
>= 65 years	54	1 (1.9) [0.0, 9.9]	52	3 (5.8) [1.2, 15.9]	0.321 [0.034, 2.988]	0.308 [0.031, 3.062]	-3.9 [-13.1, 5.3]	0.358	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSSB: TEAEs - significant SOC and PT by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Gastrointestinal disorders								
B: Sex								0.264
Male	112	30 (26.8) [18.9, 36.0]	118	21 (17.8) [11.4, 25.9]	1.505 [0.918, 2.467]	1.690 [0.900, 3.174]	9.0 [-2.6, 20.6]	0.102
Female	77	17 (22.1) [13.4, 33.0]	70	16 (22.9) [13.7, 34.4]	0.966 [0.530, 1.762]	0.956 [0.440, 2.076]	-0.8 [-15.7, 14.1]	0.910

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSSB: TEAEs - significant SOC and PT by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
PT: Diarrhoea								
B: Sex								0.678
Male	112	8 (7.1) [3.1, 13.6]	118	4 (3.4) [0.9, 8.5]	2.107 [0.653, 6.803]	2.192 [0.641, 7.495]	3.8 [-2.9, 10.4]	0.202
Female	77	10 (13.0) [6.4, 22.6]	70	3 (4.3) [0.9, 12.0]	3.030 [0.869, 10.566]	3.333 [0.878, 12.653]	8.7 [-1.5, 18.9]	0.064

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSSB: TEAEs - significant SOC and PT by sex
SAF-S

	CR845		Placebo						
		n (%)		n (%)	RR	OR	RD		
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value	
SOC: Injury, poisoning and procedural complications									
B: Sex								0.113	
Male	112	4 (3.6) [1.0, 8.9]	118	18 (15.3) [9.3, 23.0]	0.234 [0.082, 0.670]	0.206 [0.067, 0.629]	-11.7 [-19.9, -3.5]	0.003	*
Female	77	9 (11.7) [5.5, 21.0]	70	12 (17.1) [9.2, 28.0]	0.682 [0.306, 1.519]	0.640 [0.252, 1.626]	-5.5 [-18.2, 7.3]	0.347	

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSSB: TEAEs - significant SOC and PT by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Nervous system disorders								
B: Sex								0.691
Male	112	19 (17.0) [10.5, 25.2]	118	12 (10.2) [5.4, 17.1]	1.668 [0.849, 3.276]	1.805 [0.832, 3.915]	6.8 [-2.9, 16.5]	0.132
Female	77	15 (19.5) [11.3, 30.1]	70	10 (14.3) [7.1, 24.7]	1.364 [0.656, 2.835]	1.452 [0.605, 3.483]	5.2 [-8.2, 18.6]	0.404

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSSB: TEAEs - significant SOC and PT by sex
SAF-S

	CR845		Placebo						
		n (%)		n (%)	RR	OR	RD		
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value	
PT: Dizziness									
B: Sex								0.482	
Male	112	7 (6.3) [2.5, 12.5]	118	2 (1.7) [0.2, 6.0]	3.688 [0.783, 17.374]	3.867 [0.786, 19.027]	4.6 [-1.4, 10.5]	0.095	#
Female	77	6 (7.8) [2.9, 16.2]	70	0 (0.0) [0.0, 5.1]	11.833 + [0.679, 206.302]	12.818 + [0.709, 231.842]	7.8 [0.4, 15.1]	0.029	*

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSSB: TEAEs - significant SOC and PT by sex
SAF-S

	CR845		Placebo						
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
SOC: Skin and subcutaneous tissue disorders									
B: Sex								0.590	
Male	112	1 (0.9) [0.0, 4.9]	118	6 (5.1) [1.9, 10.7]	0.176 [0.021, 1.436]	0.168 [0.020, 1.420]	-4.2 [-9.4, 1.0]	0.120	#
Female	77	2 (2.6) [0.3, 9.1]	70	5 (7.1) [2.4, 15.9]	0.364 [0.073, 1.815]	0.347 [0.065, 1.847]	-4.5 [-12.9, 3.8]	0.258	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSSC: TEAEs - significant SOC and PT by race
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Gastrointestinal disorders								
C: Race								0.800
Black/African American	82	23 (28.0) [18.7, 39.1]	75	15 (20.0) [11.6, 30.8]	1.402 [0.793, 2.480]	1.559 [0.742, 3.279]	8.0 [-6.5, 22.6]	0.241
White	91	21 (23.1) [14.9, 33.1]	93	20 (21.5) [13.7, 31.2]	1.073 [0.625, 1.841]	1.095 [0.547, 2.193]	1.6 [-11.5, 14.7]	0.798
Other	15	2 (13.3) [1.7, 40.5]	18	2 (11.1) [1.4, 34.7]	1.200 [0.191, 7.528]	1.231 [0.152, 9.972]	2.2 [-26.4, 30.8]	1.000 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSSC: TEAEs - significant SOC and PT by race
SAF-S

	CR845		Placebo						
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
PT: Diarrhoea									
C: Race								0.242	
Black/African American	82	10 (12.2) [6.0, 21.3]	75	5 (6.7) [2.2, 14.9]	1.829 [0.655, 5.108]	1.944 [0.633, 5.976]	5.5 [-4.8, 15.9]	0.241	
White	91	8 (8.8) [3.9, 16.6]	93	1 (1.1) [0.0, 5.8]	8.176 [1.043, 64.062]	8.867 [1.086, 72.408]	7.7 [0.4, 15.0]	0.018	*
Other	15	0 (0.0) [0.0, 21.8]	18	1 (5.6) [0.1, 27.3]	0.396 + [0.017, 9.061]	0.376 + [0.014, 9.930]	-5.6 [-22.2, 11.1]	1.000	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSSC: TEAEs - significant SOC and PT by race
SAF-S

	CR845		Placebo						
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
SOC: Injury, poisoning and procedural complications									
C: Race								0.294	
Black/African American	82	7 (8.5) [3.5, 16.8]	75	8 (10.7) [4.7, 19.9]	0.800 [0.305, 2.100]	0.782 [0.269, 2.271]	-2.1 [-12.6, 8.4]	0.651	
White	91	6 (6.6) [2.5, 13.8]	93	18 (19.4) [11.9, 28.9]	0.341 [0.142, 0.819]	0.294 [0.111, 0.780]	-12.8 [-23.4, -2.2]	0.010	*
Other	15	0 (0.0) [0.0, 21.8]	18	4 (22.2) [6.4, 47.6]	0.132 + [0.008, 2.270]	0.104 + [0.005, 2.105]	-22.2 [-47.5, 3.1]	0.108	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSSC: TEAEs - significant SOC and PT by race
SAF-S

	CR845		Placebo						
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
SOC: Nervous system disorders									
C: Race								0.123	
Black/African American	82	18 (22.0) [13.6, 32.5]	75	7 (9.3) [3.8, 18.3]	2.352 [1.041, 5.313]	2.732 [1.070, 6.976]	12.6 [0.2, 25.0]	0.031	*
White	91	13 (14.3) [7.8, 23.2]	93	15 (16.1) [9.3, 25.2]	0.886 [0.447, 1.756]	0.867 [0.387, 1.941]	-1.8 [-13.3, 9.6]	0.729	
Other	15	2 (13.3) [1.7, 40.5]	18	0 (0.0) [0.0, 18.5]	5.938 + [0.307, 114.884]	6.852 + [0.304, 154.606]	13.3 [-10.0, 36.6]	0.199	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSSC: TEAEs - significant SOC and PT by race
SAF-S

	CR845		Placebo						
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
PT: Dizziness									
C: Race								0.712	
Black/African American	82	8 (9.8) [4.3, 18.3]	75	1 (1.3) [0.0, 7.2]	7.317 [0.937, 57.131]	8.000 [0.976, 65.570]	8.4 [0.2, 16.6]	0.035	*
White	91	4 (4.4) [1.2, 10.9]	93	1 (1.1) [0.0, 5.8]	4.088 [0.466, 35.881]	4.230 [0.464, 38.590]	3.3 [-2.5, 9.1]	0.209	#
Other	15	0 (0.0) [0.0, 21.8]	18	0 (0.0) [0.0, 18.5]	1.188 + [0.025, 56.540]	1.194 + [0.022, 63.722]	NE	NE	

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSSC: TEAEs - significant SOC and PT by race
SAF-S

	CR845		Placebo						
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
SOC: Skin and subcutaneous tissue disorders									
C: Race								0.233	
Black/African American	82	1 (1.2) [0.0, 6.6]	75	4 (5.3) [1.5, 13.1]	0.229 [0.026, 2.000]	0.219 [0.024, 2.006]	-4.1 [-11.0, 2.8]	0.193	#
White	91	1 (1.1) [0.0, 6.0]	93	7 (7.5) [3.1, 14.9]	0.146 [0.018, 1.163]	0.137 [0.016, 1.133]	-6.4 [-13.3, 0.4]	0.065	#
Other	15	1 (6.7) [0.2, 31.9]	18	0 (0.0) [0.0, 18.5]	3.563 + [0.156, 81.550]	3.828 + [0.145, 101.072]	6.7 [-12.1, 25.4]	0.455	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSSD: TEAEs - significant SOC and PT by baseline WI-NRS
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Gastrointestinal disorders								
D: Baseline worst itching NRS score (WI-NRS)								0.559
>= 4 to < 7	83	20 (24.1) [15.4, 34.7]	79	13 (16.5) [9.1, 26.5]	1.464 [0.783, 2.740]	1.612 [0.740, 3.512]	7.6 [-5.9, 21.2]	0.229
>= 7	106	27 (25.5) [17.5, 34.9]	109	24 (22.0) [14.6, 31.0]	1.157 [0.715, 1.870]	1.210 [0.645, 2.271]	3.5 [-8.8, 15.8]	0.553

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSSD: TEAEs - significant SOC and PT by baseline WI-NRS
SAF-S

	CR845		Placebo						
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
PT: Diarrhoea									
D: Baseline worst itching NRS score (WI-NRS)								0.878	
>= 4 to < 7	83	6 (7.2) [2.7, 15.1]	79	2 (2.5) [0.3, 8.8]	2.855 [0.594, 13.730]	3.000 [0.587, 15.330]	4.7 [-3.1, 12.5]	0.278	#
>= 7	106	12 (11.3) [6.0, 18.9]	109	5 (4.6) [1.5, 10.4]	2.468 [0.900, 6.765]	2.655 [0.902, 7.818]	6.7 [-1.4, 14.9]	0.068	

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSSD: TEAEs - significant SOC and PT by baseline WI-NRS
SAF-S

	CR845		Placebo						
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
SOC: Injury, poisoning and procedural complications									
D: Baseline worst itching NRS score (WI-NRS)								0.314	
>= 4 to < 7	83	3 (3.6) [0.8, 10.2]	79	11 (13.9) [7.2, 23.5]	0.260 [0.075, 0.896]	0.232 [0.062, 0.865]	-10.3 [-20.2, -0.4]	0.020	*
>= 7	106	10 (9.4) [4.6, 16.7]	109	19 (17.4) [10.8, 25.9]	0.541 [0.264, 1.109]	0.493 [0.218, 1.118]	-8.0 [-18.0, 2.0]	0.087	

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSSD: TEAEs - significant SOC and PT by baseline WI-NRS
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Nervous system disorders								
D: Baseline worst itching NRS score (WI-NRS)								0.700
>= 4 to < 7	83	16 (19.3) [11.4, 29.4]	79	11 (13.9) [7.2, 23.5]	1.384 [0.685, 2.797]	1.476 [0.638, 3.415]	5.4 [-7.3, 18.0]	0.362
>= 7	106	18 (17.0) [10.4, 25.5]	109	11 (10.1) [5.1, 17.3]	1.683 [0.835, 3.391]	1.822 [0.816, 4.070]	6.9 [-3.2, 16.9]	0.140

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSSD: TEAEs - significant SOC and PT by baseline WI-NRS
SAF-S

	CR845		Placebo						
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
PT: Dizziness									
D: Baseline worst itching NRS score (WI-NRS)								0.959	
>= 4 to < 7	83	7 (8.4) [3.5, 16.6]	79	1 (1.3) [0.0, 6.9]	6.663 [0.839, 52.933]	7.184 [0.863, 59.791]	7.2 [-0.5, 14.9]	0.064	#
>= 7	106	6 (5.7) [2.1, 11.9]	109	1 (0.9) [0.0, 5.0]	6.170 [0.755, 50.386]	6.480 [0.767, 54.769]	4.7 [-0.9, 10.4]	0.063	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSSD: TEAEs - significant SOC and PT by baseline WI-NRS
SAF-S

	CR845		Placebo						
		n (%)		n (%)	RR	OR	RD		
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value	
SOC: Skin and subcutaneous tissue disorders									
D: Baseline worst itching NRS score (WI-NRS)								0.249	
>= 4 to < 7	83	2 (2.4) [0.3, 8.4]	79	3 (3.8) [0.8, 10.7]	0.635 [0.109, 3.697]	0.626 [0.102, 3.847]	-1.4 [-8.0, 5.2]	0.676	#
>= 7	106	1 (0.9) [0.0, 5.1]	109	8 (7.3) [3.2, 14.0]	0.129 [0.016, 1.010]	0.120 [0.015, 0.979]	-6.4 [-12.6, -0.2]	0.035	*

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSSE: TEAEs - significant SOC and PT by specific medical condition
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Gastrointestinal disorders								
E: Presence of specific medical conditions								0.338
No	164	42 (25.6) [19.1, 33.0]	160	30 (18.8) [13.0, 25.7]	1.366 [0.902, 2.068]	1.492 [0.878, 2.534]	6.9 [-2.8, 16.5]	0.138
Yes	25	5 (20.0) [6.8, 40.7]	28	7 (25.0) [10.7, 44.9]	0.800 [0.290, 2.203]	0.750 [0.204, 2.754]	-5.0 [-31.2, 21.2]	0.667

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSSE: TEAEs - significant SOC and PT by specific medical condition
SAF-S

	CR845		Placebo						
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
PT: Diarrhoea									
E: Presence of specific medical conditions								0.537	
No	164	17 (10.4) [6.2, 16.1]	160	6 (3.8) [1.4, 8.0]	2.764 [1.118, 6.832]	2.968 [1.139, 7.735]	6.6 [0.5, 12.7]	0.021	*
Yes	25	1 (4.0) [0.1, 20.4]	28	1 (3.6) [0.1, 18.3]	1.120 [0.074, 16.982]	1.125 [0.067, 18.984]	0.4 [-13.7, 14.5]	1.000	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSSE: TEAEs - significant SOC and PT by specific medical condition
SAF-S

	CR845		Placebo						
		n (%)		n (%)	RR	OR	RD		
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value	
SOC: Injury, poisoning and procedural complications									
E: Presence of specific medical conditions								0.477	
No	164	10 (6.1) [3.0, 10.9]	160	25 (15.6) [10.4, 22.2]	0.390 [0.194, 0.786]	0.351 [0.163, 0.756]	-9.5 [-16.9, -2.2]	0.006	*
Yes	25	3 (12.0) [2.5, 31.2]	28	5 (17.9) [6.1, 36.9]	0.672 [0.178, 2.530]	0.627 [0.134, 2.944]	-5.9 [-28.7, 17.0]	0.708	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSSE: TEAEs - significant SOC and PT by specific medical condition
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Nervous system disorders								
E: Presence of specific medical conditions								0.683
No	164	27 (16.5) [11.1, 23.0]	160	16 (10.0) [5.8, 15.7]	1.646 [0.923, 2.937]	1.774 [0.916, 3.436]	6.5 [-1.5, 14.4]	0.087
Yes	25	7 (28.0) [12.1, 49.4]	28	6 (21.4) [8.3, 41.0]	1.307 [0.506, 3.371]	1.426 [0.406, 5.006]	6.6 [-20.5, 33.6]	0.582

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSSE: TEAEs - significant SOC and PT by specific medical condition
SAF-S

	CR845		Placebo						
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
PT: Dizziness									
E: Presence of specific medical conditions								0.065	
No	164	13 (7.9) [4.3, 13.2]	160	1 (0.6) [0.0, 3.4]	12.683 [1.679, 95.824]	13.689 [1.769, 105.920]	7.3 [2.4, 12.2]	0.001	*
Yes	25	0 (0.0) [0.0, 13.7]	28	1 (3.6) [0.1, 18.3]	0.372 + [0.016, 8.733]	0.359 + [0.014, 9.231]	-3.6 [-14.2, 7.1]	1.000	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSSE: TEAEs - significant SOC and PT by specific medical condition
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Skin and subcutaneous tissue disorders								
E: Presence of specific medical conditions								0.610
No	164	3 (1.8) [0.4, 5.3]	160	8 (5.0) [2.2, 9.6]	0.366 [0.099, 1.354]	0.354 [0.092, 1.359]	-3.2 [-7.7, 1.4]	0.116
Yes	25	0 (0.0) [0.0, 13.7]	28	3 (10.7) [2.3, 28.2]	0.159 + [0.009, 2.941]	0.143 + [0.007, 2.909]	-10.7 [-26.0, 4.5]	0.238 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSSF: TEAEs - significant SOC and PT by use of concomitant itch medication
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Gastrointestinal disorders								
F: Use of concomitant itch medication								0.468
No	117	24 (20.5) [13.6, 29.0]	110	15 (13.6) [7.8, 21.5]	1.504 [0.834, 2.714]	1.634 [0.807, 3.310]	6.9 [-3.7, 17.5]	0.171
Yes	72	23 (31.9) [21.4, 44.0]	78	22 (28.2) [18.6, 39.5]	1.133 [0.695, 1.847]	1.195 [0.594, 2.404]	3.7 [-12.3, 19.8]	0.619

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSSF: TEAEs - significant SOC and PT by use of concomitant itch medication
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
PT: Diarrhoea								
F: Use of concomitant itch medication								0.623
No	117	9 (7.7) [3.6, 14.1]	110	4 (3.6) [1.0, 9.0]	2.115 [0.671, 6.672]	2.208 [0.660, 7.390]	4.1 [-2.8, 10.9]	0.190
Yes	72	9 (12.5) [5.9, 22.4]	78	3 (3.8) [0.8, 10.8]	3.250 [0.916, 11.535]	3.571 [0.927, 13.761]	8.7 [-1.4, 18.7]	0.052

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSSF: TEAEs - significant SOC and PT by use of concomitant itch medication
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Injury, poisoning and procedural complications								
F: Use of concomitant itch medication								0.551
No	117	9 (7.7) [3.6, 14.1]	110	17 (15.5) [9.3, 23.6]	0.498 [0.232, 1.070]	0.456 [0.194, 1.071]	-7.8 [-16.9, 1.4]	0.067
Yes	72	4 (5.6) [1.5, 13.6]	78	13 (16.7) [9.2, 26.8]	0.333 [0.114, 0.976]	0.294 [0.091, 0.949]	-11.1 [-22.3, 0.0]	0.033 *

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSSF: TEAEs - significant SOC and PT by use of concomitant itch medication
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Nervous system disorders								
F: Use of concomitant itch medication								0.684
No	117	18 (15.4) [9.4, 23.2]	110	12 (10.9) [5.8, 18.3]	1.410 [0.713, 2.791]	1.485 [0.679, 3.246]	4.5 [-5.2, 14.1]	0.321
Yes	72	16 (22.2) [13.3, 33.6]	78	10 (12.8) [6.3, 22.3]	1.733 [0.842, 3.569]	1.943 [0.818, 4.617]	9.4 [-4.1, 22.9]	0.130

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSSF: TEAEs - significant SOC and PT by use of concomitant itch medication
SAF-S

	CR845		Placebo						
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
PT: Dizziness									
F: Use of concomitant itch medication								0.844	
No	117	6 (5.1) [1.9, 10.8]	110	1 (0.9) [0.0, 5.0]	5.641 [0.690, 46.109]	5.892 [0.698, 49.750]	4.2 [-1.0, 9.5]	0.120	#
Yes	72	7 (9.7) [4.0, 19.0]	78	1 (1.3) [0.0, 6.9]	7.583 [0.956, 60.136]	8.292 [0.994, 69.163]	8.4 [-0.2, 17.1]	0.029	*

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table AT2A_SSSF: TEAEs - significant SOC and PT by use of concomitant itch medication
SAF-S

	CR845		Placebo						
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
SOC: Skin and subcutaneous tissue disorders									
F: Use of concomitant itch medication								0.256	
No	117	0 (0.0) [0.0, 3.1]	110	5 (4.5) [1.5, 10.3]	0.086 + [0.005, 1.529]	0.082 + [0.004, 1.494]	-4.5 [-9.3, 0.2]	0.025	*
Yes	72	3 (4.2) [0.9, 11.7]	78	6 (7.7) [2.9, 16.0]	0.542 [0.141, 2.086]	0.522 [0.126, 2.169]	-3.5 [-12.4, 5.3]	0.498	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table AT2AEF_SSIA: Incidence of AESI falls/injuries by age
SAF-S

	CR845		Placebo					
AESI falls/injuries	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
A: Age								0.723
< 65 years	135	4 (3.0) [0.8, 7.4]	136	6 (4.4) [1.6, 9.4]	0.672 [0.194, 2.327]	0.662 [0.182, 2.399]	-1.4 [-6.7, 3.8]	0.749 #
>= 65 years	54	3 (5.6) [1.2, 15.4]	52	3 (5.8) [1.2, 15.9]	0.963 [0.204, 4.557]	0.961 [0.185, 4.991]	-0.2 [-10.9, 10.5]	1.000 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEF_SSIB: Incidence of AESI falls/injuries by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI falls/injuries	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
B: Sex		n<10 for all subgroups						NE
Male	112	2 (1.8) [0.2, 6.3]	118	6 (5.1) [1.9, 10.7]				
Female	77	5 (6.5) [2.1, 14.5]	70	3 (4.3) [0.9, 12.0]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEF_SSIC: Incidence of AESI falls/injuries by race
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI falls/injuries	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
C: Race		n<10 for all subgroups						NE
Black/African American	82	4 (4.9) [1.3, 12.0]	75	2 (2.7) [0.3, 9.3]				
White	91	3 (3.3) [0.7, 9.3]	93	6 (6.5) [2.4, 13.5]				
Other	15	0 (0.0) [0.0, 21.8]	18	1 (5.6) [0.1, 27.3]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEF_SSID: Incidence of AESI falls/injuries by baseline WI-NRS
SAF-S

	CR845		Placebo						
AESI falls/injuries	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
D: Baseline worst itching NRS score (WI-NRS)								0.189	
>= 4 to < 7	83	1 (1.2) [0.0, 6.5]	79	4 (5.1) [1.4, 12.5]	0.238 [0.027, 2.083]	0.229 [0.025, 2.092]	-3.9 [-10.5, 2.8]	0.202	#
>= 7	106	6 (5.7) [2.1, 11.9]	109	5 (4.6) [1.5, 10.4]	1.234 [0.388, 3.922]	1.248 [0.369, 4.219]	1.1 [-5.8, 7.9]	0.722	

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEF_SSIE: Incidence of AESI falls/injuries by specific medical condition
SAF-S

	CR845		Placebo					
AESI falls/injuries	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
E: Presence of specific medical conditions								0.129
No	164	4 (2.4) [0.7, 6.1]	160	8 (5.0) [2.2, 9.6]	0.488 [0.150, 1.588]	0.475 [0.140, 1.610]	-2.6 [-7.3, 2.2]	0.223
Yes	25	3 (12.0) [2.5, 31.2]	28	1 (3.6) [0.1, 18.3]	3.360 [0.373, 30.263]	3.682 [0.357, 37.922]	8.4 [-9.8, 26.7]	0.333 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEF_SSIF: Incidence of AESI falls/injuries by use of concomitant itch medication
SAF-S

	CR845		Placebo						
AESI falls/injuries	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
F: Use of concomitant itch medication								0.591	
No	117	4 (3.4) [0.9, 8.5]	110	6 (5.5) [2.0, 11.5]	0.627 [0.182, 2.162]	0.614 [0.168, 2.235]	-2.0 [-8.3, 4.2]	0.529	#
Yes	72	3 (4.2) [0.9, 11.7]	78	3 (3.8) [0.8, 10.8]	1.083 [0.226, 5.196]	1.087 [0.212, 5.566]	0.3 [-7.3, 7.9]	1.000	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEFN_SSIA: Incidence of AESI falls/injuries - non-severe by age
SAF-S

	CR845		Placebo					
AESI falls/injuries - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
A: Age								0.723
< 65 years	135	4 (3.0) [0.8, 7.4]	136	6 (4.4) [1.6, 9.4]	0.672 [0.194, 2.327]	0.662 [0.182, 2.399]	-1.4 [-6.7, 3.8]	0.749 #
>= 65 years	54	3 (5.6) [1.2, 15.4]	52	3 (5.8) [1.2, 15.9]	0.963 [0.204, 4.557]	0.961 [0.185, 4.991]	-0.2 [-10.9, 10.5]	1.000 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEFN_SSIB: Incidence of AESI falls/injuries - non-severe by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI falls/injuries - non-severe	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
B: Sex		n<10 for all subgroups						NE
Male	112	2 (1.8) [0.2, 6.3]	118	6 (5.1) [1.9, 10.7]				
Female	77	5 (6.5) [2.1, 14.5]	70	3 (4.3) [0.9, 12.0]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEFN_SSIC: Incidence of AESI falls/injuries - non-severe by race
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI falls/injuries - non-severe	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
C: Race		n<10 for all subgroups						NE
Black/African American	82	4 (4.9) [1.3, 12.0]	75	2 (2.7) [0.3, 9.3]				
White	91	3 (3.3) [0.7, 9.3]	93	6 (6.5) [2.4, 13.5]				
Other	15	0 (0.0) [0.0, 21.8]	18	1 (5.6) [0.1, 27.3]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEFN_SSID: Incidence of AESI falls/injuries - non-severe by baseline WI-NRS
SAF-S

	CR845		Placebo						
AESI falls/injuries - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
D: Baseline worst itching NRS score (WI-NRS)								0.189	
>= 4 to < 7	83	1 (1.2) [0.0, 6.5]	79	4 (5.1) [1.4, 12.5]	0.238 [0.027, 2.083]	0.229 [0.025, 2.092]	-3.9 [-10.5, 2.8]	0.202	#
>= 7	106	6 (5.7) [2.1, 11.9]	109	5 (4.6) [1.5, 10.4]	1.234 [0.388, 3.922]	1.248 [0.369, 4.219]	1.1 [-5.8, 7.9]	0.722	

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEFN_SSIE: Incidence of AESI falls/injuries - non-severe by specific medical condition
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI falls/injuries - non-severe	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
E: Presence of specific medical conditions								0.129
No	164	4 (2.4) [0.7, 6.1]	160	8 (5.0) [2.2, 9.6]	0.488 [0.150, 1.588]	0.475 [0.140, 1.610]	-2.6 [-7.3, 2.2]	0.223
Yes	25	3 (12.0) [2.5, 31.2]	28	1 (3.6) [0.1, 18.3]	3.360 [0.373, 30.263]	3.682 [0.357, 37.922]	8.4 [-9.8, 26.7]	0.333 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEFN_SSIF: Incidence of AESI falls/injuries - non-severe by use of concomitant itch medication
SAF-S

	CR845		Placebo					
AESI falls/injuries - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
F: Use of concomitant itch medication								0.591
No	117	4 (3.4) [0.9, 8.5]	110	6 (5.5) [2.0, 11.5]	0.627 [0.182, 2.162]	0.614 [0.168, 2.235]	-2.0 [-8.3, 4.2]	0.529 #
Yes	72	3 (4.2) [0.9, 11.7]	78	3 (3.8) [0.8, 10.8]	1.083 [0.226, 5.196]	1.087 [0.212, 5.566]	0.3 [-7.3, 7.9]	1.000 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEV_SSIA: Incidence of AESI dizziness by age
SAF-S

	CR845		Placebo						
AESI dizziness	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
A: Age								0.526	
< 65 years	135	10 (7.4) [3.6, 13.2]	136	1 (0.7) [0.0, 4.0]	10.074 [1.308, 77.615]	10.800 [1.363, 85.586]	6.7 [1.3, 12.1]	0.005	*
>= 65 years	54	4 (7.4) [2.1, 17.9]	52	1 (1.9) [0.0, 10.3]	3.852 [0.445, 33.332]	4.080 [0.441, 37.783]	5.5 [-4.3, 15.3]	0.363	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEV_SSIB: Incidence of AESI dizziness by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI dizziness	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
B: Sex		n<10 for all subgroups						NE
Male	112	7 (6.3) [2.5, 12.5]	118	2 (1.7) [0.2, 6.0]				
Female	77	7 (9.1) [3.7, 17.8]	70	0 (0.0) [0.0, 5.1]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEV_SSIC: Incidence of AESI dizziness by race
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI dizziness	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
C: Race		n<10 for all subgroups						NE
Black/African American	82	8 (9.8) [4.3, 18.3]	75	1 (1.3) [0.0, 7.2]				
White	91	5 (5.5) [1.8, 12.4]	93	1 (1.1) [0.0, 5.8]				
Other	15	0 (0.0) [0.0, 21.8]	18	0 (0.0) [0.0, 18.5]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEV_SSID: Incidence of AESI dizziness by baseline WI-NRS
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI dizziness	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)		n<10 for all subgroups						NE
>= 4 to < 7	83	8 (9.6) [4.3, 18.1]	79	1 (1.3) [0.0, 6.9]				
>= 7	106	6 (5.7) [2.1, 11.9]	109	1 (0.9) [0.0, 5.0]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEV_SSIE: Incidence of AESI dizziness by specific medical condition
SAF-S

	CR845		Placebo						
AESI dizziness	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
E: Presence of specific medical conditions								0.059	
No	164	14 (8.5) [4.7, 13.9]	160	1 (0.6) [0.0, 3.4]	13.659 [1.817, 102.657]	14.840 [1.928, 114.241]	7.9 [2.8, 13.0]	<0.001	*
Yes	25	0 (0.0) [0.0, 13.7]	28	1 (3.6) [0.1, 18.3]	0.372 + [0.016, 8.733]	0.359 + [0.014, 9.231]	-3.6 [-14.2, 7.1]	1.000	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEV_SSIF: Incidence of AESI dizziness by use of concomitant itch medication
SAF-S

	CR845		Placebo					
AESI dizziness	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
F: Use of concomitant itch medication		n<10 for all subgroups						NE
No	117	7 (6.0) [2.4, 11.9]	110	1 (0.9) [0.0, 5.0]				
Yes	72	7 (9.7) [4.0, 19.0]	78	1 (1.3) [0.0, 6.9]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEVN_SSIA: Incidence of AESI dizziness - non-severe by age
SAF-S

	CR845		Placebo						
AESI dizziness - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
A: Age								0.573	
< 65 years	135	9 (6.7) [3.1, 12.3]	136	1 (0.7) [0.0, 4.0]	9.067 [1.165, 70.585]	9.643 [1.204, 77.201]	5.9 [0.7, 11.1]	0.010	*
>= 65 years	54	4 (7.4) [2.1, 17.9]	52	1 (1.9) [0.0, 10.3]	3.852 [0.445, 33.332]	4.080 [0.441, 37.783]	5.5 [-4.3, 15.3]	0.363	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEVN_SSIB: Incidence of AESI dizziness - non-severe by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI dizziness - non-severe	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
B: Sex		n<10 for all subgroups						NE
Male	112	7 (6.3) [2.5, 12.5]	118	2 (1.7) [0.2, 6.0]				
Female	77	6 (7.8) [2.9, 16.2]	70	0 (0.0) [0.0, 5.1]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEVN_SSIC: Incidence of AESI dizziness - non-severe by race
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI dizziness - non-severe	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
C: Race		n<10 for all subgroups						NE
Black/African American	82	8 (9.8) [4.3, 18.3]	75	1 (1.3) [0.0, 7.2]				
White	91	4 (4.4) [1.2, 10.9]	93	1 (1.1) [0.0, 5.8]				
Other	15	0 (0.0) [0.0, 21.8]	18	0 (0.0) [0.0, 18.5]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEVN_SSID: Incidence of AESI dizziness - non-severe by baseline WI-NRS
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI dizziness - non-severe	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)		n<10 for all subgroups						NE
>= 4 to < 7	83	7 (8.4) [3.5, 16.6]	79	1 (1.3) [0.0, 6.9]				
>= 7	106	6 (5.7) [2.1, 11.9]	109	1 (0.9) [0.0, 5.0]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEVN_SSIE: Incidence of AESI dizziness - non-severe by specific medical condition
SAF-S

	CR845		Placebo						
AESI dizziness - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
E: Presence of specific medical conditions								0.065	
No	164	13 (7.9) [4.3, 13.2]	160	1 (0.6) [0.0, 3.4]	12.683 [1.679, 95.824]	13.689 [1.769, 105.920]	7.3 [2.4, 12.2]	0.001	*
Yes	25	0 (0.0) [0.0, 13.7]	28	1 (3.6) [0.1, 18.3]	0.372 + [0.016, 8.733]	0.359 + [0.014, 9.231]	-3.6 [-14.2, 7.1]	1.000	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEVN_SSIF: Incidence of AESI dizziness - non-severe by use of concomitant itch medication
SAF-S

	CR845		Placebo					
AESI dizziness - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
F: Use of concomitant itch medication		n<10 for all subgroups						NE
No	117	6 (5.1) [1.9, 10.8]	110	1 (0.9) [0.0, 5.0]				
Yes	72	7 (9.7) [4.0, 19.0]	78	1 (1.3) [0.0, 6.9]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEO_SSIA: Incidence of AESI somnolence by age
SAF-S

	CR845		Placebo					
AESI somnolence	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
A: Age		n<10 for all subgroups						NE
< 65 years	135	4 (3.0) [0.8, 7.4]	136	4 (2.9) [0.8, 7.4]				
>= 65 years	54	2 (3.7) [0.5, 12.7]	52	0 (0.0) [0.0, 6.8]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEO_SSIB: Incidence of AESI somnolence by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI somnolence	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
B: Sex		n<10 for all subgroups						NE
Male	112	4 (3.6) [1.0, 8.9]	118	3 (2.5) [0.5, 7.3]				
Female	77	2 (2.6) [0.3, 9.1]	70	1 (1.4) [0.0, 7.7]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEO_SSIC: Incidence of AESI somnolence by race
SAF-S

	CR845		Placebo					
AESI somnolence	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
C: Race		n<10 for all subgroups						NE
Black/African American	82	3 (3.7) [0.8, 10.3]	75	1 (1.3) [0.0, 7.2]				
White	91	2 (2.2) [0.3, 7.7]	93	3 (3.2) [0.7, 9.1]				
Other	15	1 (6.7) [0.2, 31.9]	18	0 (0.0) [0.0, 18.5]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEO_SSID: Incidence of AESI somnolence by baseline WI-NRS
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI somnolence	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)		n<10 for all subgroups						NE
>= 4 to < 7	83	2 (2.4) [0.3, 8.4]	79	2 (2.5) [0.3, 8.8]				
>= 7	106	4 (3.8) [1.0, 9.4]	109	2 (1.8) [0.2, 6.5]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEO_SSIE: Incidence of AESI somnolence by specific medical condition
SAF-S

	CR845		Placebo					
AESI somnolence	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
E: Presence of specific medical conditions		n<10 for all subgroups						NE
No	164	4 (2.4) [0.7, 6.1]	160	3 (1.9) [0.4, 5.4]				
Yes	25	2 (8.0) [1.0, 26.0]	28	1 (3.6) [0.1, 18.3]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEO_SSIF: Incidence of AESI somnolence by use of concomitant itch medication
SAF-S

	CR845		Placebo					
AESI somnolence	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
F: Use of concomitant itch medication		n<10 for all subgroups						NE
No	117	2 (1.7) [0.2, 6.0]	110	3 (2.7) [0.6, 7.8]				
Yes	72	4 (5.6) [1.5, 13.6]	78	1 (1.3) [0.0, 6.9]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEON_SSIA: Incidence of AESI somnolence - non-severe by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI somnolence - non-severe	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
A: Age		n<10 for all subgroups						NE
< 65 years	135	4 (3.0) [0.8, 7.4]	136	4 (2.9) [0.8, 7.4]				
>= 65 years	54	2 (3.7) [0.5, 12.7]	52	0 (0.0) [0.0, 6.8]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEON_SSIB: Incidence of AESI somnolence - non-severe by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI somnolence - non-severe	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
B: Sex		n<10 for all subgroups						NE
Male	112	4 (3.6) [1.0, 8.9]	118	3 (2.5) [0.5, 7.3]				
Female	77	2 (2.6) [0.3, 9.1]	70	1 (1.4) [0.0, 7.7]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEON_SSIC: Incidence of AESI somnolence - non-severe by race
SAF-S

	CR845		Placebo					
AESI somnolence - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
C: Race		n<10 for all subgroups						NE
Black/African American	82	3 (3.7) [0.8, 10.3]	75	1 (1.3) [0.0, 7.2]				
White	91	2 (2.2) [0.3, 7.7]	93	3 (3.2) [0.7, 9.1]				
Other	15	1 (6.7) [0.2, 31.9]	18	0 (0.0) [0.0, 18.5]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEON_SSID: Incidence of AESI somnolence - non-severe by baseline WI-NRS
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI somnolence - non-severe	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)		n<10 for all subgroups						NE
>= 4 to < 7	83	2 (2.4) [0.3, 8.4]	79	2 (2.5) [0.3, 8.8]				
>= 7	106	4 (3.8) [1.0, 9.4]	109	2 (1.8) [0.2, 6.5]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEON_SSIE: Incidence of AESI somnolence - non-severe by specific medical condition
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI somnolence - non-severe	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
E: Presence of specific medical conditions		n<10 for all subgroups						NE
No	164	4 (2.4) [0.7, 6.1]	160	3 (1.9) [0.4, 5.4]				
Yes	25	2 (8.0) [1.0, 26.0]	28	1 (3.6) [0.1, 18.3]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEON_SSIF: Incidence of AESI somnolence - non-severe by use of concomitant itch medication
SAF-S

	CR845		Placebo					
AESI somnolence - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
F: Use of concomitant itch medication		n<10 for all subgroups						NE
No	117	2 (1.7) [0.2, 6.0]	110	3 (2.7) [0.6, 7.8]				
Yes	72	4 (5.6) [1.5, 13.6]	78	1 (1.3) [0.0, 6.9]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEM_SSIA: Incidence of AESI mental status change by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI mental status change	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
A: Age		n<10 for all subgroups						NE
< 65 years	135	4 (3.0) [0.8, 7.4]	136	5 (3.7) [1.2, 8.4]				
>= 65 years	54	3 (5.6) [1.2, 15.4]	52	2 (3.8) [0.5, 13.2]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEM_SSIB: Incidence of AESI mental status change by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI mental status change	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
B: Sex		n<10 for all subgroups						NE
Male	112	4 (3.6) [1.0, 8.9]	118	4 (3.4) [0.9, 8.5]				
Female	77	3 (3.9) [0.8, 11.0]	70	3 (4.3) [0.9, 12.0]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEM_SSIC: Incidence of AESI mental status change by race
SAF-S

	CR845		Placebo					
AESI mental status change	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
C: Race		n<10 for all subgroups						NE
Black/African American	82	4 (4.9) [1.3, 12.0]	75	2 (2.7) [0.3, 9.3]				
White	91	3 (3.3) [0.7, 9.3]	93	5 (5.4) [1.8, 12.1]				
Other	15	0 (0.0) [0.0, 21.8]	18	0 (0.0) [0.0, 18.5]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEM_SSID: Incidence of AESI mental status change by baseline WI-NRS
SAF-S

	CR845		Placebo					
AESI mental status change	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)		n<10 for all subgroups						NE
>= 4 to < 7	83	3 (3.6) [0.8, 10.2]	79	4 (5.1) [1.4, 12.5]				
>= 7	106	4 (3.8) [1.0, 9.4]	109	3 (2.8) [0.6, 7.8]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEM_SSIE: Incidence of AESI mental status change by specific medical condition
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI mental status change	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
E: Presence of specific medical conditions								0.927
No	164	6 (3.7) [1.4, 7.8]	160	6 (3.8) [1.4, 8.0]	0.976 [0.321, 2.962]	0.975 [0.308, 3.088]	-0.1 [-4.8, 4.6]	0.965
Yes	25	1 (4.0) [0.1, 20.4]	28	1 (3.6) [0.1, 18.3]	1.120 [0.074, 16.982]	1.125 [0.067, 18.984]	0.4 [-13.7, 14.5]	1.000 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEM_SSIF: Incidence of AESI mental status change by use of concomitant itch medication
SAF-S

	CR845		Placebo						
AESI mental status change	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
F: Use of concomitant itch medication								0.051	
No	117	3 (2.6) [0.5, 7.3]	110	7 (6.4) [2.6, 12.7]	0.403 [0.107, 1.519]	0.387 [0.098, 1.537]	-3.8 [-10.1, 2.5]	0.204	#
Yes	72	4 (5.6) [1.5, 13.6]	78	0 (0.0) [0.0, 4.6]	9.740 + [0.534, 177.785]	10.314 + [0.545, 195.029]	5.6 [-1.1, 12.2]	0.051	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEMN_SSIA: Incidence of AESI mental status change - non-severe by age
SAF-S

AESI mental status change - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
A: Age		n<10 for all subgroups						NE
< 65 years	135	3 (2.2) [0.5, 6.4]	136	5 (3.7) [1.2, 8.4]				
>= 65 years	54	2 (3.7) [0.5, 12.7]	52	1 (1.9) [0.0, 10.3]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEMN_SSIB: Incidence of AESI mental status change - non-severe by sex
SAF-S

AESI mental status change - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
B: Sex		n<10 for all subgroups						NE
Male	112	4 (3.6) [1.0, 8.9]	118	4 (3.4) [0.9, 8.5]				
Female	77	1 (1.3) [0.0, 7.0]	70	2 (2.9) [0.3, 9.9]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEMN_SSIC: Incidence of AESI mental status change - non-severe by race
SAF-S

AESI mental status change - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
C: Race		n<10 for all subgroups						NE
Black/African American	82	2 (2.4) [0.3, 8.5]	75	2 (2.7) [0.3, 9.3]				
White	91	3 (3.3) [0.7, 9.3]	93	4 (4.3) [1.2, 10.6]				
Other	15	0 (0.0) [0.0, 21.8]	18	0 (0.0) [0.0, 18.5]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEMN_SSID: Incidence of AESI mental status change - non-severe by baseline WI-NRS
SAF-S

AESI mental status change - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)		n<10 for all subgroups						NE
>= 4 to < 7	83	2 (2.4) [0.3, 8.4]	79	4 (5.1) [1.4, 12.5]				
>= 7	106	3 (2.8) [0.6, 8.0]	109	2 (1.8) [0.2, 6.5]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEMN_SSIE: Incidence of AESI mental status change - non-severe by specific medical condition
SAF-S

AESI mental status change - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
E: Presence of specific medical conditions		n<10 for all subgroups						NE
No	164	4 (2.4) [0.7, 6.1]	160	5 (3.1) [1.0, 7.1]				
Yes	25	1 (4.0) [0.1, 20.4]	28	1 (3.6) [0.1, 18.3]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEMN_SSIF: Incidence of AESI mental status change - non-severe by use of concomitant itch medication
SAF-S

AESI mental status change - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
F: Use of concomitant itch medication		n<10 for all subgroups						NE
No	117	2 (1.7) [0.2, 6.0]	110	6 (5.5) [2.0, 11.5]				
Yes	72	3 (4.2) [0.9, 11.7]	78	0 (0.0) [0.0, 4.6]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEU_SSIA: Incidence of AESI unusual feeling/sensation by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI unusual feeling/sensation	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
A: Age		n<10 for all subgroups						NE
< 65 years	135	3 (2.2) [0.5, 6.4]	136	4 (2.9) [0.8, 7.4]				
>= 65 years	54	2 (3.7) [0.5, 12.7]	52	3 (5.8) [1.2, 15.9]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEU_SSIB: Incidence of AESI unusual feeling/sensation by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI unusual feeling/sensation	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
B: Sex		n<10 for all subgroups						NE
Male	112	3 (2.7) [0.6, 7.6]	118	4 (3.4) [0.9, 8.5]				
Female	77	2 (2.6) [0.3, 9.1]	70	3 (4.3) [0.9, 12.0]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEU_SSIC: Incidence of AESI unusual feeling/sensation by race
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI unusual feeling/sensation	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
C: Race		n<10 for all subgroups						NE
Black/African American	82	4 (4.9) [1.3, 12.0]	75	3 (4.0) [0.8, 11.2]				
White	91	1 (1.1) [0.0, 6.0]	93	4 (4.3) [1.2, 10.6]				
Other	15	0 (0.0) [0.0, 21.8]	18	0 (0.0) [0.0, 18.5]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEU_SSID: Incidence of AESI unusual feeling/sensation by baseline WI-NRS
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI unusual feeling/sensation	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)								0.831
>= 4 to < 7	83	1 (1.2) [0.0, 6.5]	79	1 (1.3) [0.0, 6.9]	0.952 [0.061, 14.958]	0.951 [0.058, 15.473]	-0.1 [-4.7, 4.6]	1.000 #
>= 7	106	4 (3.8) [1.0, 9.4]	109	6 (5.5) [2.0, 11.6]	0.686 [0.199, 2.361]	0.673 [0.184, 2.456]	-1.7 [-8.3, 4.8]	0.748 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEU_SSIE: Incidence of AESI unusual feeling/sensation by specific medical condition
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI unusual feeling/sensation	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
E: Presence of specific medical conditions								0.299
No	164	4 (2.4) [0.7, 6.1]	160	7 (4.4) [1.8, 8.8]	0.557 [0.166, 1.868]	0.546 [0.157, 1.904]	-1.9 [-6.5, 2.6]	0.337
Yes	25	1 (4.0) [0.1, 20.4]	28	0 (0.0) [0.0, 12.3]	3.346 + [0.142, 78.598]	3.490 + [0.136, 89.629]	4.0 [-7.5, 15.5]	0.472 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEU_SSIF: Incidence of AESI unusual feeling/sensation by use of concomitant itch medication
SAF-S

	CR845		Placebo					
AESI unusual feeling/sensation	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
F: Use of concomitant itch medication		n<10 for all subgroups						NE
No	117	2 (1.7) [0.2, 6.0]	110	4 (3.6) [1.0, 9.0]				
Yes	72	3 (4.2) [0.9, 11.7]	78	3 (3.8) [0.8, 10.8]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEUN_SSIA: Incidence of AESI unusual feeling/sensation - non-severe by age
SAF-S

AESI unusual feeling/sensation - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
A: Age		n<10 for all subgroups						NE
< 65 years	135	3 (2.2) [0.5, 6.4]	136	4 (2.9) [0.8, 7.4]				
>= 65 years	54	2 (3.7) [0.5, 12.7]	52	3 (5.8) [1.2, 15.9]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEUN_SSIB: Incidence of AESI unusual feeling/sensation - non-severe by sex
SAF-S

AESI unusual feeling/sensation - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
B: Sex		n<10 for all subgroups						NE
Male	112	3 (2.7) [0.6, 7.6]	118	4 (3.4) [0.9, 8.5]				
Female	77	2 (2.6) [0.3, 9.1]	70	3 (4.3) [0.9, 12.0]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEUN_SSIC: Incidence of AESI unusual feeling/sensation - non-severe by race
SAF-S

AESI unusual feeling/sensation - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
C: Race		n<10 for all subgroups						NE
Black/African American	82	4 (4.9) [1.3, 12.0]	75	3 (4.0) [0.8, 11.2]				
White	91	1 (1.1) [0.0, 6.0]	93	4 (4.3) [1.2, 10.6]				
Other	15	0 (0.0) [0.0, 21.8]	18	0 (0.0) [0.0, 18.5]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEUN_SSID: Incidence of AESI unusual feeling/sensation - non-severe by baseline WI-NRS
SAF-S

AESI unusual feeling/sensation - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
D: Baseline worst itching NRS score (WI-NRS)								0.831	
>= 4 to < 7	83	1 (1.2) [0.0, 6.5]	79	1 (1.3) [0.0, 6.9]	0.952 [0.061, 14.958]	0.951 [0.058, 15.473]	-0.1 [-4.7, 4.6]	1.000	#
>= 7	106	4 (3.8) [1.0, 9.4]	109	6 (5.5) [2.0, 11.6]	0.686 [0.199, 2.361]	0.673 [0.184, 2.456]	-1.7 [-8.3, 4.8]	0.748	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEUN_SSIE: Incidence of AESI unusual feeling/sensation - non-severe by specific medical condition
SAF-S

AESI unusual feeling/sensation - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
E: Presence of specific medical conditions								0.299	
No	164	4 (2.4) [0.7, 6.1]	160	7 (4.4) [1.8, 8.8]	0.557 [0.166, 1.868]	0.546 [0.157, 1.904]	-1.9 [-6.5, 2.6]	0.337	
Yes	25	1 (4.0) [0.1, 20.4]	28	0 (0.0) [0.0, 12.3]	3.346 + [0.142, 78.598]	3.490 + [0.136, 89.629]	4.0 [-7.5, 15.5]	0.472	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table AT2AEUN_SSIF: Incidence of AESI unusual feeling/sensation - non-severe by use of concomitant itch medication
SAF-S

	CR845		Placebo					
AESI unusual feeling/sensation - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
F: Use of concomitant itch medication		n<10 for all subgroups						NE
No	117	2 (1.7) [0.2, 6.0]	110	4 (3.6) [1.0, 9.0]				
Yes	72	3 (4.2) [0.9, 11.7]	78	3 (3.8) [0.8, 10.8]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Anhang 4-H-2:
Zusatzauswertungen der Studie KALM-2 (DB)

Table BT2WIB_IOA0: Baseline weekly WI-NRS (categorical)
ITT

		CR845		Placebo	
	Category	N	n (%)	N	n (%)
Baseline weekly WI-NRS	< 3 points	237	0 (0.0)	236	0 (0.0)
	3 - < 4 points	237	0 (0.0)	236	0 (0.0)
	4 - 6 points	237	51 (21.5)	236	69 (29.2)
	> 6 - 7 points	237	64 (27.0)	236	52 (22.0)
	> 7 points	237	122 (51.5)	236	115 (48.7)
	Missing	237	0 (0.0)	236	0 (0.0)

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients in category. WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 11FEB2022

Table BT2DTB_IOA0: Baseline 5-D total score (categorical)
ITT

		CR845		Placebo	
	Category	N	n (%)	N	n (%)
Baseline 5-D total score	< 10 points	237	5 (2.1)	236	4 (1.7)
	10 - 20 points	237	192 (81.0)	236	207 (87.7)
	> 20 points	237	35 (14.8)	236	25 (10.6)
	Missing	237	5 (2.1)	236	0 (0.0)

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients in category.
Source Data: afived, created on: 10FEB2022

Table BT2DDB_IOA0: Baseline 5-D degree score (categorical)
ITT

		CR845		Placebo	
	Category	N	n (%)	N	n (%)
Baseline 5-D degree score	1 point	237	2 (0.8)	236	0 (0.0)
	2 - 4 points	237	213 (89.9)	236	218 (92.4)
	5 points	237	19 (8.0)	236	18 (7.6)
	Missing	237	3 (1.3)	236	0 (0.0)

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients in category.
Source Data: afived, created on: 10FEB2022

Table BT2DLB_IOA0: Baseline 5-D duration score (categorical)
ITT

		CR845		Placebo	
	Category	N	n (%)	N	n (%)
Baseline 5-D duration score	1 point	237	51 (21.5)	236	65 (27.5)
	2 - 4 points	237	136 (57.4)	236	139 (58.9)
	5 points	237	46 (19.4)	236	32 (13.6)
	Missing	237	4 (1.7)	236	0 (0.0)

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients in category.
Source Data: afived, created on: 10FEB2022

Table BT2DWB_IOA0: Baseline 5-D direction score (categorical)
ITT

		CR845		Placebo	
	Category	N	n (%)	N	n (%)
Baseline 5-D direction score	1 point	237	1 (0.4)	236	0 (0.0)
	2 - 4 points	237	209 (88.2)	236	208 (88.1)
	5 points	237	24 (10.1)	236	28 (11.9)
	Missing	237	3 (1.3)	236	0 (0.0)

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients in category.
Source Data: afived, created on: 10FEB2022

Table BT2DNB_IOA0: Baseline 5-D disability score (categorical)
ITT

		CR845		Placebo	
	Category	N	n (%)	N	n (%)
Baseline 5-D disability score	1 point	237	14 (5.9)	236	17 (7.2)
	2 - 4 points	237	169 (71.3)	236	170 (72.0)
	5 points	237	50 (21.1)	236	49 (20.8)
	Missing	237	4 (1.7)	236	0 (0.0)

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients in category.
Source Data: afived, created on: 10FEB2022

Table BT2DVB_IOA0: Baseline 5-D distribution score (categorical)
ITT

		CR845		Placebo	
	Category	N	n (%)	N	n (%)
Baseline 5-D distribution score	1 point	237	19 (8.0)	236	16 (6.8)
	2 - 4 points	237	174 (73.4)	236	200 (84.7)
	5 points	237	41 (17.3)	236	20 (8.5)
	Missing	237	3 (1.3)	236	0 (0.0)

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients in category.
Source Data: afived, created on: 10FEB2022

Table BT2DDC_IMH0: Change from baseline in 5-D degree score
ITT

		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
5-D degree score	Baseline	CR845	237	234 (98.7)	3.5 (0.8)	1	4.0	5	
		Placebo	236	236 (100.0)	3.5 (0.7)	2	3.0	5	
	Week 4	CR845	237	214 (90.3)	2.8 (0.8)	1	3.0	5	
		Placebo	236	225 (95.3)	3.0 (0.8)	1	3.0	5	
	Week 8	CR845	237	210 (88.6)	2.7 (0.9)	1	3.0	5	
		Placebo	236	222 (94.1)	2.9 (0.8)	1	3.0	5	
	Week 10	CR845	237	206 (86.9)	2.6 (0.9)	1	3.0	5	
		Placebo	236	217 (91.9)	2.8 (0.8)	1	3.0	5	
	Week 12	CR845	237	205 (86.5)	2.6 (0.9)	1	3.0	5	
		Placebo	236	219 (92.8)	2.7 (0.8)	1	3.0	5	
Change from baseline in 5-D degree score	Week 4	CR845	237	212 (89.5)	-0.8 (1.0)	-4	-1.0	3	-0.29 [-0.48, -0.10]
		Placebo	236	225 (95.3)	-0.5 (0.8)	-3	0.0	2	
	Week 8	CR845	237	208 (87.8)	-0.8 (1.1)	-4	-1.0	3	-0.19 [-0.38, -0.00]
		Placebo	236	222 (94.1)	-0.6 (0.9)	-3	0.0	1	
	Week 10	CR845	237	204 (86.1)	-0.9 (1.1)	-4	-1.0	3	-0.25 [-0.44, -0.05]
		Placebo	236	217 (91.9)	-0.7 (0.9)	-3	-1.0	2	
	Week 12	CR845	237	203 (85.7)	-0.9 (1.1)	-4	-1.0	3	-0.17 [-0.36, 0.02]
		Placebo	236	219 (92.8)	-0.8 (0.9)	-3	-1.0	2	

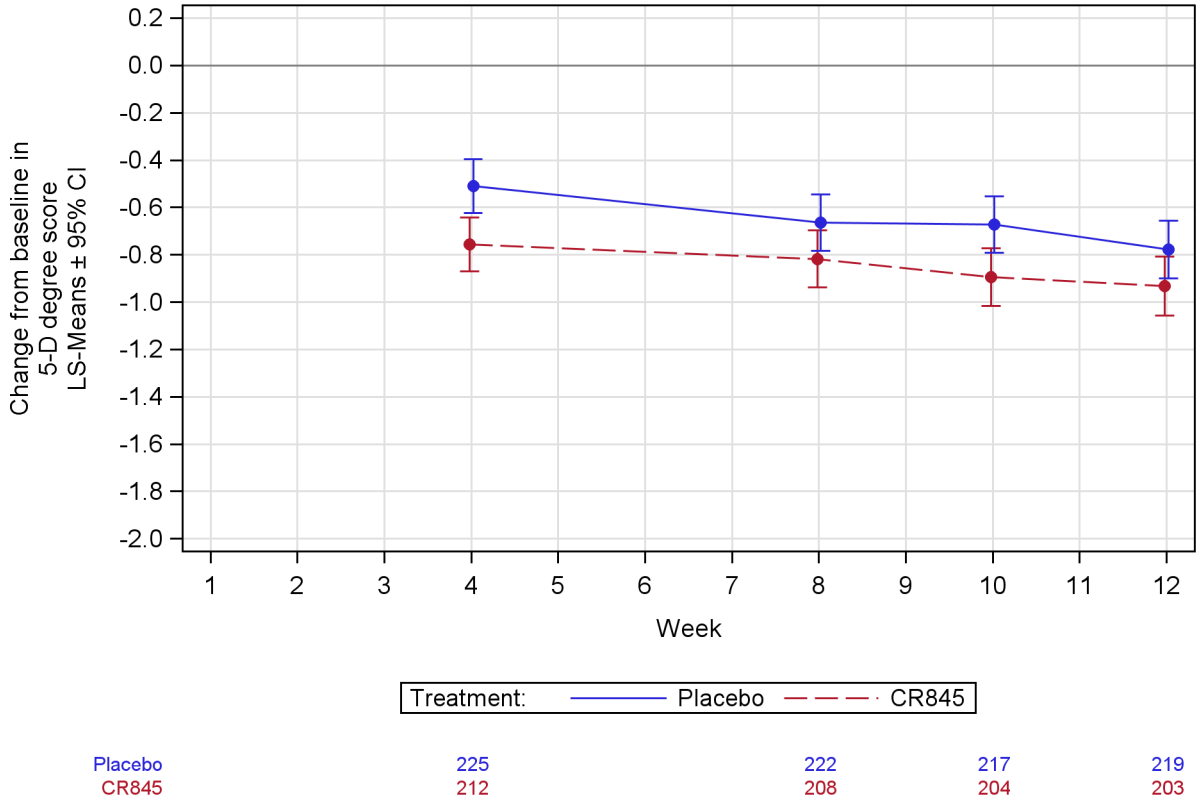
Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DDC_IMC0: Change from baseline in 5-D degree score - MMRM results
ITT

Change from baseline in 5-D degree score				Repeated measures analysis				
				Change from Baseline		Treatment Difference		
Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Week 4	CR845	237	212 (89.5)	-0.8 (0.1)	(-0.9, -0.6)	-0.2 (0.1)	(-0.4, -0.1)	<0.001 *
	Placebo	236	225 (95.3)	-0.5 (0.1)	(-0.6, -0.4)			
Week 8	CR845	237	208 (87.8)	-0.8 (0.1)	(-0.9, -0.7)	-0.2 (0.1)	(-0.3, -0.0)	0.047 *
	Placebo	236	222 (94.1)	-0.7 (0.1)	(-0.8, -0.5)			
Week 10	CR845	237	204 (86.1)	-0.9 (0.1)	(-1.0, -0.8)	-0.2 (0.1)	(-0.4, -0.1)	0.005 *
	Placebo	236	217 (91.9)	-0.7 (0.1)	(-0.8, -0.6)			
Week 12	CR845	237	203 (85.7)	-0.9 (0.1)	(-1.1, -0.8)	-0.2 (0.1)	(-0.3, 0.0)	0.055
	Placebo	236	219 (92.8)	-0.8 (0.1)	(-0.9, -0.7)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval . * = significant treatment effect.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Figure BF2DDC_IMG0: Course of change from baseline in 5-D degree score
ITT



Note: ITT = Intent-to-treat Set.
Symbols present least square mean (LS-Mean), bars present 95% confidence intervals (CI).
CR845 = Difelikefalin.
Source Table: BT2DDC_IMC0
Source Data: afived, created on: 17FEB2022

Table BT2DLC_IMH0: Change from baseline in 5-D duration score
ITT

		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
5-D duration score	Baseline	CR845	237	233 (98.3)	2.8 (1.4)	1	2.0	5	
		Placebo	236	236 (100.0)	2.5 (1.3)	1	2.0	5	
	Week 4	CR845	237	214 (90.3)	2.0 (1.2)	1	2.0	5	
		Placebo	236	225 (95.3)	2.2 (1.3)	1	2.0	5	
	Week 8	CR845	237	210 (88.6)	1.8 (1.2)	1	1.0	5	
		Placebo	236	222 (94.1)	1.9 (1.1)	1	2.0	5	
	Week 10	CR845	237	206 (86.9)	1.9 (1.2)	1	1.0	5	
		Placebo	236	217 (91.9)	1.9 (1.2)	1	2.0	5	
	Week 12	CR845	237	205 (86.5)	1.8 (1.1)	1	1.0	5	
		Placebo	236	219 (92.8)	2.0 (1.3)	1	2.0	5	
Change from baseline in 5-D duration score	Week 4	CR845	237	211 (89.0)	-0.8 (1.4)	-4	-1.0	2	-0.30 [-0.49, -0.11]
		Placebo	236	225 (95.3)	-0.3 (1.5)	-4	0.0	4	
	Week 8	CR845	237	207 (87.3)	-0.9 (1.4)	-4	-1.0	2	-0.23 [-0.42, -0.04]
		Placebo	236	222 (94.1)	-0.6 (1.4)	-4	0.0	4	
	Week 10	CR845	237	203 (85.7)	-0.9 (1.5)	-4	-1.0	4	-0.21 [-0.40, -0.01]
		Placebo	236	217 (91.9)	-0.6 (1.4)	-4	0.0	4	
	Week 12	CR845	237	202 (85.2)	-1.0 (1.5)	-4	-1.0	4	-0.29 [-0.48, -0.10]
		Placebo	236	219 (92.8)	-0.5 (1.5)	-4	0.0	4	

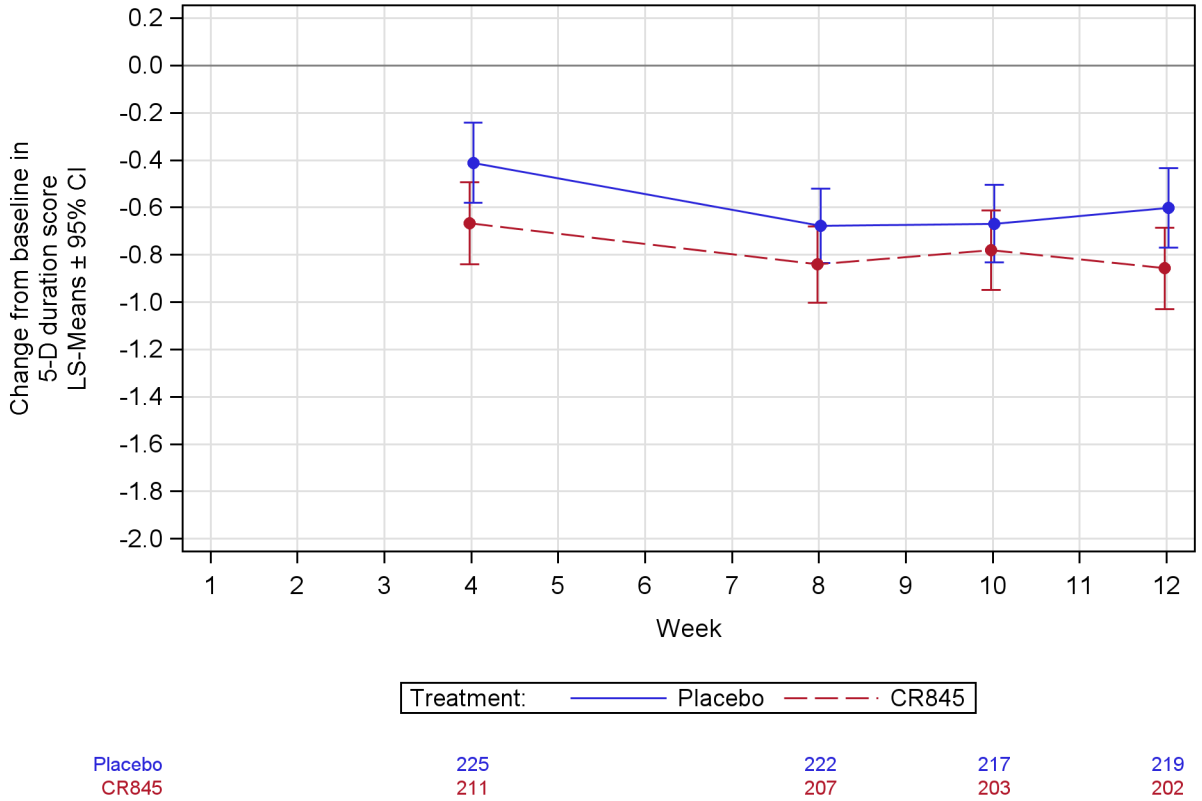
Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DLC_IMC0: Change from baseline in 5-D duration score - MMRM results
ITT

Change from baseline in 5-D duration score				Repeated measures analysis				
				Change from Baseline		Treatment Difference		
Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Week 4	CR845	237	211 (89.0)	-0.7 (0.1)	(-0.8, -0.5)	-0.3 (0.1)	(-0.5, -0.0)	0.021 *
	Placebo	236	225 (95.3)	-0.4 (0.1)	(-0.6, -0.2)			
Week 8	CR845	237	207 (87.3)	-0.8 (0.1)	(-1.0, -0.7)	-0.2 (0.1)	(-0.4, 0.0)	0.109
	Placebo	236	222 (94.1)	-0.7 (0.1)	(-0.8, -0.5)			
Week 10	CR845	237	203 (85.7)	-0.8 (0.1)	(-0.9, -0.6)	-0.1 (0.1)	(-0.3, 0.1)	0.288
	Placebo	236	217 (91.9)	-0.7 (0.1)	(-0.8, -0.5)			
Week 12	CR845	237	202 (85.2)	-0.9 (0.1)	(-1.0, -0.7)	-0.3 (0.1)	(-0.5, -0.0)	0.021 *
	Placebo	236	219 (92.8)	-0.6 (0.1)	(-0.8, -0.4)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval . * = significant treatment effect.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Figure BF2DLC_IMG0: Course of change from baseline in 5-D duration score
ITT



Note: ITT = Intent-to-treat Set.
Symbols present least square mean (LS-Mean), bars present 95% confidence intervals (CI).
CR845 = Difelikefalin.
Source Table: BT2DLC_IMC0
Source Data: afived, created on: 17FEB2022

Table BT2DWC_IMH0: Change from baseline in 5-D direction score
ITT

		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
5-D direction score	Baseline	CR845	237	234 (98.7)	3.9 (0.6)	1	4.0	5	
		Placebo	236	236 (100.0)	3.8 (0.7)	2	4.0	5	
	Week 4	CR845	237	215 (90.7)	2.7 (0.8)	1	3.0	5	
		Placebo	236	225 (95.3)	3.1 (0.9)	1	3.0	5	
	Week 8	CR845	237	209 (88.2)	2.7 (0.9)	1	3.0	5	
		Placebo	236	222 (94.1)	2.9 (0.9)	1	3.0	5	
	Week 10	CR845	237	206 (86.9)	2.6 (0.9)	1	2.0	5	
		Placebo	236	217 (91.9)	3.0 (0.9)	1	3.0	5	
	Week 12	CR845	237	204 (86.1)	2.6 (1.0)	1	2.0	5	
		Placebo	236	219 (92.8)	2.9 (1.0)	1	3.0	5	
Change from baseline in 5-D direction score	Week 4	CR845	237	213 (89.9)	-1.2 (1.0)	-4	-1.0	2	-0.45 [-0.64, -0.26]
		Placebo	236	225 (95.3)	-0.7 (1.0)	-3	-1.0	2	
	Week 8	CR845	237	207 (87.3)	-1.2 (1.0)	-4	-1.0	2	-0.32 [-0.51, -0.12]
		Placebo	236	222 (94.1)	-0.9 (1.1)	-3	-1.0	2	
	Week 10	CR845	237	204 (86.1)	-1.3 (1.0)	-4	-1.0	1	-0.40 [-0.59, -0.21]
		Placebo	236	217 (91.9)	-0.8 (1.1)	-3	-1.0	3	
	Week 12	CR845	237	202 (85.2)	-1.2 (1.1)	-4	-1.0	2	-0.28 [-0.48, -0.09]
		Placebo	236	219 (92.8)	-0.9 (1.1)	-4	-1.0	2	

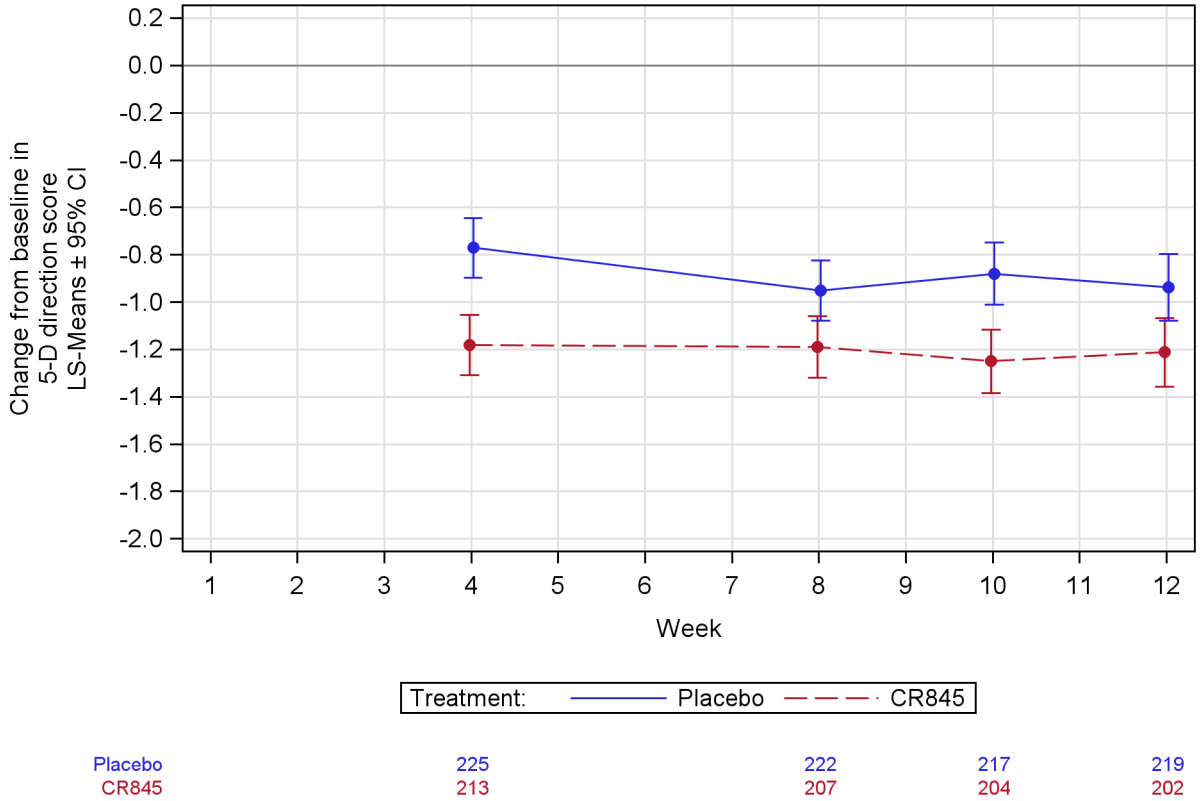
Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DWC_IMC0: Change from baseline in 5-D direction score - MMRM results
ITT

Change from baseline in 5-D direction score				Repeated measures analysis				
				Change from Baseline		Treatment Difference		
Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Week 4	CR845	237	213 (89.9)	-1.2 (0.1)	(-1.3, -1.1)	-0.4 (0.1)	(-0.6, -0.3)	<0.001 *
	Placebo	236	225 (95.3)	-0.8 (0.1)	(-0.9, -0.6)			
Week 8	CR845	237	207 (87.3)	-1.2 (0.1)	(-1.3, -1.1)	-0.2 (0.1)	(-0.4, -0.1)	0.004 *
	Placebo	236	222 (94.1)	-1.0 (0.1)	(-1.1, -0.8)			
Week 10	CR845	237	204 (86.1)	-1.2 (0.1)	(-1.4, -1.1)	-0.4 (0.1)	(-0.5, -0.2)	<0.001 *
	Placebo	236	217 (91.9)	-0.9 (0.1)	(-1.0, -0.7)			
Week 12	CR845	237	202 (85.2)	-1.2 (0.1)	(-1.4, -1.1)	-0.3 (0.1)	(-0.5, -0.1)	0.003 *
	Placebo	236	219 (92.8)	-0.9 (0.1)	(-1.1, -0.8)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval . * = significant treatment effect.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Figure BF2DWC_IMG0: Course of change from baseline in 5-D direction score
ITT



Note: ITT = Intent-to-treat Set.
Symbols present least square mean (LS-Mean), bars present 95% confidence intervals (CI).
CR845 = Difelikefalin.
Source Table: BT2DWC_IMC0
Source Data: afived, created on: 17FEB2022

Table BT2DNC_IMH0: Change from baseline in 5-D disability score
ITT

		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
5-D disability score	Baseline	CR845	237	233 (98.3)	3.5 (1.1)	1	4.0	5	
		Placebo	236	236 (100.0)	3.5 (1.2)	1	4.0	5	
	Week 4	CR845	237	215 (90.7)	2.8 (1.2)	1	3.0	5	
		Placebo	236	225 (95.3)	2.9 (1.2)	1	3.0	5	
	Week 8	CR845	237	210 (88.6)	2.6 (1.2)	1	2.0	5	
		Placebo	236	222 (94.1)	2.7 (1.2)	1	3.0	5	
	Week 10	CR845	237	206 (86.9)	2.4 (1.2)	1	2.0	5	
		Placebo	236	217 (91.9)	2.7 (1.2)	1	2.0	5	
	Week 12	CR845	237	205 (86.5)	2.4 (1.3)	1	2.0	5	
		Placebo	236	219 (92.8)	2.5 (1.2)	1	2.0	5	
Change from baseline in 5-D disability score	Week 4	CR845	237	213 (89.9)	-0.7 (1.2)	-4	-1.0	3	-0.09 [-0.28, 0.10]
		Placebo	236	225 (95.3)	-0.6 (1.3)	-4	0.0	3	
	Week 8	CR845	237	208 (87.8)	-0.9 (1.3)	-4	-1.0	3	-0.13 [-0.32, 0.06]
		Placebo	236	222 (94.1)	-0.8 (1.4)	-4	-1.0	4	
	Week 10	CR845	237	204 (86.1)	-1.1 (1.3)	-4	-1.0	3	-0.18 [-0.37, 0.01]
		Placebo	236	217 (91.9)	-0.8 (1.3)	-4	-1.0	3	
	Week 12	CR845	237	203 (85.7)	-1.1 (1.4)	-4	-1.0	4	-0.10 [-0.29, 0.09]
		Placebo	236	219 (92.8)	-0.9 (1.3)	-4	-1.0	3	

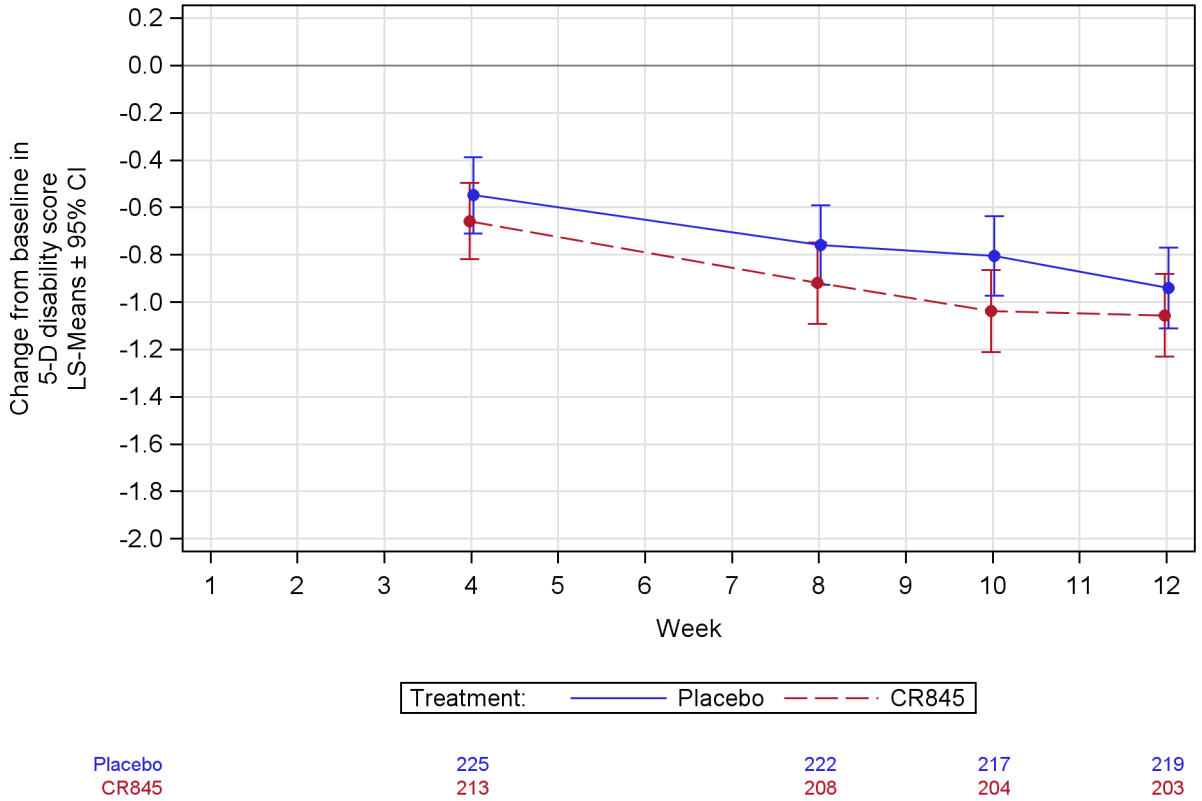
Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DNC_IMC0: Change from baseline in 5-D disability score - MMRM results
ITT

Change from baseline in 5-D disability score				Repeated measures analysis				
				Change from Baseline		Treatment Difference		
Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Week 4	CR845	237	213 (89.9)	-0.7 (0.1)	(-0.8, -0.5)	-0.1 (0.1)	(-0.3, 0.1)	0.286
	Placebo	236	225 (95.3)	-0.5 (0.1)	(-0.7, -0.4)			
Week 8	CR845	237	208 (87.8)	-0.9 (0.1)	(-1.1, -0.7)	-0.2 (0.1)	(-0.4, 0.1)	0.141
	Placebo	236	222 (94.1)	-0.8 (0.1)	(-0.9, -0.6)			
Week 10	CR845	237	204 (86.1)	-1.0 (0.1)	(-1.2, -0.9)	-0.2 (0.1)	(-0.4, -0.0)	0.034 *
	Placebo	236	217 (91.9)	-0.8 (0.1)	(-1.0, -0.6)			
Week 12	CR845	237	203 (85.7)	-1.1 (0.1)	(-1.2, -0.9)	-0.1 (0.1)	(-0.3, 0.1)	0.298
	Placebo	236	219 (92.8)	-0.9 (0.1)	(-1.1, -0.8)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval . * = significant treatment effect.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Figure BF2DNC_IMG0: Course of change from baseline in 5-D disability score
ITT



Note: ITT = Intent-to-treat Set.
Symbols present least square mean (LS-Mean), bars present 95% confidence intervals (CI).
CR845 = Difelikefalin.
Source Table: BT2DNC_IMC0
Source Data: afived, created on: 17FEB2022

Table BT2DVC_IMH0: Change from baseline in 5-D distribution score
ITT

		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
5-D distribution score	Baseline	CR845	237	234 (98.7)	3.1 (1.2)	1	3.0	5	
		Placebo	236	236 (100.0)	2.9 (1.0)	1	3.0	5	
	Week 4	CR845	237	215 (90.7)	2.5 (1.2)	1	2.0	5	
		Placebo	236	225 (95.3)	2.7 (1.1)	1	3.0	5	
	Week 8	CR845	237	210 (88.6)	2.5 (1.3)	1	2.0	5	
		Placebo	236	222 (94.1)	2.6 (1.1)	1	2.5	5	
	Week 10	CR845	237	206 (86.9)	2.5 (1.2)	1	2.0	5	
		Placebo	236	217 (91.9)	2.6 (1.1)	1	2.0	5	
	Week 12	CR845	237	205 (86.5)	2.4 (1.2)	1	2.0	5	
		Placebo	236	219 (92.8)	2.6 (1.2)	1	2.0	5	
Change from baseline in 5-D distribution score	Week 4	CR845	237	213 (89.9)	-0.5 (1.0)	-4	0.0	2	-0.27 [-0.46, -0.09]
		Placebo	236	225 (95.3)	-0.2 (1.0)	-4	0.0	2	
	Week 8	CR845	237	208 (87.8)	-0.6 (1.2)	-4	0.0	3	-0.20 [-0.39, -0.01]
		Placebo	236	222 (94.1)	-0.3 (1.1)	-4	0.0	3	
	Week 10	CR845	237	204 (86.1)	-0.6 (1.3)	-4	0.0	3	-0.25 [-0.44, -0.06]
		Placebo	236	217 (91.9)	-0.3 (1.0)	-4	0.0	3	
	Week 12	CR845	237	203 (85.7)	-0.6 (1.3)	-4	0.0	4	-0.28 [-0.47, -0.09]
		Placebo	236	219 (92.8)	-0.3 (1.0)	-3	0.0	3	

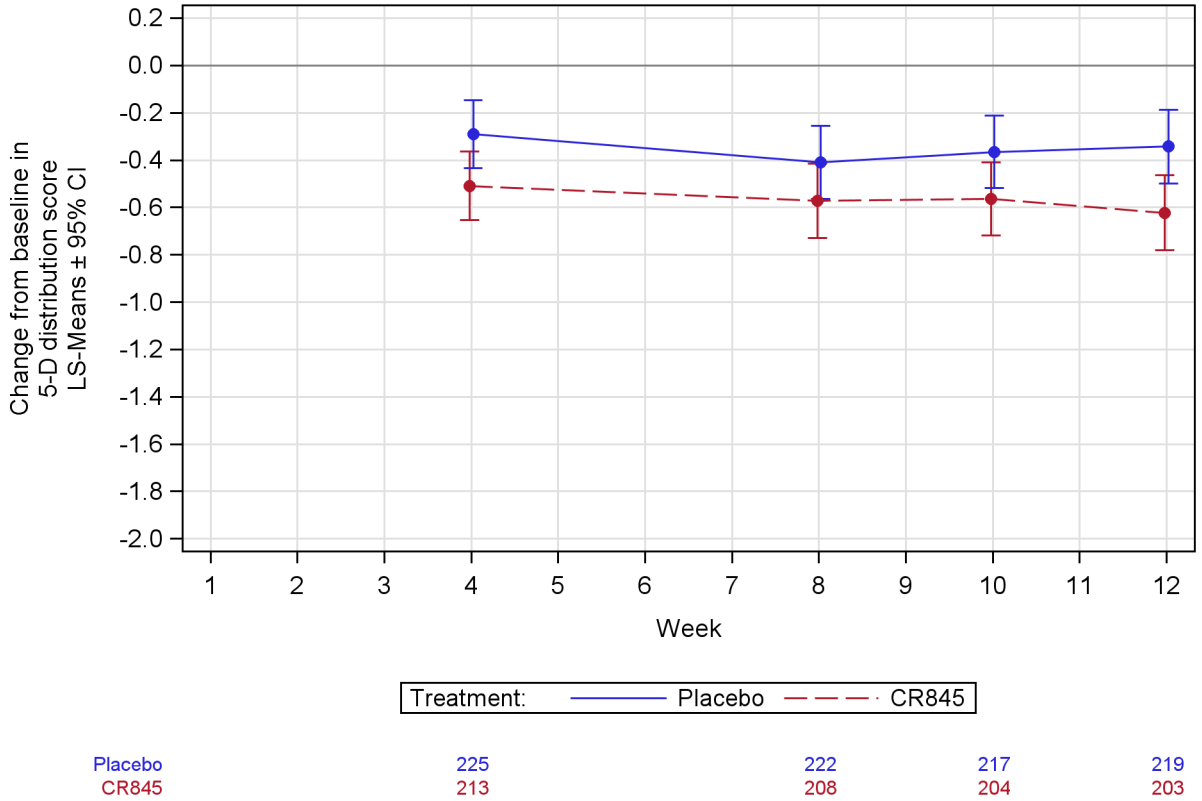
Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DVC_IMC0: Change from baseline in 5-D distribution score - MMRM results
ITT

Change from baseline in 5-D distribution score				Repeated measures analysis				
				Change from Baseline		Treatment Difference		
Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Week 4	CR845	237	213 (89.9)	-0.5 (0.1)	(-0.7, -0.4)	-0.2 (0.1)	(-0.4, -0.0)	0.015 *
	Placebo	236	225 (95.3)	-0.3 (0.1)	(-0.4, -0.1)			
Week 8	CR845	237	208 (87.8)	-0.6 (0.1)	(-0.7, -0.4)	-0.2 (0.1)	(-0.4, 0.0)	0.101
	Placebo	236	222 (94.1)	-0.4 (0.1)	(-0.6, -0.3)			
Week 10	CR845	237	204 (86.1)	-0.6 (0.1)	(-0.7, -0.4)	-0.2 (0.1)	(-0.4, -0.0)	0.043 *
	Placebo	236	217 (91.9)	-0.4 (0.1)	(-0.5, -0.2)			
Week 12	CR845	237	203 (85.7)	-0.6 (0.1)	(-0.8, -0.5)	-0.3 (0.1)	(-0.5, -0.1)	0.006 *
	Placebo	236	219 (92.8)	-0.3 (0.1)	(-0.5, -0.2)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval . * = significant treatment effect.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Figure BF2DVC_IMG0: Course of change from baseline in 5-D distribution score
ITT



Note: ITT = Intent-to-treat Set.
Symbols present least square mean (LS-Mean), bars present 95% confidence intervals (CI).
CR845 = Difelikefalin.
Source Table: BT2DVC_IMC0
Source Data: afived, created on: 17FEB2022

Table BT2DDCD1_IMP0: Decrease of 5-D degree score of at least 1 point
ITT

		CR845			Placebo						
Variable	Time	N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Decrease of 5-D degree score of at least 1 point	Week 12	237	203 (85.7)	136 (57.4) [50.8, 63.8]	236	219 (92.8)	132 (55.9) [49.3, 62.4]	1.026 [0.876, 1.201]	1.061 [0.737, 1.526]	1.5 [-7.9, 10.8]	0.750

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: afived, created on: 10FEB2022

Table BT2DLCD1_IMP0: Decrease of 5-D duration score of at least 1 point
ITT

		CR845			Placebo						
Variable	Time	N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Decrease of 5-D duration score of at least 1 point	Week 12	237	202 (85.2)	115 (48.5) [42.0, 55.1]	236	219 (92.8)	103 (43.6) [37.2, 50.2]	1.112 [0.914, 1.352]	1.217 [0.847, 1.748]	4.9 [-4.5, 14.3]	0.288

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: afived, created on: 10FEB2022

Table BT2DWCD1_IMP0: Decrease of 5-D direction score of at least 1 point
ITT

		CR845			Placebo						
Variable	Time	N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Decrease of 5-D direction score of at least 1 point	Week 12	237	202 (85.2)	155 (65.4) [59.0, 71.4]	236	219 (92.8)	136 (57.6) [51.0, 64.0]	1.135 [0.983, 1.310]	1.390 [0.958, 2.016]	7.8 [-1.4, 16.9]	0.083

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: afived, created on: 10FEB2022

Table BT2DNCD1_IMP0: Decrease of 5-D disability score of at least 1 point
ITT

		CR845			Placebo						
Variable	Time	N	nval	n (%) [95 % CI]	N	nval	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Decrease of 5-D disability score of at least 1 point	Week 12	237	203 (85.7)	135 (57.0) [50.4, 63.4]	236	219 (92.8)	135 (57.2) [50.6, 63.6]	0.996 [0.852, 1.164]	0.990 [0.688, 1.425]	-0.2 [-9.6, 9.1]	0.958

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: afived, created on: 10FEB2022

Table BT2DVCD1_IMP0: Decrease of 5-D distribution score of at least 1 point
ITT

		CR845			Placebo						
Variable	Time	N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Decrease of 5-D distribution score of at least 1 point	Week 12	237	203 (85.7)	97 (40.9) [34.6, 47.5]	236	219 (92.8)	84 (35.6) [29.5, 42.1]	1.150 [0.914, 1.447]	1.254 [0.865, 1.818]	5.3 [-3.8, 14.5]	0.233

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: afived, created on: 10FEB2022

Table BT2STB_IOA0: Baseline Skindex-10 total score (categorical)
ITT

		CR845		Placebo	
	Category	N	n (%)	N	n (%)
Baseline Skindex-10 total score	< 15 points	237	22 (9.3)	236	24 (10.2)
	15 - 45 points	237	147 (62.0)	236	152 (64.4)
	> 45 points	237	62 (26.2)	236	54 (22.9)
	Missing	237	6 (2.5)	236	6 (2.5)

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients in category.
Source Data: askin, created on: 11FEB2022

Table BT2SDB_IOA0: Baseline Skindex-10 disease score (categorical)
ITT

		CR845		Placebo	
	Category	N	n (%)	N	n (%)
Baseline Skindex-10 disease score	< 3 points	237	6 (2.5)	236	1 (0.4)
	3 - 15 points	237	153 (64.6)	236	174 (73.7)
	> 15 points	237	74 (31.2)	236	58 (24.6)
	Missing	237	4 (1.7)	236	3 (1.3)

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients in category.
Source Data: askin, created on: 11FEB2022

Table BT2SMB_IOA0: Baseline Skindex-10 mood/emotional distress score (categorical)
ITT

		CR845		Placebo	
	Category	N	n (%)	N	n (%)
Baseline Skindex-10 mood/emotional distress score	< 3 points	237	14 (5.9)	236	14 (5.9)
	3 - 15 points	237	163 (68.8)	236	172 (72.9)
	> 15 points	237	55 (23.2)	236	47 (19.9)
	Missing	237	5 (2.1)	236	3 (1.3)

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients in category.
Source Data: askin, created on: 11FEB2022

Table BT2SSB_IOA0: Baseline Skindex-10 social functioning score (categorical)
ITT

		CR845		Placebo	
	Category	N	n (%)	N	n (%)
Baseline Skindex-10 social functioning score	< 4 points	237	55 (23.2)	236	50 (21.2)
	4 - 20 points	237	143 (60.3)	236	149 (63.1)
	> 20 points	237	36 (15.2)	236	33 (14.0)
	Missing	237	3 (1.3)	236	4 (1.7)

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients in category.
Source Data: askin, created on: 11FEB2022

Table BT2SDC_IMH0: Change from baseline in Skindex-10 disease score
ITT

		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Skindex-10 disease score	Baseline	CR845	237	233 (98.3)	12.9 (4.2)	0	13.0	18	
		Placebo	236	233 (98.7)	12.4 (4.0)	0	13.0	18	
	Week 4	CR845	237	212 (89.5)	9.0 (5.2)	0	9.0	18	
		Placebo	236	217 (91.9)	9.8 (4.9)	0	9.0	18	
	Week 8	CR845	237	209 (88.2)	8.3 (5.4)	0	8.0	18	
		Placebo	236	218 (92.4)	8.5 (4.7)	0	8.0	18	
	Week 10	CR845	237	205 (86.5)	7.3 (5.2)	0	6.0	18	
		Placebo	236	213 (90.3)	8.4 (4.6)	0	8.0	18	
	Week 12	CR845	237	203 (85.7)	7.4 (5.3)	0	7.0	18	
		Placebo	236	215 (91.1)	8.0 (4.8)	0	8.0	18	
Change from baseline in Skindex-10 disease score	Week 4	CR845	237	210 (88.6)	-3.9 (5.0)	-17	-3.5	9	-0.28 [-0.48, -0.09]
		Placebo	236	215 (91.1)	-2.5 (4.9)	-17	-2.0	12	
	Week 8	CR845	237	207 (87.3)	-4.6 (5.3)	-17	-5.0	11	-0.15 [-0.34, 0.04]
		Placebo	236	216 (91.5)	-3.8 (4.7)	-16	-3.0	9	
	Week 10	CR845	237	203 (85.7)	-5.5 (5.1)	-17	-6.0	9	-0.32 [-0.52, -0.13]
		Placebo	236	211 (89.4)	-3.9 (4.7)	-15	-3.0	8	
	Week 12	CR845	237	201 (84.8)	-5.5 (5.5)	-18	-6.0	9	-0.22 [-0.41, -0.03]
		Placebo	236	214 (90.7)	-4.3 (5.0)	-18	-4.0	12	

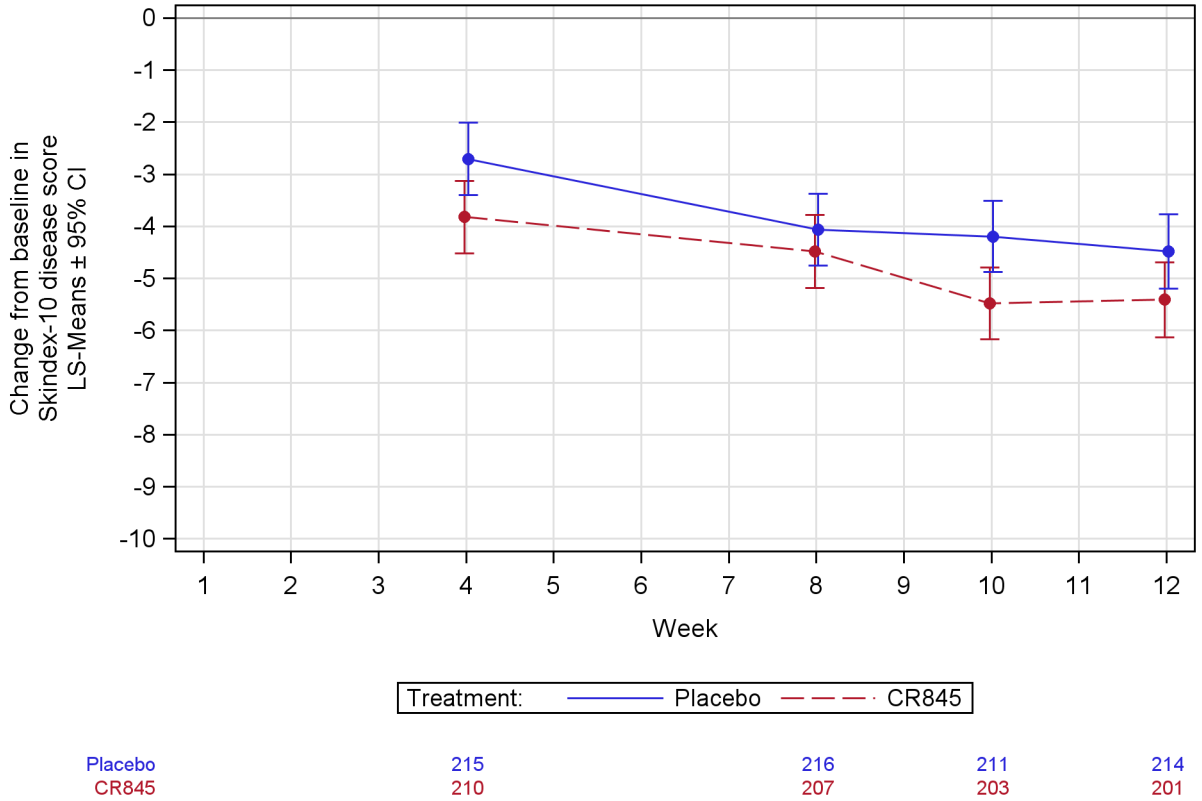
Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SDC_IMC0: Change from baseline in Skindex-10 disease score - MMRM results
ITT

Change from baseline in Skindex-10 disease score				Repeated measures analysis				
				Change from Baseline		Treatment Difference		
Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Week 4	CR845	237	210 (88.6)	-3.8 (0.4)	(-4.5, -3.1)	-1.1 (0.4)	(-2.0, -0.3)	0.012 *
	Placebo	236	215 (91.1)	-2.7 (0.4)	(-3.4, -2.0)			
Week 8	CR845	237	207 (87.3)	-4.5 (0.4)	(-5.2, -3.8)	-0.4 (0.4)	(-1.3, 0.4)	0.340
	Placebo	236	216 (91.5)	-4.1 (0.4)	(-4.8, -3.4)			
Week 10	CR845	237	203 (85.7)	-5.5 (0.3)	(-6.2, -4.8)	-1.3 (0.4)	(-2.1, -0.4)	0.003 *
	Placebo	236	211 (89.4)	-4.2 (0.3)	(-4.9, -3.5)			
Week 12	CR845	237	201 (84.8)	-5.4 (0.4)	(-6.1, -4.7)	-0.9 (0.5)	(-1.8, -0.0)	0.044 *
	Placebo	236	214 (90.7)	-4.5 (0.4)	(-5.2, -3.8)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval . * = significant treatment effect.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Figure BF2SDC_IMG0: Course of change from baseline in Skindex-10 disease score
ITT



Note: ITT = Intent-to-treat Set.
Symbols present least square mean (LS-Mean), bars present 95% confidence intervals (CI).
CR845 = Difelikefalin.
Source Table: BT2SDC_IMC0
Source Data: askin, created on: 17FEB2022

Table BT2SMC_IMH0: Change from baseline in Skindex-10 mood/emotional distress score
ITT

		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Skindex-10 mood/emotional distress score	Baseline	CR845	237	232 (97.9)	11.4 (5.0)	0	12.0	18	
		Placebo	236	233 (98.7)	11.0 (4.9)	0	11.0	18	
	Week 4	CR845	237	212 (89.5)	7.7 (5.4)	0	7.0	18	
		Placebo	236	222 (94.1)	8.3 (5.3)	0	8.0	18	
	Week 8	CR845	237	205 (86.5)	6.9 (5.6)	0	6.0	18	
		Placebo	236	219 (92.8)	6.9 (5.2)	0	6.0	18	
	Week 10	CR845	237	204 (86.1)	6.2 (5.5)	0	5.0	18	
		Placebo	236	214 (90.7)	7.0 (5.1)	0	6.0	18	
	Week 12	CR845	237	205 (86.5)	6.1 (5.5)	0	5.0	18	
		Placebo	236	217 (91.9)	6.4 (5.3)	0	5.0	18	
Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	237	208 (87.8)	-3.8 (5.2)	-18	-4.0	14	-0.24 [-0.43, -0.05]
		Placebo	236	219 (92.8)	-2.5 (5.3)	-17	-2.0	17	
	Week 8	CR845	237	201 (84.8)	-4.4 (5.4)	-18	-4.0	11	-0.08 [-0.27, 0.11]
		Placebo	236	217 (91.9)	-4.0 (5.2)	-17	-4.0	15	
	Week 10	CR845	237	200 (84.4)	-5.2 (5.4)	-18	-5.0	11	-0.25 [-0.44, -0.06]
		Placebo	236	212 (89.8)	-3.8 (5.3)	-18	-3.0	13	
	Week 12	CR845	237	201 (84.8)	-5.4 (5.6)	-18	-5.0	13	-0.15 [-0.34, 0.04]
		Placebo	236	215 (91.1)	-4.5 (5.6)	-18	-4.0	11	

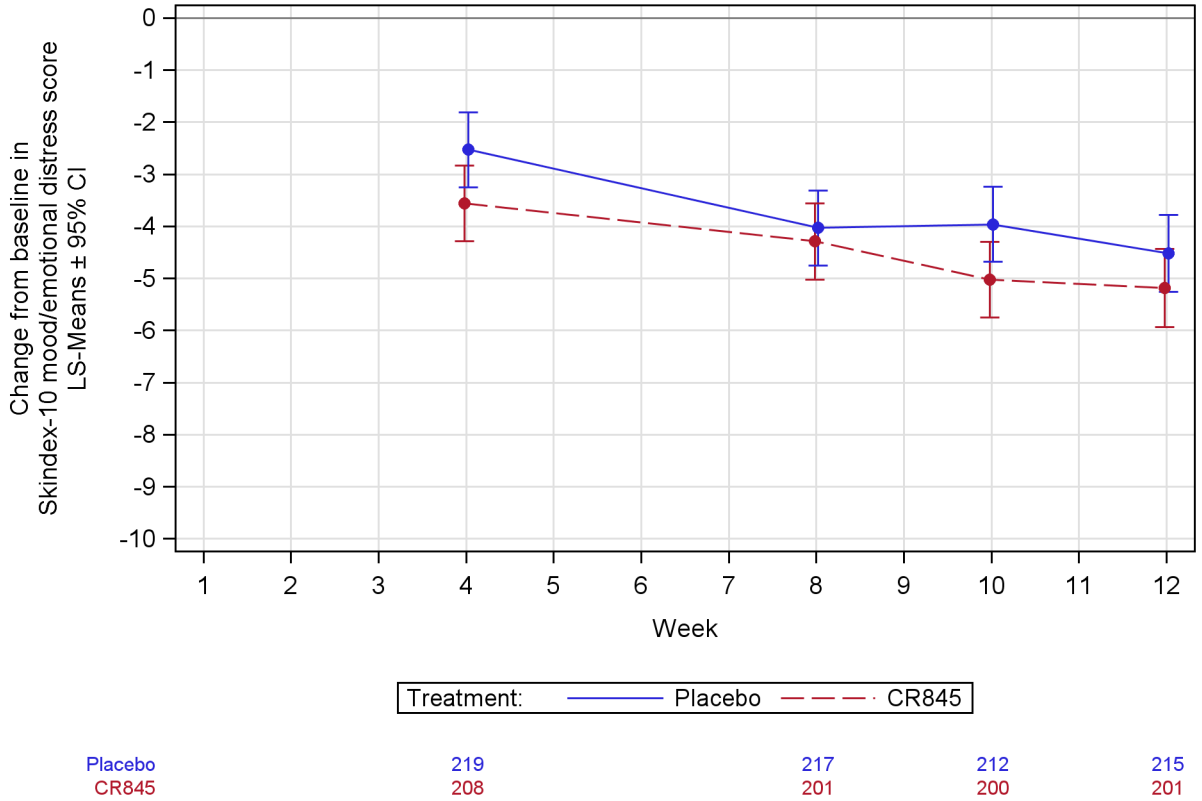
Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SMC_IMC0: Change from baseline in Skindex-10 mood/emotional distress score - MMRM results
ITT

Change from baseline in Skindex-10 mood/emotional distress score				Repeated measures analysis				
				Change from Baseline		Treatment Difference		
Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Week 4	CR845	237	208 (87.8)	-3.6 (0.4)	(-4.3, -2.8)	-1.0 (0.5)	(-1.9, -0.1)	0.024 *
	Placebo	236	219 (92.8)	-2.5 (0.4)	(-3.2, -1.8)			
Week 8	CR845	237	201 (84.8)	-4.3 (0.4)	(-5.0, -3.6)	-0.3 (0.5)	(-1.2, 0.6)	0.575
	Placebo	236	217 (91.9)	-4.0 (0.4)	(-4.7, -3.3)			
Week 10	CR845	237	200 (84.4)	-5.0 (0.4)	(-5.8, -4.3)	-1.1 (0.5)	(-2.0, -0.2)	0.021 *
	Placebo	236	212 (89.8)	-4.0 (0.4)	(-4.7, -3.2)			
Week 12	CR845	237	201 (84.8)	-5.2 (0.4)	(-5.9, -4.4)	-0.7 (0.5)	(-1.6, 0.3)	0.165
	Placebo	236	215 (91.1)	-4.5 (0.4)	(-5.3, -3.8)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval . * = significant treatment effect.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Figure BF2SMC_IMG0: Course of change from baseline in Skindex-10 mood/emotional distress score
ITT



Note: ITT = Intent-to-treat Set.
Symbols present least square mean (LS-Mean), bars present 95% confidence intervals (CI).
CR845 = Difelikefalin.
Source Table: BT2SMC_IMC0
Source Data: askin, created on: 17FEB2022

Table BT2SSC_IMH0: Change from baseline in Skindex-10 social functioning score
ITT

		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Skindex-10 social functioning score	Baseline	CR845	237	234 (98.7)	11.2 (7.9)	0	11.0	24	
		Placebo	236	232 (98.3)	10.9 (7.7)	0	11.0	24	
	Week 4	CR845	237	213 (89.9)	7.9 (7.2)	0	6.0	24	
		Placebo	236	222 (94.1)	7.5 (7.3)	0	5.0	24	
	Week 8	CR845	237	207 (87.3)	6.8 (7.1)	0	4.0	24	
		Placebo	236	220 (93.2)	6.7 (7.0)	0	5.0	24	
	Week 10	CR845	237	206 (86.9)	6.3 (7.1)	0	4.0	24	
		Placebo	236	214 (90.7)	6.8 (7.0)	0	5.0	24	
	Week 12	CR845	237	204 (86.1)	6.3 (7.1)	0	4.0	24	
		Placebo	236	216 (91.5)	6.3 (6.9)	0	4.0	24	
Change from baseline in Skindex-10 social functioning score	Week 4	CR845	237	211 (89.0)	-3.3 (7.2)	-24	-3.0	19	0.01 [-0.18, 0.20]
		Placebo	236	220 (93.2)	-3.3 (7.5)	-24	-2.0	23	
	Week 8	CR845	237	205 (86.5)	-4.5 (7.5)	-23	-4.0	24	-0.06 [-0.25, 0.13]
		Placebo	236	218 (92.4)	-4.0 (7.2)	-24	-3.0	22	
	Week 10	CR845	237	204 (86.1)	-4.9 (7.3)	-24	-4.0	20	-0.12 [-0.32, 0.07]
		Placebo	236	211 (89.4)	-3.9 (7.5)	-24	-3.0	22	
	Week 12	CR845	237	202 (85.2)	-4.8 (7.4)	-23	-4.0	20	-0.04 [-0.23, 0.15]
		Placebo	236	214 (90.7)	-4.5 (7.8)	-24	-3.0	24	

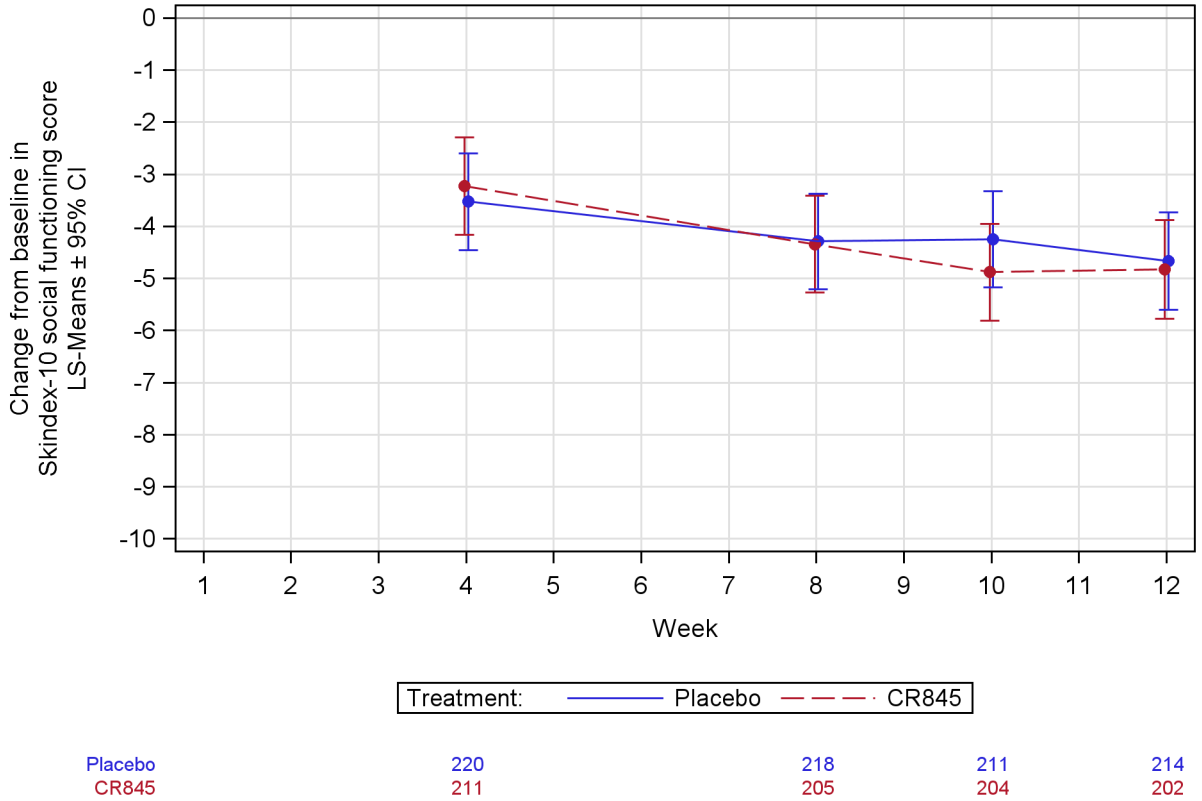
Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SSC_IMC0: Change from baseline in Skindex-10 social functioning score - MMRM results
ITT

Change from baseline in Skindex-10 social functioning score				Repeated measures analysis				
				Change from Baseline		Treatment Difference		
Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Week 4	CR845	237	211 (89.0)	-3.2 (0.5)	(-4.2, -2.3)	0.3 (0.6)	(-0.9, 1.5)	0.612
	Placebo	236	220 (93.2)	-3.5 (0.5)	(-4.5, -2.6)			
Week 8	CR845	237	205 (86.5)	-4.3 (0.5)	(-5.3, -3.4)	-0.1 (0.6)	(-1.2, 1.1)	0.927
	Placebo	236	218 (92.4)	-4.3 (0.5)	(-5.2, -3.4)			
Week 10	CR845	237	204 (86.1)	-4.9 (0.5)	(-5.8, -3.9)	-0.6 (0.6)	(-1.8, 0.5)	0.285
	Placebo	236	211 (89.4)	-4.3 (0.5)	(-5.2, -3.3)			
Week 12	CR845	237	202 (85.2)	-4.8 (0.5)	(-5.8, -3.9)	-0.2 (0.6)	(-1.3, 1.0)	0.788
	Placebo	236	214 (90.7)	-4.7 (0.5)	(-5.6, -3.7)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval . * = significant treatment effect.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Figure BF2SSC_IMG0: Course of change from baseline in Skindex-10 social functioning score
ITT



Note: ITT = Intent-to-treat Set.
Symbols present least square mean (LS-Mean), bars present 95% confidence intervals (CI).
CR845 = Difelikefalin.
Source Table: BT2SSC_IMC0
Source Data: askin, created on: 17FEB2022

Table BT2SDCD3_IMP0: Decrease of Skindex-10 disease score of at least 3 points
ITT

		CR845			Placebo						
Variable	Time	N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Decrease of Skindex-10 disease score of at least 3 points	Week 12	237	201 (84.8)	136 (57.4) [50.8, 63.8]	236	214 (90.7)	136 (57.6) [51.0, 64.0]	0.996 [0.853, 1.163]	0.990 [0.688, 1.426]	-0.2 [-9.6, 9.1]	0.957

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: askin, created on: 11FEB2022

Table BT2SMCD3_IMP0: Decrease of Skindex-10 mood/emotional distress score of at least 3 points
ITT

		CR845			Placebo						
Variable	Time	N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Decrease of Skindex-10 mood/emotional distress score of at least 3 points	Week 12	237	201 (84.8)	139 (58.6) [52.1, 65.0]	236	215 (91.1)	132 (55.9) [49.3, 62.4]	1.049 [0.897, 1.225]	1.118 [0.776, 1.609]	2.7 [-6.6, 12.1]	0.551

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: askin, created on: 11FEB2022

Table BT2SSCD4_IMP0: Decrease of Skindex-10 social functioning score of at least 4 points
ITT

		CR845			Placebo						
Variable	Time	N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Decrease of Skindex-10 social functioning score of at least 4 points	Week 12	237	202 (85.2)	110 (46.4) [39.9, 53.0]	236	214 (90.7)	102 (43.2) [36.8, 49.8]	1.074 [0.879, 1.312]	1.138 [0.792, 1.635]	3.2 [-6.2, 12.6]	0.486

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: askin, created on: 11FEB2022

Table BT2A_SMS0: TEAEs by SOC and PT
SAF-S

	CR845		Placebo					
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
SOC: Cardiac disorders	235	20 (8.5) [5.3, 12.8]	236	19 (8.1) [4.9, 12.3]	1.057 [0.579, 1.929]	1.062 [0.552, 2.047]	0.5 [-4.9, 5.9]	0.856
SOC: Gastrointestinal disorders	235	57 (24.3) [18.9, 30.3]	236	36 (15.3) [10.9, 20.5]	1.590 [1.092, 2.316]	1.779 [1.119, 2.828]	9.0 [1.4, 16.6]	0.014 *
Diarrhoea	235	19 (8.1) [4.9, 12.3]	236	13 (5.5) [3.0, 9.2]	1.468 [0.742, 2.903]	1.509 [0.727, 3.131]	2.6 [-2.4, 7.5]	0.267
Nausea	235	15 (6.4) [3.6, 10.3]	236	10 (4.2) [2.1, 7.7]	1.506 [0.691, 3.284]	1.541 [0.678, 3.504]	2.1 [-2.3, 6.6]	0.300
Vomiting	235	15 (6.4) [3.6, 10.3]	236	14 (5.9) [3.3, 9.8]	1.076 [0.531, 2.179]	1.081 [0.510, 2.293]	0.5 [-4.3, 5.2]	0.839
SOC: General disorders and administration site conditions	235	35 (14.9) [10.6, 20.1]	236	26 (11.0) [7.3, 15.7]	1.352 [0.841, 2.172]	1.413 [0.821, 2.433]	3.9 [-2.6, 10.4]	0.211
Chest pain	235	11 (4.7) [2.4, 8.2]	236	5 (2.1) [0.7, 4.9]	2.209 [0.780, 6.261]	2.269 [0.776, 6.634]	2.6 [-1.1, 6.3]	0.125
SOC: Infections and infestations	235	48 (20.4) [15.5, 26.2]	236	42 (17.8) [13.1, 23.3]	1.148 [0.791, 1.666]	1.186 [0.748, 1.879]	2.6 [-4.9, 10.2]	0.469
SOC: Injury, poisoning and procedural complications	235	51 (21.7) [16.6, 27.5]	236	44 (18.6) [13.9, 24.2]	1.164 [0.812, 1.669]	1.209 [0.770, 1.899]	3.1 [-4.6, 10.7]	0.409
Fall	235	16 (6.8) [3.9, 10.8]	236	12 (5.1) [2.7, 8.7]	1.339 [0.648, 2.768]	1.364 [0.631, 2.949]	1.7 [-3.0, 6.4]	0.429
SOC: Investigations	235	12 (5.1) [2.7, 8.7]	236	13 (5.5) [3.0, 9.2]	0.927 [0.432, 1.989]	0.923 [0.412, 2.067]	-0.4 [-4.9, 4.1]	0.846
SOC: Metabolism and nutrition disorders	235	22 (9.4) [6.0, 13.8]	236	24 (10.2) [6.6, 14.8]	0.921 [0.531, 1.595]	0.912 [0.496, 1.677]	-0.8 [-6.6, 5.0]	0.768
SOC: Musculoskeletal and connective tissue disorders	235	26 (11.1) [7.4, 15.8]	236	21 (8.9) [5.6, 13.3]	1.243 [0.720, 2.146]	1.274 [0.695, 2.334]	2.2 [-3.7, 8.0]	0.434

Note: SAF-S = Week 12 Safety Set. Only events are displayed with an incidence of at least 10 percent in a treatment group or 10 patients with an incidence of at least 1 percent in a treatment group.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 31JAN2022

Table BT2A_SMS0: TEAEs by SOC and PT
SAF-S

	CR845		Placebo					
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
SOC: Nervous system disorders	235	46 (19.6) [14.7, 25.2]	236	34 (14.4) [10.2, 19.5]	1.359 [0.906, 2.037]	1.446 [0.890, 2.350]	5.2 [-2.0, 12.4]	0.136
Dizziness	235	13 (5.5) [3.0, 9.3]	236	12 (5.1) [2.7, 8.7]	1.088 [0.507, 2.335]	1.093 [0.488, 2.448]	0.4 [-4.0, 4.9]	0.829
Headache	235	10 (4.3) [2.1, 7.7]	236	6 (2.5) [0.9, 5.5]	1.674 [0.618, 4.531]	1.704 [0.609, 4.766]	1.7 [-2.0, 5.4]	0.305
Somnolence	235	11 (4.7) [2.4, 8.2]	236	5 (2.1) [0.7, 4.9]	2.209 [0.780, 6.261]	2.269 [0.776, 6.634]	2.6 [-1.1, 6.3]	0.125
SOC: Psychiatric disorders	235	18 (7.7) [4.6, 11.8]	236	14 (5.9) [3.3, 9.8]	1.291 [0.658, 2.535]	1.315 [0.638, 2.711]	1.7 [-3.2, 6.7]	0.457
SOC: Respiratory, thoracic and mediastinal disorders	235	23 (9.8) [6.3, 14.3]	236	21 (8.9) [5.6, 13.3]	1.100 [0.626, 1.932]	1.111 [0.597, 2.067]	0.9 [-4.8, 6.6]	0.741
SOC: Skin and subcutaneous tissue disorders	235	13 (5.5) [3.0, 9.3]	236	10 (4.2) [2.1, 7.7]	1.306 [0.584, 2.918]	1.323 [0.569, 3.081]	1.3 [-3.0, 5.6]	0.515
SOC: Vascular disorders	235	25 (10.6) [7.0, 15.3]	236	28 (11.9) [8.0, 16.7]	0.897 [0.539, 1.490]	0.884 [0.499, 1.567]	-1.2 [-7.4, 4.9]	0.674
Hypertension	235	6 (2.6) [0.9, 5.5]	236	11 (4.7) [2.3, 8.2]	0.548 [0.206, 1.457]	0.536 [0.195, 1.474]	-2.1 [-5.9, 1.7]	0.221

Note: SAF-S = Week 12 Safety Set. Only events are displayed with an incidence of at least 10 percent in a treatment group or 10 patients with an incidence of at least 1 percent in a treatment group.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 31JAN2022

Table BT2AD_SMSD: Fatal TEAEs by SOC and PT
SAF-S

	CR845		Placebo	
Fatal TEAEs	N	n (%)	N	n (%)
SOC: Blood and lymphatic system disorders	235	1 (0.4)	236	0 (0.0)
Anaemia	235	1 (0.4)	236	0 (0.0)
SOC: Cardiac disorders	235	2 (0.9)	236	1 (0.4)
Cardiac arrest	235	1 (0.4)	236	1 (0.4)
Cardiac failure	235	1 (0.4)	236	0 (0.0)
Cardiopulmonary failure	235	1 (0.4)	236	0 (0.0)
SOC: Respiratory, thoracic and mediastinal disorders	235	0 (0.0)	236	1 (0.4)
Dyspnoea	235	0 (0.0)	236	1 (0.4)
SOC: Vascular disorders	235	0 (0.0)	236	1 (0.4)
Hypotension	235	0 (0.0)	236	1 (0.4)

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term.
Source Data: aae, created on: 31JAN2022

Table BT2AEGN_SMI0: Incidence of AESI gait disturbance - non-severe
SAF-S

	CR845		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
AESI gait disturbance - non-severe	235	8 (3.4) [1.5, 6.6]	236	2 (0.8) [0.1, 3.0]	4.017 [0.862, 18.718]	4.123 [0.866, 19.626]	2.6 [-0.5, 5.6]	0.062 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 31JAN2022

Table BT2AEFN_SMI0: Incidence of AESI falls/injuries - non-severe
SAF-S

	CR845		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
AESI falls/injuries - non-severe	235	22 (9.4) [6.0, 13.8]	236	12 (5.1) [2.7, 8.7]	1.841 [0.933, 3.633]	1.928 [0.931, 3.993]	4.3 [-0.8, 9.4]	0.073

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 31JAN2022

Table BT2AEVN_SMI0: Incidence of AESI dizziness - non-severe
SAF-S

	CR845		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
AESI dizziness - non-severe	235	12 (5.1) [2.7, 8.7]	236	13 (5.5) [3.0, 9.2]	0.927 [0.432, 1.989]	0.923 [0.412, 2.067]	-0.4 [-4.9, 4.1]	0.846

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 31JAN2022

Table BT2AEYN_SMI0: Incidence of AESI syncope - non-severe
SAF-S

	CR845		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
AESI syncope - non-severe	235	4 (1.7) [0.5, 4.3]	236	2 (0.8) [0.1, 3.0]	2.009 [0.371, 10.861]	2.026 [0.367, 11.169]	0.9 [-1.6, 3.3]	0.450 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 31JAN2022

Table BT2AEON_SMI0: Incidence of AESI somnolence - non-severe
SAF-S

	CR845		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
AESI somnolence - non-severe	235	12 (5.1) [2.7, 8.7]	236	5 (2.1) [0.7, 4.9]	2.410 [0.863, 6.734]	2.486 [0.862, 7.171]	3.0 [-0.8, 6.8]	0.083

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 31JAN2022

Table BT2AEKN_SMI0: Incidence of AESI seizures - non-severe
SAF-S

	CR845		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
AESI seizures - non-severe	235	0 (0.0) [0.0, 1.6]	236	0 (0.0) [0.0, 1.6]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 31JAN2022

Table BT2AEMN_SMI0: Incidence of AESI mental status change - non-severe
SAF-S

	CR845		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
AESI mental status change - non-severe	235	8 (3.4) [1.5, 6.6]	236	5 (2.1) [0.7, 4.9]	1.607 [0.533, 4.840]	1.628 [0.525, 5.052]	1.3 [-2.1, 4.7]	0.395

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 31JAN2022

Table BT2AEEN_SMI0: Incidence of AESI mood change - non-severe
SAF-S

	CR845		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
AESI mood change - non-severe	235	4 (1.7) [0.5, 4.3]	236	3 (1.3) [0.3, 3.7]	1.339 [0.303, 5.918]	1.345 [0.298, 6.076]	0.4 [-2.2, 3.0]	0.724 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 31JAN2022

Table BT2AEUN_SMI0: Incidence of AESI unusual feeling/sensation - non-severe
SAF-S

	CR845		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
AESI unusual feeling/sensation - non-severe	235	10 (4.3) [2.1, 7.7]	236	6 (2.5) [0.9, 5.5]	1.674 [0.618, 4.531]	1.704 [0.609, 4.766]	1.7 [-2.0, 5.4]	0.305

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 31JAN2022

Table BT2AERN_SMI0: Incidence of AESI tachycardia/palpitation - non-severe
SAF-S

	CR845		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
AESI tachycardia/palpitation - non-severe	235	5 (2.1) [0.7, 4.9]	236	7 (3.0) [1.2, 6.0]	0.717 [0.231, 2.228]	0.711 [0.222, 2.273]	-0.8 [-4.1, 2.4]	0.564

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 31JAN2022

Table BT2WIC_ISHA: Change from baseline in weekly WI-NRS by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
< 65 years	Weekly WI-NRS	Baseline	CR845	147	147 (100.0)	7.34 (1.37)	4.5	7.38	10.0	
			Placebo	153	153 (100.0)	7.15 (1.39)	4.8	7.13	10.0	
		Week 1	CR845	147	144 (98.0)	6.72 (1.72)	2.7	6.64	10.0	
			Placebo	153	150 (98.0)	6.68 (1.56)	2.0	6.71	10.0	
		Week 2	CR845	147	138 (93.9)	5.94 (2.19)	0.0	5.71	10.0	
			Placebo	153	151 (98.7)	6.15 (1.93)	1.1	6.29	10.0	
		Week 3	CR845	147	138 (93.9)	5.52 (2.38)	0.0	5.43	10.0	
			Placebo	153	146 (95.4)	5.81 (2.09)	1.0	5.86	10.0	
		Week 4	CR845	147	134 (91.2)	5.04 (2.50)	0.0	5.14	10.0	
			Placebo	153	146 (95.4)	5.57 (2.25)	1.0	5.57	10.0	
		Week 5	CR845	147	136 (92.5)	4.91 (2.58)	0.0	5.14	10.0	
			Placebo	153	146 (95.4)	5.36 (2.33)	0.6	5.50	10.0	
		Week 6	CR845	147	132 (89.8)	4.74 (2.61)	0.0	4.93	10.0	
			Placebo	153	146 (95.4)	5.30 (2.47)	0.0	5.57	10.0	
		Week 7	CR845	147	133 (90.5)	4.65 (2.66)	0.0	5.00	10.0	
			Placebo	153	145 (94.8)	5.17 (2.37)	0.0	5.29	9.9	
		Week 8	CR845	147	131 (89.1)	4.56 (2.62)	0.0	4.57	10.0	
			Placebo	153	144 (94.1)	5.07 (2.40)	0.0	5.15	10.0	
		Week 9	CR845	147	131 (89.1)	4.51 (2.66)	0.0	4.43	10.0	
			Placebo	153	144 (94.1)	4.91 (2.41)	0.0	5.00	10.0	
		Week 10	CR845	147	133 (90.5)	4.43 (2.71)	0.0	4.00	10.0	
			Placebo	153	143 (93.5)	4.97 (2.42)	0.0	5.00	10.0	
		Week 11	CR845	147	129 (87.8)	4.33 (2.75)	0.0	3.71	9.9	
			Placebo	153	144 (94.1)	4.84 (2.49)	0.0	4.71	10.0	
		Week 12	CR845	147	122 (83.0)	4.17 (2.75)	0.0	3.71	10.0	
			Placebo	153	137 (89.5)	4.73 (2.52)	0.0	4.57	10.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	147	144 (98.0)	-0.62 (1.16)	-3.8	-0.51	2.4	-0.11 [-0.34, 0.12]
			Placebo	153	150 (98.0)	-0.49 (1.23)	-4.8	-0.38	2.9	
		Week 2	CR845	147	138 (93.9)	-1.38 (1.81)	-8.9	-1.00	2.0	-0.21 [-0.44, 0.02]
			Placebo	153	151 (98.7)	-1.03 (1.55)	-5.0	-0.79	2.8	
		Week 3	CR845	147	138 (93.9)	-1.81 (1.99)	-7.9	-1.43	2.1	-0.22 [-0.46, 0.01]
			Placebo	153	146 (95.4)	-1.39 (1.84)	-6.1	-1.29	3.1	
		Week 4	CR845	147	134 (91.2)	-2.28 (2.19)	-9.3	-1.92	1.5	-0.32 [-0.55, -0.08]
			Placebo	153	146 (95.4)	-1.60 (2.05)	-7.1	-1.38	2.9	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISHA: Change from baseline in weekly WI-NRS by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 5	CR845	147	136 (92.5)	-2.41 (2.44)	-10.0	-2.00	2.9	-0.26 [-0.50, -0.03]
			Placebo	153	146 (95.4)	-1.81 (2.14)	-7.8	-1.63	3.5	
		Week 6	CR845	147	132 (89.8)	-2.58 (2.53)	-9.9	-2.03	3.8	-0.30 [-0.54, -0.07]
			Placebo	153	146 (95.4)	-1.86 (2.24)	-7.1	-1.68	3.1	
		Week 7	CR845	147	133 (90.5)	-2.66 (2.55)	-10.0	-2.14	1.6	-0.28 [-0.52, -0.05]
			Placebo	153	145 (94.8)	-1.98 (2.27)	-7.2	-1.66	3.3	
		Week 8	CR845	147	131 (89.1)	-2.76 (2.42)	-8.8	-2.58	1.9	-0.29 [-0.53, -0.05]
			Placebo	153	144 (94.1)	-2.08 (2.31)	-7.6	-1.88	3.5	
		Week 9	CR845	147	131 (89.1)	-2.81 (2.48)	-10.0	-2.52	2.0	-0.24 [-0.48, -0.00]
			Placebo	153	144 (94.1)	-2.25 (2.30)	-7.9	-2.00	3.5	
		Week 10	CR845	147	133 (90.5)	-2.89 (2.57)	-10.0	-2.80	3.0	-0.30 [-0.53, -0.06]
			Placebo	153	143 (93.5)	-2.16 (2.32)	-8.0	-2.00	3.5	
		Week 11	CR845	147	129 (87.8)	-2.96 (2.55)	-10.0	-2.73	3.0	-0.27 [-0.51, -0.03]
			Placebo	153	144 (94.1)	-2.29 (2.37)	-7.9	-2.21	3.6	
		Week 12	CR845	147	122 (83.0)	-3.15 (2.57)	-10.0	-3.00	2.0	-0.30 [-0.55, -0.06]
			Placebo	153	137 (89.5)	-2.40 (2.40)	-8.6	-2.34	3.6	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISHA: Change from baseline in weekly WI-NRS by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 65 years	Weekly WI-NRS	Baseline	CR845	90	90 (100.0)	7.14 (1.34)	5.0	7.06	10.0	
			Placebo	83	83 (100.0)	7.06 (1.32)	5.0	7.00	10.0	
		Week 1	CR845	90	87 (96.7)	6.09 (1.89)	0.9	6.14	10.0	
			Placebo	83	82 (98.8)	6.51 (1.78)	0.0	6.57	9.9	
		Week 2	CR845	90	87 (96.7)	5.38 (2.36)	0.0	6.00	10.0	
			Placebo	83	81 (97.6)	6.00 (2.08)	0.0	6.14	9.9	
		Week 3	CR845	90	83 (92.2)	5.07 (2.61)	0.0	5.17	10.0	
			Placebo	83	81 (97.6)	5.76 (2.16)	0.0	5.86	10.0	
		Week 4	CR845	90	80 (88.9)	4.83 (2.50)	0.0	5.14	10.0	
			Placebo	83	79 (95.2)	5.54 (2.24)	0.0	5.86	9.6	
		Week 5	CR845	90	80 (88.9)	4.65 (2.57)	0.0	4.71	10.0	
			Placebo	83	80 (96.4)	5.08 (2.32)	0.0	4.93	9.9	
		Week 6	CR845	90	80 (88.9)	4.44 (2.55)	0.0	4.57	10.0	
			Placebo	83	78 (94.0)	5.02 (2.41)	0.0	4.86	9.9	
		Week 7	CR845	90	80 (88.9)	4.32 (2.61)	0.0	4.57	10.0	
			Placebo	83	79 (95.2)	5.18 (2.34)	0.0	5.00	10.0	
		Week 8	CR845	90	78 (86.7)	4.34 (2.60)	0.0	4.29	10.0	
			Placebo	83	77 (92.8)	5.03 (2.33)	0.0	5.00	10.0	
		Week 9	CR845	90	76 (84.4)	4.35 (2.68)	0.0	4.57	10.0	
			Placebo	83	78 (94.0)	4.88 (2.41)	0.0	4.77	10.0	
		Week 10	CR845	90	74 (82.2)	4.30 (2.69)	0.0	4.43	10.0	
			Placebo	83	77 (92.8)	4.72 (2.44)	0.0	4.29	10.0	
		Week 11	CR845	90	73 (81.1)	4.11 (2.70)	0.0	4.14	10.0	
			Placebo	83	75 (90.4)	4.82 (2.42)	0.0	4.86	10.0	
		Week 12	CR845	90	69 (76.7)	4.11 (2.64)	0.0	3.86	10.0	
			Placebo	83	70 (84.3)	4.63 (2.45)	0.0	4.54	10.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	90	87 (96.7)	-1.05 (1.49)	-5.6	-1.00	1.2	-0.36 [-0.66, -0.05]
			Placebo	83	82 (98.8)	-0.55 (1.34)	-6.3	-0.39	2.8	
		Week 2	CR845	90	87 (96.7)	-1.76 (2.07)	-10.0	-1.21	1.7	-0.35 [-0.66, -0.05]
			Placebo	83	81 (97.6)	-1.07 (1.79)	-6.5	-0.91	3.5	
		Week 3	CR845	90	83 (92.2)	-2.05 (2.37)	-10.0	-1.79	1.8	-0.37 [-0.68, -0.06]
			Placebo	83	81 (97.6)	-1.28 (1.77)	-7.1	-1.07	3.3	
		Week 4	CR845	90	80 (88.9)	-2.31 (2.32)	-10.0	-2.01	1.3	-0.37 [-0.69, -0.06]
			Placebo	83	79 (95.2)	-1.50 (2.02)	-8.0	-1.32	3.5	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISHA: Change from baseline in weekly WI-NRS by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 5	CR845	90	80 (88.9)	-2.49 (2.38)	-10.0	-2.16	1.8	-0.25 [-0.56, 0.06]
			Placebo	83	80 (96.4)	-1.92 (2.15)	-8.1	-1.88	3.4	
		Week 6	CR845	90	80 (88.9)	-2.69 (2.43)	-10.0	-2.28	1.3	-0.28 [-0.59, 0.04]
			Placebo	83	78 (94.0)	-2.05 (2.21)	-8.1	-1.86	2.9	
		Week 7	CR845	90	80 (88.9)	-2.81 (2.55)	-10.0	-2.32	1.6	-0.40 [-0.71, -0.08]
			Placebo	83	79 (95.2)	-1.89 (2.07)	-7.1	-1.75	2.8	
		Week 8	CR845	90	78 (86.7)	-2.77 (2.49)	-10.0	-2.63	1.9	-0.32 [-0.63, -0.00]
			Placebo	83	77 (92.8)	-2.03 (2.11)	-7.1	-1.68	2.8	
		Week 9	CR845	90	76 (84.4)	-2.76 (2.54)	-10.0	-2.73	1.6	-0.23 [-0.55, 0.09]
			Placebo	83	78 (94.0)	-2.21 (2.19)	-7.1	-1.96	2.8	
		Week 10	CR845	90	74 (82.2)	-2.81 (2.53)	-10.0	-2.90	2.8	-0.20 [-0.52, 0.12]
			Placebo	83	77 (92.8)	-2.35 (2.17)	-6.7	-2.20	2.8	
		Week 11	CR845	90	73 (81.1)	-3.05 (2.63)	-10.0	-3.14	1.2	-0.34 [-0.66, -0.01]
			Placebo	83	75 (90.4)	-2.23 (2.24)	-7.0	-2.04	2.8	
		Week 12	CR845	90	69 (76.7)	-3.04 (2.63)	-10.0	-2.86	3.0	-0.29 [-0.62, 0.05]
			Placebo	83	70 (84.3)	-2.34 (2.22)	-7.0	-2.22	2.8	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISHB: Change from baseline in weekly WI-NRS by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Male	Weekly WI-NRS	Baseline	CR845	137	137 (100.0)	7.18 (1.37)	4.5	7.00	10.0	
			Placebo	139	139 (100.0)	7.00 (1.31)	5.0	6.88	10.0	
		Week 1	CR845	137	132 (96.4)	6.50 (1.78)	3.0	6.29	10.0	
			Placebo	139	138 (99.3)	6.41 (1.55)	0.0	6.50	9.4	
		Week 2	CR845	137	129 (94.2)	5.77 (2.18)	0.1	5.71	10.0	
			Placebo	139	138 (99.3)	5.86 (1.92)	0.0	6.14	9.3	
		Week 3	CR845	137	128 (93.4)	5.53 (2.40)	0.0	5.57	10.0	
			Placebo	139	134 (96.4)	5.61 (2.00)	0.0	5.80	9.6	
		Week 4	CR845	137	125 (91.2)	5.19 (2.38)	0.0	5.57	10.0	
			Placebo	139	134 (96.4)	5.32 (2.17)	0.0	5.57	9.6	
		Week 5	CR845	137	126 (92.0)	5.15 (2.48)	0.0	5.14	10.0	
			Placebo	139	133 (95.7)	5.09 (2.32)	0.0	5.14	9.6	
		Week 6	CR845	137	125 (91.2)	5.09 (2.49)	0.0	5.29	10.0	
			Placebo	139	131 (94.2)	5.10 (2.39)	0.0	5.43	9.7	
		Week 7	CR845	137	125 (91.2)	5.06 (2.53)	0.0	5.29	10.0	
			Placebo	139	131 (94.2)	5.07 (2.31)	0.0	5.29	9.9	
		Week 8	CR845	137	123 (89.8)	5.08 (2.55)	0.0	5.14	10.0	
			Placebo	139	131 (94.2)	4.94 (2.28)	0.0	5.14	10.0	
		Week 9	CR845	137	120 (87.6)	4.98 (2.55)	0.0	5.07	10.0	
			Placebo	139	131 (94.2)	4.76 (2.31)	0.0	4.86	10.0	
		Week 10	CR845	137	120 (87.6)	4.81 (2.71)	0.0	4.69	10.0	
			Placebo	139	130 (93.5)	4.68 (2.26)	0.0	4.86	10.0	
		Week 11	CR845	137	117 (85.4)	4.75 (2.71)	0.0	4.57	10.0	
			Placebo	139	129 (92.8)	4.68 (2.30)	0.0	4.71	9.2	
		Week 12	CR845	137	110 (80.3)	4.67 (2.67)	0.0	4.62	10.0	
			Placebo	139	125 (89.9)	4.65 (2.30)	0.0	4.71	9.9	
	Change from baseline in weekly WI-NRS	Week 1	CR845	137	132 (96.4)	-0.69 (1.21)	-4.1	-0.49	1.7	-0.07 [-0.31, 0.17]
			Placebo	139	138 (99.3)	-0.60 (1.28)	-6.3	-0.39	2.8	
		Week 2	CR845	137	129 (94.2)	-1.40 (1.71)	-6.9	-1.09	1.7	-0.15 [-0.39, 0.09]
			Placebo	139	138 (99.3)	-1.15 (1.73)	-6.5	-0.87	2.8	
		Week 3	CR845	137	128 (93.4)	-1.64 (1.93)	-7.6	-1.40	2.1	-0.14 [-0.38, 0.11]
			Placebo	139	134 (96.4)	-1.38 (1.85)	-7.1	-1.07	2.8	
		Week 4	CR845	137	125 (91.2)	-1.98 (1.92)	-7.8	-1.71	1.5	-0.15 [-0.40, 0.09]
			Placebo	139	134 (96.4)	-1.67 (2.11)	-8.0	-1.42	3.1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISHB: Change from baseline in weekly WI-NRS by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 5	CR845	137	126 (92.0)	-2.01 (2.05)	-8.6	-1.86	2.0	-0.05 [-0.29, 0.20]
			Placebo	139	133 (95.7)	-1.91 (2.23)	-8.1	-1.71	3.5	
		Week 6	CR845	137	125 (91.2)	-2.08 (2.10)	-8.6	-1.86	1.7	-0.08 [-0.33, 0.16]
			Placebo	139	131 (94.2)	-1.90 (2.21)	-8.1	-1.64	3.1	
		Week 7	CR845	137	125 (91.2)	-2.11 (2.14)	-8.6	-1.70	1.6	-0.10 [-0.34, 0.15]
			Placebo	139	131 (94.2)	-1.91 (2.24)	-7.1	-1.77	3.3	
		Week 8	CR845	137	123 (89.8)	-2.10 (2.11)	-7.4	-2.00	1.9	-0.02 [-0.26, 0.23]
			Placebo	139	131 (94.2)	-2.06 (2.21)	-7.1	-2.00	3.3	
		Week 9	CR845	137	120 (87.6)	-2.22 (2.11)	-7.7	-2.02	2.0	0.02 [-0.23, 0.27]
			Placebo	139	131 (94.2)	-2.26 (2.18)	-7.1	-2.00	3.5	
		Week 10	CR845	137	120 (87.6)	-2.38 (2.31)	-8.2	-2.13	3.0	-0.02 [-0.27, 0.22]
			Placebo	139	130 (93.5)	-2.32 (2.15)	-7.0	-2.20	3.5	
		Week 11	CR845	137	117 (85.4)	-2.44 (2.31)	-7.9	-2.39	3.0	-0.05 [-0.30, 0.20]
			Placebo	139	129 (92.8)	-2.32 (2.20)	-7.0	-2.14	3.6	
		Week 12	CR845	137	110 (80.3)	-2.51 (2.28)	-8.0	-2.35	3.0	-0.08 [-0.34, 0.17]
			Placebo	139	125 (89.9)	-2.32 (2.17)	-7.0	-2.43	3.6	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISHB: Change from baseline in weekly WI-NRS by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Female	Weekly WI-NRS	Baseline	CR845	100	100 (100.0)	7.37 (1.33)	5.0	7.25	10.0	
			Placebo	97	97 (100.0)	7.29 (1.43)	4.8	7.38	10.0	
		Week 1	CR845	100	99 (99.0)	6.46 (1.85)	0.9	6.57	10.0	
			Placebo	97	94 (96.9)	6.93 (1.73)	2.0	6.93	10.0	
		Week 2	CR845	100	96 (96.0)	5.68 (2.39)	0.0	6.07	10.0	
			Placebo	97	94 (96.9)	6.43 (2.03)	2.0	6.66	10.0	
		Week 3	CR845	100	93 (93.0)	5.11 (2.57)	0.0	5.14	10.0	
			Placebo	97	93 (95.9)	6.04 (2.24)	1.3	5.86	10.0	
		Week 4	CR845	100	89 (89.0)	4.64 (2.64)	0.0	4.86	10.0	
			Placebo	97	91 (93.8)	5.90 (2.31)	1.3	5.86	10.0	
		Week 5	CR845	100	90 (90.0)	4.33 (2.65)	0.0	4.62	9.6	
			Placebo	97	93 (95.9)	5.50 (2.33)	0.7	5.43	10.0	
		Week 6	CR845	100	87 (87.0)	3.95 (2.59)	0.0	3.71	10.0	
			Placebo	97	93 (95.9)	5.35 (2.53)	0.1	5.43	10.0	
		Week 7	CR845	100	88 (88.0)	3.78 (2.63)	0.0	3.64	10.0	
			Placebo	97	93 (95.9)	5.31 (2.42)	0.1	5.14	10.0	
		Week 8	CR845	100	86 (86.0)	3.62 (2.46)	0.0	3.46	8.4	
			Placebo	97	90 (92.8)	5.23 (2.50)	0.0	5.36	10.0	
		Week 9	CR845	100	87 (87.0)	3.73 (2.65)	0.0	3.43	9.3	
			Placebo	97	91 (93.8)	5.10 (2.53)	0.0	5.29	10.0	
		Week 10	CR845	100	87 (87.0)	3.79 (2.58)	0.0	3.60	9.9	
			Placebo	97	90 (92.8)	5.17 (2.63)	0.0	4.79	10.0	
		Week 11	CR845	100	85 (85.0)	3.57 (2.62)	0.0	3.14	9.1	
			Placebo	97	90 (92.8)	5.06 (2.68)	0.0	4.57	10.0	
		Week 12	CR845	100	81 (81.0)	3.43 (2.60)	0.0	3.00	9.0	
			Placebo	97	82 (84.5)	4.77 (2.76)	0.0	4.37	10.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	100	99 (99.0)	-0.92 (1.42)	-5.6	-0.71	2.4	-0.40 [-0.68, -0.11]
			Placebo	97	94 (96.9)	-0.38 (1.24)	-3.1	-0.38	2.9	
		Week 2	CR845	100	96 (96.0)	-1.69 (2.16)	-10.0	-1.11	2.0	-0.43 [-0.72, -0.14]
			Placebo	97	94 (96.9)	-0.90 (1.49)	-4.5	-0.82	3.5	
		Week 3	CR845	100	93 (93.0)	-2.26 (2.37)	-10.0	-1.80	1.7	-0.46 [-0.76, -0.17]
			Placebo	97	93 (95.9)	-1.29 (1.76)	-5.5	-1.29	3.3	
		Week 4	CR845	100	89 (89.0)	-2.72 (2.56)	-10.0	-2.71	1.3	-0.58 [-0.88, -0.28]
			Placebo	97	91 (93.8)	-1.41 (1.93)	-6.0	-1.23	3.5	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISHB: Change from baseline in weekly WI-NRS by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 5	CR845	100	90 (90.0)	-3.03 (2.75)	-10.0	-2.73	2.9	-0.53 [-0.83, -0.24]
			Placebo	97	93 (95.9)	-1.76 (2.01)	-6.5	-1.50	3.4	
		Week 6	CR845	100	87 (87.0)	-3.41 (2.79)	-10.0	-3.55	3.8	-0.57 [-0.87, -0.27]
			Placebo	97	93 (95.9)	-1.96 (2.27)	-7.5	-1.95	2.9	
		Week 7	CR845	100	88 (88.0)	-3.57 (2.83)	-10.0	-3.65	1.4	-0.63 [-0.93, -0.33]
			Placebo	97	93 (95.9)	-2.00 (2.15)	-7.2	-1.68	2.3	
		Week 8	CR845	100	86 (86.0)	-3.72 (2.57)	-10.0	-3.65	0.8	-0.68 [-0.98, -0.38]
			Placebo	97	90 (92.8)	-2.07 (2.29)	-7.6	-1.61	3.5	
		Week 9	CR845	100	87 (87.0)	-3.58 (2.77)	-10.0	-3.43	1.1	-0.54 [-0.84, -0.24]
			Placebo	97	91 (93.8)	-2.19 (2.36)	-7.9	-1.93	3.1	
		Week 10	CR845	100	87 (87.0)	-3.53 (2.72)	-10.0	-3.50	1.2	-0.56 [-0.86, -0.26]
			Placebo	97	90 (92.8)	-2.10 (2.43)	-8.0	-1.78	3.1	
		Week 11	CR845	100	85 (85.0)	-3.76 (2.73)	-10.0	-3.80	1.0	-0.60 [-0.90, -0.29]
			Placebo	97	90 (92.8)	-2.20 (2.50)	-7.9	-2.08	2.9	
		Week 12	CR845	100	81 (81.0)	-3.92 (2.76)	-10.0	-4.00	0.9	-0.55 [-0.86, -0.23]
			Placebo	97	82 (84.5)	-2.46 (2.57)	-8.6	-2.19	2.7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISHC: Change from baseline in weekly WI-NRS by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Black/African American	Weekly WI-NRS	Baseline	CR845	53	53 (100.0)	7.46 (1.27)	5.0	7.38	10.0	
			Placebo	38	38 (100.0)	7.65 (1.37)	5.0	7.63	10.0	
		Week 1	CR845	53	52 (98.1)	6.64 (1.52)	3.1	6.36	10.0	
			Placebo	38	38 (100.0)	7.01 (1.63)	3.4	7.00	9.9	
		Week 2	CR845	53	49 (92.5)	6.33 (1.94)	0.0	6.57	10.0	
			Placebo	38	37 (97.4)	6.48 (2.02)	2.7	6.43	10.0	
		Week 3	CR845	53	49 (92.5)	5.91 (2.15)	0.0	6.00	10.0	
			Placebo	38	37 (97.4)	6.08 (2.04)	2.0	5.86	10.0	
		Week 4	CR845	53	47 (88.7)	5.49 (2.33)	0.0	5.80	10.0	
			Placebo	38	35 (92.1)	5.87 (2.27)	1.2	5.57	10.0	
		Week 5	CR845	53	49 (92.5)	5.44 (2.31)	0.0	5.83	10.0	
			Placebo	38	36 (94.7)	5.51 (2.42)	1.0	5.86	9.9	
		Week 6	CR845	53	45 (84.9)	5.03 (2.37)	0.0	4.86	10.0	
			Placebo	38	37 (97.4)	5.73 (2.59)	0.6	5.71	10.0	
		Week 7	CR845	53	46 (86.8)	4.77 (2.58)	0.0	4.86	10.0	
			Placebo	38	36 (94.7)	5.53 (2.50)	0.1	5.36	10.0	
		Week 8	CR845	53	45 (84.9)	4.58 (2.53)	0.0	4.43	10.0	
			Placebo	38	36 (94.7)	5.47 (2.71)	0.0	5.71	9.8	
		Week 9	CR845	53	45 (84.9)	4.65 (2.56)	0.0	4.71	10.0	
			Placebo	38	37 (97.4)	5.32 (2.59)	0.0	5.14	10.0	
		Week 10	CR845	53	45 (84.9)	4.35 (2.47)	0.0	4.00	10.0	
			Placebo	38	37 (97.4)	5.31 (2.55)	0.0	5.00	9.9	
		Week 11	CR845	53	43 (81.1)	4.29 (2.60)	0.0	3.86	10.0	
			Placebo	38	36 (94.7)	5.20 (2.53)	0.7	4.93	9.8	
		Week 12	CR845	53	39 (73.6)	3.97 (2.56)	0.0	3.60	9.7	
			Placebo	38	35 (92.1)	5.03 (2.54)	0.0	4.86	10.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	53	52 (98.1)	-0.82 (1.42)	-5.4	-0.77	1.7	-0.13 [-0.55, 0.28]
			Placebo	38	38 (100.0)	-0.64 (1.11)	-2.8	-0.49	2.3	
		Week 2	CR845	53	49 (92.5)	-1.09 (1.91)	-10.0	-0.68	1.3	0.07 [-0.35, 0.50]
			Placebo	38	37 (97.4)	-1.23 (1.63)	-5.6	-1.07	1.4	
		Week 3	CR845	53	49 (92.5)	-1.52 (2.18)	-10.0	-1.34	2.1	0.01 [-0.42, 0.44]
			Placebo	38	37 (97.4)	-1.54 (1.86)	-7.1	-1.33	2.6	
		Week 4	CR845	53	47 (88.7)	-1.92 (2.31)	-10.0	-1.71	1.5	-0.06 [-0.50, 0.38]
			Placebo	38	35 (92.1)	-1.78 (2.08)	-8.0	-1.36	2.5	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISHC: Change from baseline in weekly WI-NRS by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 5	CR845	53	49 (92.5)	-1.95 (2.31)	-10.0	-1.71	2.0	0.04 [-0.39, 0.47]
			Placebo	38	36 (94.7)	-2.04 (2.30)	-8.1	-1.71	1.7	
		Week 6	CR845	53	45 (84.9)	-2.36 (2.36)	-10.0	-1.96	1.0	-0.16 [-0.60, 0.27]
			Placebo	38	37 (97.4)	-1.98 (2.31)	-8.1	-1.71	2.0	
		Week 7	CR845	53	46 (86.8)	-2.61 (2.57)	-10.0	-2.22	1.0	-0.19 [-0.63, 0.24]
			Placebo	38	36 (94.7)	-2.14 (2.25)	-7.2	-1.85	1.8	
		Week 8	CR845	53	45 (84.9)	-2.87 (2.58)	-10.0	-3.43	1.4	-0.25 [-0.69, 0.19]
			Placebo	38	36 (94.7)	-2.25 (2.46)	-7.4	-1.46	2.1	
		Week 9	CR845	53	45 (84.9)	-2.77 (2.65)	-10.0	-2.84	1.5	-0.15 [-0.59, 0.28]
			Placebo	38	37 (97.4)	-2.39 (2.37)	-7.4	-1.84	2.0	
		Week 10	CR845	53	45 (84.9)	-3.13 (2.47)	-10.0	-3.30	1.2	-0.30 [-0.74, 0.13]
			Placebo	38	37 (97.4)	-2.40 (2.29)	-7.4	-2.00	2.0	
		Week 11	CR845	53	43 (81.1)	-3.26 (2.57)	-10.0	-3.43	1.0	-0.33 [-0.77, 0.12]
			Placebo	38	36 (94.7)	-2.45 (2.30)	-6.7	-2.29	2.0	
		Week 12	CR845	53	39 (73.6)	-3.58 (2.59)	-10.0	-3.71	0.9	-0.41 [-0.87, 0.05]
			Placebo	38	35 (92.1)	-2.57 (2.29)	-7.4	-2.21	1.8	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISHC: Change from baseline in weekly WI-NRS by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
White	Weekly WI-NRS	Baseline	CR845	164	164 (100.0)	7.24 (1.39)	4.5	7.16	10.0	
			Placebo	169	169 (100.0)	7.04 (1.36)	4.8	6.86	10.0	
		Week 1	CR845	164	159 (97.0)	6.47 (1.88)	0.9	6.43	10.0	
			Placebo	169	166 (98.2)	6.57 (1.59)	0.0	6.57	9.9	
		Week 2	CR845	164	158 (96.3)	5.62 (2.31)	0.0	5.64	10.0	
			Placebo	169	167 (98.8)	6.02 (1.93)	0.0	6.14	9.6	
		Week 3	CR845	164	155 (94.5)	5.22 (2.54)	0.0	5.29	10.0	
			Placebo	169	163 (96.4)	5.74 (2.12)	0.0	6.00	9.6	
		Week 4	CR845	164	150 (91.5)	4.87 (2.55)	0.0	5.14	10.0	
			Placebo	169	162 (95.9)	5.50 (2.24)	0.0	5.71	10.0	
		Week 5	CR845	164	151 (92.1)	4.65 (2.69)	0.0	5.00	10.0	
			Placebo	169	162 (95.9)	5.21 (2.34)	0.0	5.43	9.9	
		Week 6	CR845	164	150 (91.5)	4.55 (2.69)	0.0	4.86	10.0	
			Placebo	169	160 (94.7)	5.12 (2.43)	0.0	5.43	9.9	
		Week 7	CR845	164	150 (91.5)	4.50 (2.71)	0.0	4.93	10.0	
			Placebo	169	161 (95.3)	5.10 (2.34)	0.0	5.29	10.0	
		Week 8	CR845	164	147 (89.6)	4.51 (2.68)	0.0	4.86	10.0	
			Placebo	169	158 (93.5)	5.02 (2.32)	0.0	5.21	10.0	
		Week 9	CR845	164	147 (89.6)	4.44 (2.74)	0.0	4.43	10.0	
			Placebo	169	159 (94.1)	4.88 (2.41)	0.0	5.00	10.0	
		Week 10	CR845	164	146 (89.0)	4.44 (2.81)	0.0	4.36	10.0	
			Placebo	169	158 (93.5)	4.83 (2.43)	0.0	4.86	10.0	
		Week 11	CR845	164	143 (87.2)	4.29 (2.81)	0.0	4.43	10.0	
			Placebo	169	158 (93.5)	4.84 (2.44)	0.0	4.86	10.0	
		Week 12	CR845	164	136 (82.9)	4.22 (2.81)	0.0	3.86	10.0	
			Placebo	169	150 (88.8)	4.72 (2.50)	0.0	4.79	10.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	164	159 (97.0)	-0.77 (1.25)	-5.6	-0.62	2.4	-0.22 [-0.44, -0.00]
			Placebo	169	166 (98.2)	-0.49 (1.27)	-6.3	-0.38	2.9	
		Week 2	CR845	164	158 (96.3)	-1.62 (1.90)	-8.9	-1.21	2.0	-0.33 [-0.55, -0.11]
			Placebo	169	167 (98.8)	-1.04 (1.63)	-6.5	-0.79	3.5	
		Week 3	CR845	164	155 (94.5)	-2.02 (2.14)	-7.9	-1.70	2.0	-0.35 [-0.57, -0.13]
			Placebo	169	163 (96.4)	-1.33 (1.83)	-6.3	-1.09	3.3	
		Week 4	CR845	164	150 (91.5)	-2.38 (2.25)	-9.3	-2.00	1.4	-0.38 [-0.61, -0.16]
			Placebo	169	162 (95.9)	-1.56 (2.08)	-7.2	-1.26	3.5	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISHC: Change from baseline in weekly WI-NRS by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 5	CR845	164	151 (92.1)	-2.60 (2.50)	-10.0	-2.11	2.9	-0.32 [-0.55, -0.10]
			Placebo	169	162 (95.9)	-1.84 (2.17)	-7.8	-1.68	3.5	
		Week 6	CR845	164	150 (91.5)	-2.69 (2.57)	-9.9	-2.24	3.8	-0.32 [-0.55, -0.10]
			Placebo	169	160 (94.7)	-1.91 (2.26)	-7.5	-1.86	3.1	
		Week 7	CR845	164	150 (91.5)	-2.74 (2.58)	-10.0	-2.23	1.6	-0.34 [-0.56, -0.11]
			Placebo	169	161 (95.3)	-1.93 (2.23)	-7.1	-1.75	3.3	
		Week 8	CR845	164	147 (89.6)	-2.72 (2.44)	-8.3	-2.27	1.9	-0.30 [-0.53, -0.07]
			Placebo	169	158 (93.5)	-2.01 (2.27)	-7.6	-1.73	3.5	
		Week 9	CR845	164	147 (89.6)	-2.79 (2.48)	-10.0	-2.52	2.0	-0.27 [-0.49, -0.04]
			Placebo	169	159 (94.1)	-2.15 (2.31)	-7.9	-1.93	3.5	
		Week 10	CR845	164	146 (89.0)	-2.77 (2.58)	-10.0	-2.59	3.0	-0.24 [-0.47, -0.02]
			Placebo	169	158 (93.5)	-2.17 (2.34)	-8.0	-2.00	3.5	
		Week 11	CR845	164	143 (87.2)	-2.92 (2.59)	-10.0	-2.73	3.0	-0.30 [-0.53, -0.07]
			Placebo	169	158 (93.5)	-2.17 (2.39)	-7.9	-2.01	3.6	
		Week 12	CR845	164	136 (82.9)	-3.00 (2.62)	-10.0	-2.87	3.0	-0.29 [-0.52, -0.06]
			Placebo	169	150 (88.8)	-2.27 (2.41)	-8.6	-2.17	3.6	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISHC: Change from baseline in weekly WI-NRS by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Other	Weekly WI-NRS	Baseline	CR845	20	20 (100.0)	6.97 (1.27)	5.0	7.00	10.0	
			Placebo	29	29 (100.0)	6.88 (1.24)	5.0	6.88	10.0	
		Week 1	CR845	20	20 (100.0)	6.15 (1.95)	3.0	5.86	10.0	
			Placebo	29	28 (96.6)	6.41 (1.89)	3.0	5.86	10.0	
		Week 2	CR845	20	18 (90.0)	5.05 (2.50)	1.3	5.00	10.0	
			Placebo	29	28 (96.6)	6.00 (2.19)	2.7	6.00	10.0	
		Week 3	CR845	20	17 (85.0)	4.97 (2.60)	1.3	4.57	10.0	
			Placebo	29	27 (93.1)	5.70 (2.15)	2.4	5.50	10.0	
		Week 4	CR845	20	17 (85.0)	4.39 (2.37)	1.0	4.29	8.9	
			Placebo	29	28 (96.6)	5.50 (2.22)	1.7	5.50	9.9	
		Week 5	CR845	20	16 (80.0)	4.37 (1.99)	1.0	4.21	7.9	
			Placebo	29	28 (96.6)	5.20 (2.18)	1.7	4.92	10.0	
		Week 6	CR845	20	17 (85.0)	4.19 (2.17)	0.1	4.00	8.5	
			Placebo	29	27 (93.1)	4.98 (2.34)	1.4	4.71	10.0	
		Week 7	CR845	20	17 (85.0)	4.11 (2.30)	0.1	3.83	8.1	
			Placebo	29	27 (93.1)	5.11 (2.31)	1.4	5.00	9.9	
		Week 8	CR845	20	17 (85.0)	3.99 (2.27)	1.0	3.29	8.3	
			Placebo	29	27 (93.1)	4.74 (2.19)	1.3	4.43	10.0	
		Week 9	CR845	20	15 (75.0)	4.01 (2.22)	1.1	4.00	8.1	
			Placebo	29	26 (89.7)	4.39 (2.01)	1.4	4.14	10.0	
		Week 10	CR845	20	16 (80.0)	3.87 (2.36)	0.4	3.93	8.0	
			Placebo	29	25 (86.2)	4.58 (2.22)	1.1	4.29	10.0	
		Week 11	CR845	20	16 (80.0)	3.84 (2.39)	0.3	3.71	8.0	
			Placebo	29	25 (86.2)	4.27 (2.48)	0.6	4.00	10.0	
		Week 12	CR845	20	16 (80.0)	3.99 (2.26)	0.1	3.86	8.1	
			Placebo	29	22 (75.9)	4.00 (2.27)	1.1	3.43	10.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	20	20 (100.0)	-0.82 (1.50)	-4.1	-0.09	0.9	-0.25 [-0.82, 0.33]
			Placebo	29	28 (96.6)	-0.45 (1.46)	-4.8	-0.28	2.8	
		Week 2	CR845	20	18 (90.0)	-1.88 (2.05)	-5.9	-0.88	1.1	-0.55 [-1.15, 0.05]
			Placebo	29	28 (96.6)	-0.86 (1.73)	-5.0	-0.63	2.8	
		Week 3	CR845	20	17 (85.0)	-1.90 (1.98)	-5.9	-1.43	1.0	-0.41 [-1.03, 0.20]
			Placebo	29	27 (93.1)	-1.16 (1.64)	-5.3	-1.33	2.5	
		Week 4	CR845	20	17 (85.0)	-2.47 (1.85)	-6.6	-2.16	-0.3	-0.62 [-1.24, -0.00]
			Placebo	29	28 (96.6)	-1.36 (1.74)	-5.0	-1.20	2.1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISHC: Change from baseline in weekly WI-NRS by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 5	CR845	20	16 (80.0)	-2.44 (1.64)	-5.4	-1.73	-0.2	-0.47 [-1.09, 0.15]
			Placebo	29	28 (96.6)	-1.66 (1.69)	-5.2	-1.41	1.9	
		Week 6	CR845	20	17 (85.0)	-2.68 (2.12)	-6.3	-2.04	0.8	-0.38 [-0.99, 0.23]
			Placebo	29	27 (93.1)	-1.91 (1.99)	-6.8	-1.64	1.9	
		Week 7	CR845	20	17 (85.0)	-2.76 (2.32)	-6.9	-1.79	-0.0	-0.48 [-1.09, 0.14]
			Placebo	29	27 (93.1)	-1.75 (1.98)	-6.7	-1.34	1.9	
		Week 8	CR845	20	17 (85.0)	-2.88 (2.20)	-6.7	-2.48	-0.0	-0.39 [-1.00, 0.22]
			Placebo	29	27 (93.1)	-2.12 (1.77)	-6.1	-2.02	1.6	
		Week 9	CR845	20	15 (75.0)	-2.92 (2.36)	-7.4	-2.75	-0.1	-0.21 [-0.85, 0.43]
			Placebo	29	26 (89.7)	-2.51 (1.69)	-6.6	-2.29	0.4	
		Week 10	CR845	20	16 (80.0)	-2.99 (2.52)	-8.4	-2.13	-0.6	-0.31 [-0.94, 0.33]
			Placebo	29	25 (86.2)	-2.35 (1.73)	-6.6	-2.48	1.8	
		Week 11	CR845	20	16 (80.0)	-3.02 (2.52)	-8.0	-2.38	-0.1	-0.16 [-0.79, 0.46]
			Placebo	29	25 (86.2)	-2.67 (1.90)	-6.6	-2.30	1.8	
		Week 12	CR845	20	16 (80.0)	-2.87 (2.31)	-7.7	-2.18	-0.7	-0.03 [-0.67, 0.62]
			Placebo	29	22 (75.9)	-2.81 (1.78)	-6.7	-2.99	1.8	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISHD: Change from baseline in weekly WI-NRS by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 4 to < 7	Weekly WI-NRS	Baseline	CR845	102	102 (100.0)	6.00 (0.60)	4.5	6.06	6.9	
			Placebo	113	113 (100.0)	5.93 (0.56)	4.8	6.00	6.9	
		Week 1	CR845	102	100 (98.0)	5.26 (1.41)	0.9	5.43	8.9	
			Placebo	113	111 (98.2)	5.68 (1.36)	0.0	5.71	8.4	
		Week 2	CR845	102	99 (97.1)	4.56 (1.85)	0.0	4.71	8.4	
			Placebo	113	110 (97.3)	5.13 (1.69)	0.0	5.43	8.7	
		Week 3	CR845	102	97 (95.1)	4.18 (1.97)	0.0	4.29	8.7	
			Placebo	113	108 (95.6)	4.88 (1.82)	0.0	4.86	8.6	
		Week 4	CR845	102	96 (94.1)	3.93 (1.91)	0.0	3.93	8.0	
			Placebo	113	108 (95.6)	4.73 (1.92)	0.0	4.83	8.7	
		Week 5	CR845	102	98 (96.1)	3.89 (2.11)	0.4	3.93	8.4	
			Placebo	113	108 (95.6)	4.45 (1.96)	0.0	4.57	8.9	
		Week 6	CR845	102	96 (94.1)	3.77 (2.08)	0.1	3.86	9.0	
			Placebo	113	106 (93.8)	4.33 (2.03)	0.0	4.29	8.4	
		Week 7	CR845	102	97 (95.1)	3.65 (2.16)	0.0	3.60	8.4	
			Placebo	113	107 (94.7)	4.46 (2.07)	0.0	4.57	8.7	
		Week 8	CR845	102	94 (92.2)	3.51 (2.12)	0.0	3.14	8.6	
			Placebo	113	106 (93.8)	4.36 (2.09)	0.0	4.57	8.9	
		Week 9	CR845	102	93 (91.2)	3.43 (2.08)	0.0	3.14	8.7	
			Placebo	113	105 (92.9)	4.20 (2.13)	0.0	4.14	8.9	
		Week 10	CR845	102	93 (91.2)	3.36 (2.19)	0.0	3.00	9.3	
			Placebo	113	105 (92.9)	4.13 (2.17)	0.0	4.00	9.4	
		Week 11	CR845	102	90 (88.2)	3.17 (2.14)	0.0	3.00	9.7	
			Placebo	113	104 (92.0)	4.07 (2.21)	0.0	4.00	9.3	
		Week 12	CR845	102	84 (82.4)	3.10 (2.07)	0.0	2.64	8.2	
			Placebo	113	101 (89.4)	3.96 (2.20)	0.0	4.00	9.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	102	100 (98.0)	-0.74 (1.32)	-4.9	-0.70	2.4	-0.36 [-0.63, -0.09]
			Placebo	113	111 (98.2)	-0.26 (1.36)	-6.3	-0.21	2.9	
		Week 2	CR845	102	99 (97.1)	-1.43 (1.72)	-5.4	-1.21	1.7	-0.36 [-0.63, -0.08]
			Placebo	113	110 (97.3)	-0.82 (1.70)	-6.3	-0.71	3.5	
		Week 3	CR845	102	97 (95.1)	-1.79 (1.85)	-5.6	-1.80	2.0	-0.39 [-0.67, -0.12]
			Placebo	113	108 (95.6)	-1.06 (1.85)	-6.3	-1.04	3.3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISHD: Change from baseline in weekly WI-NRS by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 4	CR845	102	96 (94.1)	-2.05 (1.83)	-5.8	-2.03	1.5	-0.43 [-0.71, -0.15]
			Placebo	113	108 (95.6)	-1.22 (2.02)	-6.3	-1.13	3.5	
		Week 5	CR845	102	98 (96.1)	-2.10 (2.04)	-5.9	-2.13	2.9	-0.30 [-0.58, -0.03]
			Placebo	113	108 (95.6)	-1.49 (2.04)	-6.3	-1.41	3.5	
		Week 6	CR845	102	96 (94.1)	-2.22 (2.04)	-6.5	-2.20	3.8	-0.29 [-0.57, -0.02]
			Placebo	113	106 (93.8)	-1.61 (2.13)	-6.6	-1.86	3.1	
		Week 7	CR845	102	97 (95.1)	-2.34 (2.09)	-6.3	-2.25	1.6	-0.41 [-0.69, -0.13]
			Placebo	113	107 (94.7)	-1.47 (2.14)	-6.9	-1.34	3.3	
		Week 8	CR845	102	94 (92.2)	-2.48 (2.04)	-6.1	-2.65	1.9	-0.43 [-0.71, -0.15]
			Placebo	113	106 (93.8)	-1.58 (2.16)	-6.9	-1.26	3.5	
		Week 9	CR845	102	93 (91.2)	-2.57 (2.02)	-6.1	-2.75	2.0	-0.39 [-0.67, -0.11]
			Placebo	113	105 (92.9)	-1.74 (2.20)	-6.9	-1.48	3.5	
		Week 10	CR845	102	93 (91.2)	-2.62 (2.12)	-6.1	-2.95	3.0	-0.37 [-0.65, -0.09]
			Placebo	113	105 (92.9)	-1.81 (2.25)	-6.9	-1.88	3.5	
		Week 11	CR845	102	90 (88.2)	-2.80 (2.13)	-6.2	-2.98	3.0	-0.42 [-0.71, -0.14]
			Placebo	113	104 (92.0)	-1.86 (2.28)	-6.9	-2.00	3.6	
		Week 12	CR845	102	84 (82.4)	-2.86 (2.11)	-6.0	-3.31	3.0	-0.40 [-0.70, -0.11]
			Placebo	113	101 (89.4)	-1.97 (2.26)	-6.9	-2.14	3.6	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISHD: Change from baseline in weekly WI-NRS by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 7	Weekly WI-NRS	Baseline	CR845	135	135 (100.0)	8.22 (0.91)	7.0	8.00	10.0	
			Placebo	123	123 (100.0)	8.21 (0.88)	7.0	8.13	10.0	
		Week 1	CR845	135	131 (97.0)	7.42 (1.48)	2.0	7.43	10.0	
			Placebo	123	121 (98.4)	7.48 (1.39)	3.0	7.57	10.0	
		Week 2	CR845	135	126 (93.3)	6.65 (2.15)	0.0	7.00	10.0	
			Placebo	123	122 (99.2)	6.97 (1.80)	0.8	7.31	10.0	
		Week 3	CR845	135	124 (91.9)	6.27 (2.45)	0.0	6.86	10.0	
			Placebo	123	119 (96.7)	6.62 (2.01)	1.0	6.86	10.0	
		Week 4	CR845	135	118 (87.4)	5.81 (2.61)	0.0	6.46	10.0	
			Placebo	123	117 (95.1)	6.32 (2.25)	0.1	6.57	10.0	
		Week 5	CR845	135	118 (87.4)	5.57 (2.68)	0.0	6.00	10.0	
			Placebo	123	118 (95.9)	5.99 (2.40)	0.0	6.15	10.0	
		Week 6	CR845	135	116 (85.9)	5.33 (2.76)	0.0	5.71	10.0	
			Placebo	123	118 (95.9)	5.99 (2.53)	0.0	6.50	10.0	
		Week 7	CR845	135	116 (85.9)	5.26 (2.79)	0.0	6.00	10.0	
			Placebo	123	117 (95.1)	5.82 (2.42)	0.0	6.00	10.0	
		Week 8	CR845	135	115 (85.2)	5.27 (2.71)	0.0	5.71	10.0	
			Placebo	123	115 (93.5)	5.70 (2.44)	0.0	5.71	10.0	
		Week 9	CR845	135	114 (84.4)	5.29 (2.79)	0.0	5.71	10.0	
			Placebo	123	117 (95.1)	5.53 (2.46)	0.0	5.57	10.0	
		Week 10	CR845	135	114 (84.4)	5.21 (2.80)	0.0	5.36	10.0	
			Placebo	123	115 (93.5)	5.57 (2.44)	0.0	5.71	10.0	
		Week 11	CR845	135	112 (83.0)	5.12 (2.85)	0.0	5.86	10.0	
			Placebo	123	115 (93.5)	5.53 (2.48)	0.0	5.57	10.0	
		Week 12	CR845	135	107 (79.3)	4.97 (2.86)	0.0	5.14	10.0	
			Placebo	123	106 (86.2)	5.40 (2.55)	0.0	5.49	10.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	135	131 (97.0)	-0.82 (1.30)	-5.6	-0.52	2.1	-0.06 [-0.31, 0.19]
			Placebo	123	121 (98.4)	-0.75 (1.13)	-4.8	-0.46	2.8	
		Week 2	CR845	135	126 (93.3)	-1.60 (2.07)	-10.0	-0.96	2.0	-0.19 [-0.44, 0.06]
			Placebo	123	122 (99.2)	-1.25 (1.56)	-6.5	-1.00	2.8	
		Week 3	CR845	135	124 (91.9)	-1.99 (2.34)	-10.0	-1.43	2.1	-0.18 [-0.44, 0.07]
			Placebo	123	119 (96.7)	-1.61 (1.74)	-7.1	-1.38	2.5	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISHD: Change from baseline in weekly WI-NRS by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 4	CR845	135	118 (87.4)	-2.48 (2.51)	-10.0	-1.85	1.3	-0.26 [-0.52, -0.00]
			Placebo	123	117 (95.1)	-1.89 (2.01)	-8.0	-1.50	1.5	
		Week 5	CR845	135	118 (87.4)	-2.72 (2.67)	-10.0	-2.00	1.3	-0.22 [-0.48, 0.04]
			Placebo	123	118 (95.9)	-2.18 (2.18)	-8.1	-1.76	1.5	
		Week 6	CR845	135	116 (85.9)	-2.96 (2.77)	-10.0	-2.00	1.4	-0.29 [-0.55, -0.04]
			Placebo	123	118 (95.9)	-2.21 (2.28)	-8.1	-1.63	1.6	
		Week 7	CR845	135	116 (85.9)	-3.03 (2.84)	-10.0	-2.12	1.4	-0.26 [-0.52, -0.00]
			Placebo	123	117 (95.1)	-2.38 (2.17)	-7.2	-2.13	1.8	
		Week 8	CR845	135	115 (85.2)	-3.00 (2.71)	-10.0	-2.36	1.3	-0.20 [-0.45, 0.06]
			Placebo	123	115 (93.5)	-2.52 (2.22)	-7.6	-2.43	1.6	
		Week 9	CR845	135	114 (84.4)	-2.98 (2.82)	-10.0	-2.28	1.4	-0.12 [-0.38, 0.14]
			Placebo	123	117 (95.1)	-2.67 (2.22)	-7.9	-2.39	1.4	
		Week 10	CR845	135	114 (84.4)	-3.06 (2.84)	-10.0	-2.59	1.3	-0.17 [-0.43, 0.08]
			Placebo	123	115 (93.5)	-2.61 (2.22)	-8.0	-2.29	1.8	
		Week 11	CR845	135	112 (83.0)	-3.15 (2.88)	-10.0	-2.67	2.1	-0.20 [-0.46, 0.07]
			Placebo	123	115 (93.5)	-2.64 (2.30)	-7.9	-2.38	1.8	
		Week 12	CR845	135	107 (79.3)	-3.30 (2.90)	-10.0	-2.70	2.0	-0.20 [-0.47, 0.07]
			Placebo	123	106 (86.2)	-2.77 (2.34)	-8.6	-2.58	1.8	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISHE: Change from baseline in weekly WI-NRS by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	Weekly WI-NRS	Baseline	CR845	195	195 (100.0)	7.22 (1.38)	4.5	7.00	10.0	
			Placebo	199	199 (100.0)	7.05 (1.38)	4.8	6.88	10.0	
		Week 1	CR845	195	191 (97.9)	6.43 (1.82)	0.9	6.29	10.0	
			Placebo	199	195 (98.0)	6.53 (1.66)	0.0	6.57	10.0	
		Week 2	CR845	195	187 (95.9)	5.74 (2.21)	0.0	5.86	10.0	
			Placebo	199	195 (98.0)	6.06 (1.99)	0.0	6.14	10.0	
		Week 3	CR845	195	183 (93.8)	5.36 (2.40)	0.0	5.29	10.0	
			Placebo	199	190 (95.5)	5.73 (2.10)	0.0	5.83	10.0	
		Week 4	CR845	195	176 (90.3)	4.97 (2.42)	0.0	5.14	10.0	
			Placebo	199	190 (95.5)	5.52 (2.23)	0.0	5.57	10.0	
		Week 5	CR845	195	178 (91.3)	4.85 (2.46)	0.0	5.00	10.0	
			Placebo	199	191 (96.0)	5.25 (2.32)	0.0	5.40	10.0	
		Week 6	CR845	195	177 (90.8)	4.64 (2.49)	0.0	4.71	10.0	
			Placebo	199	189 (95.0)	5.20 (2.47)	0.0	5.29	10.0	
		Week 7	CR845	195	177 (90.8)	4.56 (2.56)	0.0	4.86	10.0	
			Placebo	199	188 (94.5)	5.16 (2.38)	0.0	5.14	10.0	
		Week 8	CR845	195	173 (88.7)	4.46 (2.56)	0.0	4.43	10.0	
			Placebo	199	186 (93.5)	5.03 (2.39)	0.0	5.14	10.0	
		Week 9	CR845	195	173 (88.7)	4.44 (2.62)	0.0	4.43	10.0	
			Placebo	199	186 (93.5)	4.90 (2.46)	0.0	5.00	10.0	
		Week 10	CR845	195	172 (88.2)	4.41 (2.67)	0.0	4.21	10.0	
			Placebo	199	184 (92.5)	4.87 (2.50)	0.0	4.86	10.0	
		Week 11	CR845	195	169 (86.7)	4.25 (2.72)	0.0	3.86	10.0	
			Placebo	199	183 (92.0)	4.86 (2.52)	0.0	4.71	10.0	
		Week 12	CR845	195	160 (82.1)	4.13 (2.71)	0.0	3.64	10.0	
			Placebo	199	175 (87.9)	4.69 (2.53)	0.0	4.43	10.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	195	191 (97.9)	-0.80 (1.30)	-5.6	-0.64	2.4	-0.20 [-0.40, -0.00]
			Placebo	199	195 (98.0)	-0.54 (1.30)	-6.3	-0.39	2.9	
		Week 2	CR845	195	187 (95.9)	-1.46 (1.80)	-8.9	-1.09	2.0	-0.26 [-0.46, -0.06]
			Placebo	199	195 (98.0)	-1.01 (1.63)	-6.5	-0.91	3.5	
		Week 3	CR845	195	183 (93.8)	-1.83 (2.00)	-7.9	-1.43	2.1	-0.26 [-0.46, -0.06]
			Placebo	199	190 (95.5)	-1.34 (1.78)	-6.3	-1.33	3.3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISHE: Change from baseline in weekly WI-NRS by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 4	CR845	195	176 (90.3)	-2.22 (2.10)	-9.3	-1.98	1.4	-0.34 [-0.54, -0.13]
			Placebo	199	190 (95.5)	-1.53 (2.01)	-7.2	-1.35	3.5	
		Week 5	CR845	195	178 (91.3)	-2.34 (2.26)	-10.0	-2.00	2.9	-0.26 [-0.47, -0.06]
			Placebo	199	191 (96.0)	-1.77 (2.10)	-7.1	-1.63	3.5	
		Week 6	CR845	195	177 (90.8)	-2.54 (2.34)	-9.9	-2.11	3.8	-0.30 [-0.51, -0.10]
			Placebo	199	189 (95.0)	-1.85 (2.22)	-7.5	-1.79	3.1	
		Week 7	CR845	195	177 (90.8)	-2.62 (2.41)	-10.0	-2.18	1.6	-0.32 [-0.53, -0.12]
			Placebo	199	188 (94.5)	-1.88 (2.19)	-7.2	-1.67	3.3	
		Week 8	CR845	195	173 (88.7)	-2.72 (2.32)	-8.8	-2.58	1.9	-0.30 [-0.51, -0.09]
			Placebo	199	186 (93.5)	-2.03 (2.24)	-7.6	-1.77	3.5	
		Week 9	CR845	195	173 (88.7)	-2.74 (2.39)	-10.0	-2.57	2.0	-0.25 [-0.46, -0.04]
			Placebo	199	186 (93.5)	-2.16 (2.28)	-7.9	-1.89	3.5	
		Week 10	CR845	195	172 (88.2)	-2.76 (2.45)	-10.0	-2.78	3.0	-0.25 [-0.46, -0.04]
			Placebo	199	184 (92.5)	-2.17 (2.31)	-8.0	-2.00	3.5	
		Week 11	CR845	195	169 (86.7)	-2.94 (2.53)	-10.0	-2.75	3.0	-0.31 [-0.52, -0.10]
			Placebo	199	183 (92.0)	-2.18 (2.35)	-7.9	-2.04	3.6	
		Week 12	CR845	195	160 (82.1)	-3.07 (2.54)	-10.0	-2.89	3.0	-0.30 [-0.52, -0.09]
			Placebo	199	175 (87.9)	-2.33 (2.39)	-8.6	-2.21	3.6	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISHE: Change from baseline in weekly WI-NRS by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	Weekly WI-NRS	Baseline	CR845	42	42 (100.0)	7.45 (1.24)	5.0	7.63	10.0	
			Placebo	37	37 (100.0)	7.49 (1.24)	5.0	7.50	10.0	
		Week 1	CR845	42	40 (95.2)	6.77 (1.73)	3.1	7.07	10.0	
			Placebo	37	37 (100.0)	7.10 (1.47)	3.6	7.14	9.9	
		Week 2	CR845	42	38 (90.5)	5.67 (2.56)	0.0	5.67	10.0	
			Placebo	37	37 (100.0)	6.28 (1.92)	1.5	6.33	9.6	
		Week 3	CR845	42	38 (90.5)	5.30 (2.83)	0.0	6.00	10.0	
			Placebo	37	37 (100.0)	6.11 (2.13)	1.6	6.29	9.4	
		Week 4	CR845	42	38 (90.5)	4.92 (2.87)	0.0	5.36	10.0	
			Placebo	37	35 (94.6)	5.74 (2.29)	1.2	6.00	9.4	
		Week 5	CR845	42	38 (90.5)	4.64 (3.08)	0.0	5.43	10.0	
			Placebo	37	35 (94.6)	5.27 (2.42)	1.0	5.86	9.4	
		Week 6	CR845	42	35 (83.3)	4.54 (3.06)	0.0	4.71	10.0	
			Placebo	37	35 (94.6)	5.25 (2.34)	1.0	5.60	9.6	
		Week 7	CR845	42	36 (85.7)	4.38 (3.06)	0.0	4.86	10.0	
			Placebo	37	36 (97.3)	5.25 (2.23)	1.4	5.43	9.7	
		Week 8	CR845	42	36 (85.7)	4.57 (2.89)	0.0	4.71	10.0	
			Placebo	37	35 (94.6)	5.21 (2.32)	1.0	5.17	9.9	
		Week 9	CR845	42	34 (81.0)	4.50 (2.90)	0.0	4.64	10.0	
			Placebo	37	36 (97.3)	4.89 (2.09)	1.0	4.93	9.9	
		Week 10	CR845	42	35 (83.3)	4.22 (2.87)	0.0	4.57	10.0	
			Placebo	37	36 (97.3)	4.94 (2.00)	1.0	4.86	9.6	
		Week 11	CR845	42	33 (78.6)	4.28 (2.83)	0.0	4.00	10.0	
			Placebo	37	36 (97.3)	4.74 (2.17)	0.6	4.86	9.9	
		Week 12	CR845	42	31 (73.8)	4.24 (2.73)	0.0	4.50	9.0	
			Placebo	37	32 (86.5)	4.75 (2.29)	1.0	4.71	9.6	
	Change from baseline in weekly WI-NRS	Week 1	CR845	42	40 (95.2)	-0.72 (1.36)	-5.4	-0.39	1.3	-0.27 [-0.72, 0.17]
			Placebo	37	37 (100.0)	-0.38 (1.10)	-3.4	-0.29	1.4	
		Week 2	CR845	42	38 (90.5)	-1.84 (2.42)	-10.0	-1.16	1.3	-0.30 [-0.76, 0.15]
			Placebo	37	37 (100.0)	-1.20 (1.68)	-5.6	-0.79	1.1	
		Week 3	CR845	42	38 (90.5)	-2.24 (2.74)	-10.0	-1.58	1.6	-0.36 [-0.82, 0.09]
			Placebo	37	37 (100.0)	-1.38 (1.96)	-7.1	-0.79	0.9	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISHE: Change from baseline in weekly WI-NRS by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 4	CR845	42	38 (90.5)	-2.60 (2.78)	-10.0	-2.02	1.5	-0.32 [-0.79, 0.14]
			Placebo	37	35 (94.6)	-1.79 (2.18)	-8.0	-1.27	1.1	
		Week 5	CR845	42	38 (90.5)	-2.89 (3.05)	-10.0	-2.11	2.0	-0.22 [-0.68, 0.24]
			Placebo	37	35 (94.6)	-2.29 (2.32)	-8.1	-1.84	0.9	
		Week 6	CR845	42	35 (83.3)	-3.04 (3.15)	-10.0	-1.59	1.0	-0.27 [-0.74, 0.21]
			Placebo	37	35 (94.6)	-2.32 (2.24)	-8.1	-1.88	1.1	
		Week 7	CR845	42	36 (85.7)	-3.17 (3.13)	-10.0	-2.19	1.0	-0.33 [-0.80, 0.13]
			Placebo	37	36 (97.3)	-2.27 (2.24)	-7.0	-2.00	2.0	
		Week 8	CR845	42	36 (85.7)	-2.96 (2.96)	-10.0	-2.37	1.4	-0.27 [-0.74, 0.19]
			Placebo	37	35 (94.6)	-2.24 (2.24)	-6.8	-1.71	2.0	
		Week 9	CR845	42	34 (81.0)	-3.05 (2.98)	-10.0	-2.38	1.0	-0.16 [-0.63, 0.31]
			Placebo	37	36 (97.3)	-2.63 (2.12)	-6.5	-2.34	1.4	
		Week 10	CR845	42	35 (83.3)	-3.34 (2.96)	-10.0	-3.16	1.0	-0.33 [-0.80, 0.14]
			Placebo	37	36 (97.3)	-2.51 (2.01)	-6.1	-2.23	1.7	
		Week 11	CR845	42	33 (78.6)	-3.29 (2.82)	-10.0	-3.34	1.0	-0.22 [-0.69, 0.26]
			Placebo	37	36 (97.3)	-2.76 (2.12)	-6.6	-2.39	1.5	
		Week 12	CR845	42	31 (73.8)	-3.29 (2.85)	-10.0	-3.05	0.9	-0.25 [-0.75, 0.25]
			Placebo	37	32 (86.5)	-2.68 (2.01)	-6.2	-2.73	1.7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISHF: Change from baseline in weekly WI-NRS by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	Weekly WI-NRS	Baseline	CR845	150	150 (100.0)	7.20 (1.31)	5.0	7.00	10.0	
			Placebo	151	151 (100.0)	7.14 (1.32)	5.0	7.13	10.0	
		Week 1	CR845	150	146 (97.3)	6.57 (1.80)	0.9	6.43	10.0	
			Placebo	151	150 (99.3)	6.57 (1.68)	0.0	6.71	10.0	
		Week 2	CR845	150	142 (94.7)	5.79 (2.14)	0.0	5.79	10.0	
			Placebo	151	149 (98.7)	6.06 (2.04)	0.0	6.29	10.0	
		Week 3	CR845	150	140 (93.3)	5.46 (2.37)	0.0	5.43	10.0	
			Placebo	151	146 (96.7)	5.79 (2.17)	0.0	6.00	9.7	
		Week 4	CR845	150	138 (92.0)	5.15 (2.37)	0.0	5.14	10.0	
			Placebo	151	145 (96.0)	5.52 (2.25)	0.0	5.71	9.6	
		Week 5	CR845	150	140 (93.3)	4.98 (2.44)	0.0	5.14	10.0	
			Placebo	151	145 (96.0)	5.28 (2.36)	0.0	5.57	9.9	
		Week 6	CR845	150	139 (92.7)	4.84 (2.44)	0.0	5.00	10.0	
			Placebo	151	143 (94.7)	5.26 (2.52)	0.0	5.86	9.9	
		Week 7	CR845	150	139 (92.7)	4.69 (2.55)	0.0	5.00	10.0	
			Placebo	151	143 (94.7)	5.15 (2.37)	0.0	5.29	10.0	
		Week 8	CR845	150	138 (92.0)	4.58 (2.48)	0.0	4.57	10.0	
			Placebo	151	142 (94.0)	5.02 (2.39)	0.0	5.15	10.0	
		Week 9	CR845	150	134 (89.3)	4.59 (2.56)	0.0	4.71	10.0	
			Placebo	151	144 (95.4)	4.88 (2.43)	0.0	5.00	10.0	
		Week 10	CR845	150	133 (88.7)	4.50 (2.64)	0.0	4.43	10.0	
			Placebo	151	143 (94.7)	4.86 (2.47)	0.0	5.00	10.0	
		Week 11	CR845	150	133 (88.7)	4.31 (2.64)	0.0	4.29	10.0	
			Placebo	151	141 (93.4)	4.88 (2.48)	0.0	4.86	10.0	
		Week 12	CR845	150	125 (83.3)	4.24 (2.60)	0.0	4.00	10.0	
			Placebo	151	133 (88.1)	4.79 (2.57)	0.0	5.00	10.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	150	146 (97.3)	-0.65 (1.25)	-5.6	-0.47	2.1	-0.05 [-0.28, 0.17]
			Placebo	151	150 (99.3)	-0.58 (1.37)	-6.3	-0.40	2.9	
		Week 2	CR845	150	142 (94.7)	-1.42 (1.72)	-7.6	-1.08	2.0	-0.18 [-0.42, 0.05]
			Placebo	151	149 (98.7)	-1.11 (1.71)	-6.5	-1.00	3.5	
		Week 3	CR845	150	140 (93.3)	-1.76 (2.00)	-7.6	-1.36	2.1	-0.19 [-0.43, 0.04]
			Placebo	151	146 (96.7)	-1.38 (1.93)	-7.1	-1.29	3.3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISHF: Change from baseline in weekly WI-NRS by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 4	CR845	150	138 (92.0)	-2.06 (2.04)	-7.8	-1.85	1.4	-0.21 [-0.44, 0.02]
			Placebo	151	145 (96.0)	-1.62 (2.15)	-8.0	-1.45	3.5	
		Week 5	CR845	150	140 (93.3)	-2.22 (2.22)	-8.6	-2.00	2.9	-0.17 [-0.40, 0.07]
			Placebo	151	145 (96.0)	-1.85 (2.22)	-8.1	-1.63	3.5	
		Week 6	CR845	150	139 (92.7)	-2.37 (2.31)	-8.6	-2.00	3.8	-0.21 [-0.44, 0.02]
			Placebo	151	143 (94.7)	-1.88 (2.39)	-8.1	-1.63	3.1	
		Week 7	CR845	150	139 (92.7)	-2.51 (2.43)	-8.6	-2.02	1.6	-0.22 [-0.46, 0.01]
			Placebo	151	143 (94.7)	-1.99 (2.26)	-7.2	-1.68	3.3	
		Week 8	CR845	150	138 (92.0)	-2.60 (2.27)	-8.8	-2.42	1.9	-0.20 [-0.44, 0.03]
			Placebo	151	142 (94.0)	-2.14 (2.27)	-7.6	-2.02	3.3	
		Week 9	CR845	150	134 (89.3)	-2.60 (2.34)	-9.0	-2.33	2.0	-0.14 [-0.38, 0.09]
			Placebo	151	144 (95.4)	-2.27 (2.34)	-7.9	-2.00	3.5	
		Week 10	CR845	150	133 (88.7)	-2.67 (2.43)	-9.0	-2.75	3.0	-0.15 [-0.39, 0.08]
			Placebo	151	143 (94.7)	-2.29 (2.41)	-8.0	-2.20	3.5	
		Week 11	CR845	150	133 (88.7)	-2.86 (2.47)	-9.0	-2.84	3.0	-0.24 [-0.48, -0.00]
			Placebo	151	141 (93.4)	-2.28 (2.39)	-7.9	-2.14	3.6	
		Week 12	CR845	150	125 (83.3)	-2.94 (2.50)	-9.0	-2.86	3.0	-0.24 [-0.49, 0.00]
			Placebo	151	133 (88.1)	-2.34 (2.48)	-8.6	-2.30	3.6	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISHF: Change from baseline in weekly WI-NRS by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	Weekly WI-NRS	Baseline	CR845	87	87 (100.0)	7.36 (1.44)	4.5	7.38	10.0	
			Placebo	85	85 (100.0)	7.07 (1.44)	4.8	6.88	10.0	
		Week 1	CR845	87	85 (97.7)	6.34 (1.82)	3.0	6.29	10.0	
			Placebo	85	82 (96.5)	6.70 (1.58)	3.4	6.57	9.9	
		Week 2	CR845	87	83 (95.4)	5.62 (2.48)	0.0	6.00	10.0	
			Placebo	85	83 (97.6)	6.16 (1.86)	1.5	6.00	10.0	
		Week 3	CR845	87	81 (93.1)	5.16 (2.66)	0.0	5.14	10.0	
			Placebo	85	81 (95.3)	5.80 (2.01)	2.1	5.43	10.0	
		Week 4	CR845	87	76 (87.4)	4.63 (2.70)	0.0	4.86	9.4	
			Placebo	85	80 (94.1)	5.61 (2.23)	1.3	5.50	10.0	
		Week 5	CR845	87	76 (87.4)	4.49 (2.80)	0.0	4.29	10.0	
			Placebo	85	81 (95.3)	5.22 (2.28)	0.7	5.00	10.0	
		Week 6	CR845	87	73 (83.9)	4.21 (2.82)	0.0	3.86	9.6	
			Placebo	85	81 (95.3)	5.10 (2.31)	0.1	4.71	10.0	
		Week 7	CR845	87	74 (85.1)	4.23 (2.80)	0.0	3.79	9.1	
			Placebo	85	81 (95.3)	5.21 (2.33)	0.4	5.00	10.0	
		Week 8	CR845	87	71 (81.6)	4.28 (2.85)	0.0	3.57	9.1	
			Placebo	85	79 (92.9)	5.12 (2.35)	1.0	5.00	10.0	
		Week 9	CR845	87	73 (83.9)	4.20 (2.83)	0.0	3.43	9.3	
			Placebo	85	78 (91.8)	4.93 (2.36)	0.6	4.64	10.0	
		Week 10	CR845	87	74 (85.1)	4.16 (2.81)	0.0	3.86	9.6	
			Placebo	85	77 (90.6)	4.92 (2.36)	0.3	4.57	10.0	
		Week 11	CR845	87	69 (79.3)	4.14 (2.91)	0.0	3.43	9.8	
			Placebo	85	78 (91.8)	4.76 (2.44)	0.0	4.29	10.0	
		Week 12	CR845	87	66 (75.9)	3.97 (2.90)	0.0	3.21	9.7	
			Placebo	85	74 (87.1)	4.54 (2.34)	0.0	4.14	10.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	87	85 (97.7)	-1.01 (1.37)	-5.4	-1.11	2.4	-0.51 [-0.82, -0.20]
			Placebo	85	82 (96.5)	-0.39 (1.05)	-2.8	-0.23	2.6	
		Week 2	CR845	87	83 (95.4)	-1.71 (2.22)	-10.0	-1.16	1.7	-0.41 [-0.71, -0.10]
			Placebo	85	83 (97.6)	-0.94 (1.50)	-4.5	-0.70	2.6	
		Week 3	CR845	87	81 (93.1)	-2.15 (2.36)	-10.0	-1.71	1.8	-0.43 [-0.74, -0.12]
			Placebo	85	81 (95.3)	-1.29 (1.57)	-5.4	-1.00	3.1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISHF: Change from baseline in weekly WI-NRS by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 4	CR845	87	76 (87.4)	-2.71 (2.51)	-10.0	-2.13	1.5	-0.57 [-0.89, -0.25]
			Placebo	85	80 (94.1)	-1.47 (1.83)	-7.1	-1.19	3.1	
		Week 5	CR845	87	76 (87.4)	-2.84 (2.71)	-10.0	-2.88	2.0	-0.42 [-0.74, -0.10]
			Placebo	85	81 (95.3)	-1.84 (2.00)	-7.8	-1.75	3.4	
		Week 6	CR845	87	73 (83.9)	-3.11 (2.74)	-10.0	-2.77	1.1	-0.47 [-0.79, -0.15]
			Placebo	85	81 (95.3)	-2.01 (1.91)	-7.1	-1.95	2.5	
		Week 7	CR845	87	74 (85.1)	-3.09 (2.73)	-10.0	-2.34	1.0	-0.51 [-0.83, -0.19]
			Placebo	85	81 (95.3)	-1.86 (2.10)	-6.8	-1.76	2.3	
		Week 8	CR845	87	71 (81.6)	-3.09 (2.72)	-10.0	-2.86	1.9	-0.47 [-0.80, -0.15]
			Placebo	85	79 (92.9)	-1.93 (2.18)	-6.8	-1.54	3.5	
		Week 9	CR845	87	73 (83.9)	-3.15 (2.74)	-10.0	-2.71	1.5	-0.40 [-0.72, -0.08]
			Placebo	85	78 (91.8)	-2.17 (2.11)	-6.5	-1.99	3.1	
		Week 10	CR845	87	74 (85.1)	-3.21 (2.73)	-10.0	-3.00	2.8	-0.46 [-0.79, -0.14]
			Placebo	85	77 (90.6)	-2.11 (1.97)	-6.7	-2.00	3.1	
		Week 11	CR845	87	69 (79.3)	-3.26 (2.77)	-10.0	-2.96	1.0	-0.40 [-0.73, -0.08]
			Placebo	85	78 (91.8)	-2.26 (2.21)	-7.3	-2.00	2.8	
		Week 12	CR845	87	66 (75.9)	-3.43 (2.74)	-10.0	-3.62	1.0	-0.41 [-0.74, -0.07]
			Placebo	85	74 (87.1)	-2.46 (2.06)	-7.3	-2.15	2.6	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISHG: Change from baseline in weekly WI-NRS by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
USA	Weekly WI-NRS	Baseline	CR845	146	146 (100.0)	7.38 (1.32)	4.5	7.38	10.0	
			Placebo	133	133 (100.0)	7.16 (1.38)	4.8	7.13	10.0	
		Week 1	CR845	146	142 (97.3)	6.72 (1.69)	0.9	6.77	10.0	
			Placebo	133	129 (97.0)	6.75 (1.59)	2.0	6.71	10.0	
		Week 2	CR845	146	138 (94.5)	6.26 (2.00)	0.0	6.57	9.9	
			Placebo	133	129 (97.0)	6.26 (1.97)	0.8	6.43	10.0	
		Week 3	CR845	146	137 (93.8)	5.89 (2.21)	0.0	6.00	10.0	
			Placebo	133	126 (94.7)	6.02 (1.98)	1.0	6.00	9.9	
		Week 4	CR845	146	133 (91.1)	5.45 (2.26)	0.0	5.71	9.7	
			Placebo	133	123 (92.5)	5.74 (2.22)	0.1	5.83	10.0	
		Week 5	CR845	146	136 (93.2)	5.29 (2.46)	0.0	5.57	10.0	
			Placebo	133	125 (94.0)	5.45 (2.31)	0.0	5.71	9.9	
		Week 6	CR845	146	131 (89.7)	5.07 (2.50)	0.0	5.29	10.0	
			Placebo	133	123 (92.5)	5.53 (2.47)	0.0	5.86	10.0	
		Week 7	CR845	146	132 (90.4)	4.97 (2.56)	0.0	5.20	10.0	
			Placebo	133	124 (93.2)	5.33 (2.39)	0.0	5.71	10.0	
		Week 8	CR845	146	129 (88.4)	4.93 (2.49)	0.0	5.14	10.0	
			Placebo	133	123 (92.5)	5.23 (2.49)	0.0	5.57	10.0	
		Week 9	CR845	146	130 (89.0)	4.92 (2.54)	0.0	5.14	10.0	
			Placebo	133	124 (93.2)	5.02 (2.48)	0.0	5.07	10.0	
		Week 10	CR845	146	130 (89.0)	4.86 (2.60)	0.0	5.00	10.0	
			Placebo	133	123 (92.5)	4.98 (2.49)	0.0	5.14	10.0	
		Week 11	CR845	146	126 (86.3)	4.69 (2.59)	0.0	4.64	10.0	
			Placebo	133	124 (93.2)	5.00 (2.51)	0.0	5.00	10.0	
		Week 12	CR845	146	118 (80.8)	4.63 (2.62)	0.0	4.62	10.0	
			Placebo	133	115 (86.5)	4.81 (2.59)	0.0	4.86	10.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	146	142 (97.3)	-0.67 (1.26)	-5.4	-0.50	2.4	-0.19 [-0.42, 0.05]
			Placebo	133	129 (97.0)	-0.44 (1.24)	-3.4	-0.38	2.9	
		Week 2	CR845	146	138 (94.5)	-1.11 (1.70)	-10.0	-0.87	2.0	-0.10 [-0.34, 0.14]
			Placebo	133	129 (97.0)	-0.94 (1.63)	-6.5	-0.93	3.5	
		Week 3	CR845	146	137 (93.8)	-1.47 (1.91)	-10.0	-1.04	2.1	-0.17 [-0.41, 0.07]
			Placebo	133	126 (94.7)	-1.16 (1.80)	-6.1	-1.00	3.3	
		Week 4	CR845	146	133 (91.1)	-1.92 (2.03)	-10.0	-1.50	1.5	-0.23 [-0.48, 0.01]
			Placebo	133	123 (92.5)	-1.44 (2.05)	-7.2	-1.07	3.5	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISHG: Change from baseline in weekly WI-NRS by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 5	CR845	146	136 (93.2)	-2.07 (2.29)	-10.0	-1.68	2.0	-0.17 [-0.41, 0.08]
			Placebo	133	125 (94.0)	-1.70 (2.17)	-7.1	-1.45	3.5	
		Week 6	CR845	146	131 (89.7)	-2.29 (2.38)	-10.0	-1.86	1.7	-0.27 [-0.52, -0.02]
			Placebo	133	123 (92.5)	-1.66 (2.29)	-7.1	-1.38	3.1	
		Week 7	CR845	146	132 (90.4)	-2.38 (2.46)	-10.0	-1.80	1.6	-0.22 [-0.47, 0.02]
			Placebo	133	124 (93.2)	-1.85 (2.22)	-7.2	-1.52	3.3	
		Week 8	CR845	146	129 (88.4)	-2.45 (2.36)	-10.0	-1.83	1.9	-0.21 [-0.46, 0.04]
			Placebo	133	123 (92.5)	-1.95 (2.34)	-7.6	-1.54	3.5	
		Week 9	CR845	146	130 (89.0)	-2.43 (2.41)	-10.0	-1.90	1.6	-0.11 [-0.36, 0.13]
			Placebo	133	124 (93.2)	-2.17 (2.31)	-7.9	-1.82	3.5	
		Week 10	CR845	146	130 (89.0)	-2.52 (2.44)	-10.0	-2.10	3.0	-0.14 [-0.39, 0.10]
			Placebo	133	123 (92.5)	-2.18 (2.34)	-8.0	-1.92	3.5	
		Week 11	CR845	146	126 (86.3)	-2.71 (2.44)	-10.0	-2.38	2.4	-0.23 [-0.48, 0.02]
			Placebo	133	124 (93.2)	-2.16 (2.33)	-7.9	-2.00	3.6	
		Week 12	CR845	146	118 (80.8)	-2.81 (2.49)	-10.0	-2.67	2.0	-0.20 [-0.46, 0.06]
			Placebo	133	115 (86.5)	-2.32 (2.40)	-8.6	-2.21	3.6	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISHG: Change from baseline in weekly WI-NRS by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Asia	Weekly WI-NRS	Baseline	CR845	8	8 (100.0)	6.30 (0.81)	5.0	6.14	7.6	
			Placebo	12	12 (100.0)	6.76 (1.27)	5.0	6.63	9.1	
		Week 1	CR845	8	8 (100.0)	4.86 (1.26)	3.0	5.29	6.3	
			Placebo	12	12 (100.0)	6.40 (1.48)	4.7	6.14	9.1	
		Week 2	CR845	8	8 (100.0)	3.89 (1.74)	1.3	4.21	6.0	
			Placebo	12	12 (100.0)	5.83 (1.74)	3.4	6.21	8.6	
		Week 3	CR845	8	8 (100.0)	3.59 (1.53)	1.3	4.29	5.4	
			Placebo	12	12 (100.0)	5.29 (1.74)	2.9	4.79	8.0	
		Week 4	CR845	8	8 (100.0)	3.29 (1.67)	1.0	4.00	5.1	
			Placebo	12	12 (100.0)	5.25 (1.81)	2.6	4.86	8.9	
		Week 5	CR845	8	7 (87.5)	3.53 (1.59)	1.0	4.14	5.1	
			Placebo	12	12 (100.0)	4.87 (1.98)	2.3	4.64	8.7	
		Week 6	CR845	8	7 (87.5)	3.33 (1.76)	0.1	4.00	4.6	
			Placebo	12	11 (91.7)	4.48 (2.04)	2.1	4.29	8.6	
		Week 7	CR845	8	7 (87.5)	3.20 (1.89)	0.1	3.71	5.1	
			Placebo	12	12 (100.0)	4.79 (2.03)	2.0	4.66	8.9	
		Week 8	CR845	8	7 (87.5)	2.94 (1.43)	1.0	3.00	4.4	
			Placebo	12	12 (100.0)	4.49 (1.54)	1.4	4.71	6.6	
		Week 9	CR845	8	7 (87.5)	3.41 (1.65)	1.1	4.00	5.1	
			Placebo	12	11 (91.7)	3.95 (1.39)	1.4	4.00	6.4	
		Week 10	CR845	8	7 (87.5)	3.31 (1.64)	0.9	4.00	4.6	
			Placebo	12	11 (91.7)	3.95 (1.48)	1.1	4.29	5.9	
		Week 11	CR845	8	7 (87.5)	3.14 (1.82)	0.3	4.00	4.9	
			Placebo	12	11 (91.7)	3.82 (1.73)	1.0	4.00	7.7	
		Week 12	CR845	8	7 (87.5)	3.29 (1.30)	1.2	3.43	4.7	
			Placebo	12	11 (91.7)	3.66 (1.58)	1.1	3.71	6.9	
	Change from baseline in weekly WI-NRS	Week 1	CR845	8	8 (100.0)	-1.44 (1.77)	-4.1	-0.80	0.3	-0.86 [-1.80, 0.08]
			Placebo	12	12 (100.0)	-0.36 (0.79)	-1.7	-0.15	0.9	
		Week 2	CR845	8	8 (100.0)	-2.41 (2.33)	-5.9	-2.00	0.0	-0.85 [-1.79, 0.08]
			Placebo	12	12 (100.0)	-0.93 (1.20)	-2.9	-0.97	0.9	
		Week 3	CR845	8	8 (100.0)	-2.71 (2.15)	-5.9	-2.09	-0.4	-0.77 [-1.70, 0.16]
			Placebo	12	12 (100.0)	-1.47 (1.16)	-3.0	-1.71	1.0	
		Week 4	CR845	8	8 (100.0)	-3.02 (2.35)	-6.6	-2.38	-0.3	-0.84 [-1.77, 0.10]
			Placebo	12	12 (100.0)	-1.51 (1.32)	-3.9	-1.40	0.7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISHG: Change from baseline in weekly WI-NRS by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 5	CR845	8	7 (87.5)	-2.58 (2.03)	-5.4	-1.71	-0.4	-0.38 [-1.32, 0.56]
			Placebo	12	12 (100.0)	-1.89 (1.68)	-4.8	-1.68	0.4	
		Week 6	CR845	8	7 (87.5)	-2.79 (2.17)	-6.1	-1.89	-0.4	-0.21 [-1.16, 0.74]
			Placebo	12	11 (91.7)	-2.35 (1.98)	-6.8	-1.98	0.3	
		Week 7	CR845	8	7 (87.5)	-2.91 (2.31)	-6.1	-2.29	-0.3	-0.44 [-1.38, 0.51]
			Placebo	12	12 (100.0)	-1.97 (2.04)	-6.7	-1.53	0.4	
		Week 8	CR845	8	7 (87.5)	-3.17 (1.89)	-6.0	-2.75	-0.6	-0.51 [-1.45, 0.44]
			Placebo	12	12 (100.0)	-2.27 (1.72)	-6.1	-1.83	-0.4	
		Week 9	CR845	8	7 (87.5)	-2.70 (2.13)	-5.7	-2.75	-0.1	0.09 [-0.86, 1.04]
			Placebo	12	11 (91.7)	-2.88 (1.81)	-6.6	-2.73	0.4	
		Week 10	CR845	8	7 (87.5)	-2.81 (2.11)	-6.0	-2.14	-0.6	0.04 [-0.91, 0.99]
			Placebo	12	11 (91.7)	-2.88 (1.68)	-6.6	-2.59	-1.1	
		Week 11	CR845	8	7 (87.5)	-2.97 (2.28)	-6.0	-2.75	-0.1	0.02 [-0.93, 0.97]
			Placebo	12	11 (91.7)	-3.01 (1.66)	-6.6	-2.66	-1.3	
		Week 12	CR845	8	7 (87.5)	-2.82 (1.70)	-5.8	-2.32	-0.7	0.21 [-0.74, 1.16]
			Placebo	12	11 (91.7)	-3.17 (1.63)	-6.7	-2.98	-1.3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISHG: Change from baseline in weekly WI-NRS by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Eastern Europe	Weekly WI-NRS	Baseline	CR845	54	54 (100.0)	7.19 (1.51)	5.0	7.19	10.0	
			Placebo	60	60 (100.0)	7.00 (1.34)	5.0	6.88	10.0	
		Week 1	CR845	54	54 (100.0)	6.21 (1.94)	2.0	6.00	10.0	
			Placebo	60	60 (100.0)	6.39 (1.74)	0.0	6.64	9.9	
		Week 2	CR845	54	54 (100.0)	5.12 (2.33)	0.0	5.07	10.0	
			Placebo	60	60 (100.0)	5.89 (1.89)	0.0	5.93	9.1	
		Week 3	CR845	54	53 (98.1)	4.73 (2.60)	0.0	4.29	10.0	
			Placebo	60	60 (100.0)	5.44 (2.08)	0.0	5.64	9.1	
		Week 4	CR845	54	51 (94.4)	4.43 (2.63)	0.0	4.29	10.0	
			Placebo	60	60 (100.0)	5.32 (2.26)	0.0	5.29	10.0	
		Week 5	CR845	54	51 (94.4)	3.98 (2.53)	0.0	4.29	9.0	
			Placebo	60	60 (100.0)	5.07 (2.31)	0.0	5.00	9.4	
		Week 6	CR845	54	51 (94.4)	3.80 (2.53)	0.0	3.14	9.0	
			Placebo	60	60 (100.0)	4.84 (2.28)	0.0	4.50	9.3	
		Week 7	CR845	54	51 (94.4)	3.75 (2.74)	0.0	3.43	9.0	
			Placebo	60	59 (98.3)	4.86 (2.22)	0.0	4.86	9.0	
		Week 8	CR845	54	50 (92.6)	3.78 (2.70)	0.0	3.43	9.0	
			Placebo	60	59 (98.3)	4.86 (2.20)	0.0	4.71	9.0	
		Week 9	CR845	54	49 (90.7)	3.65 (2.71)	0.0	3.00	9.0	
			Placebo	60	59 (98.3)	4.77 (2.29)	0.0	4.71	9.0	
		Week 10	CR845	54	48 (88.9)	3.50 (2.76)	0.0	2.79	9.1	
			Placebo	60	59 (98.3)	4.74 (2.24)	0.0	4.43	9.4	
		Week 11	CR845	54	47 (87.0)	3.44 (2.89)	0.0	2.86	9.7	
			Placebo	60	57 (95.0)	4.72 (2.36)	0.0	4.43	9.3	
		Week 12	CR845	54	46 (85.2)	3.33 (2.76)	0.0	2.14	9.0	
			Placebo	60	57 (95.0)	4.55 (2.33)	0.0	4.29	9.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	54	54 (100.0)	-0.98 (1.41)	-5.6	-0.81	1.3	-0.27 [-0.64, 0.10]
			Placebo	60	60 (100.0)	-0.61 (1.38)	-6.3	-0.39	2.8	
		Week 2	CR845	54	54 (100.0)	-2.07 (2.16)	-8.9	-1.53	1.3	-0.50 [-0.87, -0.12]
			Placebo	60	60 (100.0)	-1.11 (1.69)	-6.3	-0.71	2.8	
		Week 3	CR845	54	53 (98.1)	-2.47 (2.35)	-7.9	-2.34	1.1	-0.44 [-0.81, -0.06]
			Placebo	60	60 (100.0)	-1.56 (1.76)	-6.3	-1.42	2.8	
		Week 4	CR845	54	51 (94.4)	-2.78 (2.48)	-9.3	-2.82	1.3	-0.48 [-0.86, -0.10]
			Placebo	60	60 (100.0)	-1.68 (2.11)	-7.1	-1.44	3.1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISHG: Change from baseline in weekly WI-NRS by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 5	CR845	54	51 (94.4)	-3.23 (2.50)	-10.0	-3.25	1.3	-0.57 [-0.95, -0.19]
			Placebo	60	60 (100.0)	-1.93 (2.11)	-7.8	-1.97	3.4	
		Week 6	CR845	54	51 (94.4)	-3.42 (2.57)	-9.9	-3.39	1.3	-0.55 [-0.93, -0.17]
			Placebo	60	60 (100.0)	-2.16 (1.98)	-6.4	-2.03	2.8	
		Week 7	CR845	54	51 (94.4)	-3.47 (2.73)	-10.0	-3.67	1.3	-0.55 [-0.94, -0.17]
			Placebo	60	59 (98.3)	-2.12 (2.16)	-6.7	-2.00	2.8	
		Week 8	CR845	54	50 (92.6)	-3.38 (2.55)	-8.0	-3.55	1.8	-0.54 [-0.93, -0.16]
			Placebo	60	59 (98.3)	-2.11 (2.13)	-6.3	-2.18	2.8	
		Week 9	CR845	54	49 (90.7)	-3.52 (2.52)	-10.0	-3.25	2.0	-0.57 [-0.95, -0.18]
			Placebo	60	59 (98.3)	-2.21 (2.15)	-6.9	-2.00	2.8	
		Week 10	CR845	54	48 (88.9)	-3.62 (2.66)	-10.0	-3.93	2.4	-0.58 [-0.97, -0.19]
			Placebo	60	59 (98.3)	-2.24 (2.09)	-6.7	-2.04	3.1	
		Week 11	CR845	54	47 (87.0)	-3.64 (2.78)	-10.0	-3.88	3.0	-0.55 [-0.94, -0.15]
			Placebo	60	57 (95.0)	-2.27 (2.28)	-7.0	-2.04	2.9	
		Week 12	CR845	54	46 (85.2)	-3.76 (2.74)	-10.0	-4.15	3.0	-0.54 [-0.94, -0.15]
			Placebo	60	57 (95.0)	-2.43 (2.21)	-7.0	-2.17	2.8	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISHG: Change from baseline in weekly WI-NRS by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Western Europe/European origin	Weekly WI-NRS	Baseline	CR845	29	29 (100.0)	7.06 (1.27)	5.1	7.00	10.0	
			Placebo	31	31 (100.0)	7.31 (1.40)	5.3	7.13	10.0	
		Week 1	CR845	29	27 (93.1)	6.28 (1.98)	3.0	6.14	10.0	
			Placebo	31	31 (100.0)	6.62 (1.75)	3.0	6.40	9.9	
		Week 2	CR845	29	25 (86.2)	4.71 (2.77)	0.0	4.57	10.0	
			Placebo	31	31 (100.0)	5.92 (2.29)	2.0	5.57	10.0	
		Week 3	CR845	29	23 (79.3)	4.17 (3.02)	0.0	3.29	10.0	
			Placebo	31	29 (93.5)	5.75 (2.74)	1.0	5.50	10.0	
		Week 4	CR845	29	22 (75.9)	3.90 (3.05)	0.0	3.07	10.0	
			Placebo	31	30 (96.8)	5.39 (2.45)	1.0	5.64	9.9	
		Week 5	CR845	29	22 (75.9)	4.19 (2.97)	0.3	3.79	10.0	
			Placebo	31	29 (93.5)	4.94 (2.58)	0.7	4.86	10.0	
		Week 6	CR845	29	23 (79.3)	4.34 (2.90)	0.4	3.67	10.0	
			Placebo	31	30 (96.8)	4.88 (2.69)	0.9	5.43	10.0	
		Week 7	CR845	29	23 (79.3)	4.14 (2.61)	0.1	3.57	10.0	
			Placebo	31	29 (93.5)	5.30 (2.62)	1.0	5.29	10.0	
		Week 8	CR845	29	23 (79.3)	3.96 (2.87)	0.0	3.29	10.0	
			Placebo	31	27 (87.1)	4.92 (2.52)	1.1	5.00	10.0	
		Week 9	CR845	29	21 (72.4)	3.76 (3.00)	0.0	2.57	10.0	
			Placebo	31	28 (90.3)	5.02 (2.62)	0.6	5.10	10.0	
		Week 10	CR845	29	22 (75.9)	3.80 (2.85)	0.0	2.79	10.0	
			Placebo	31	27 (87.1)	5.12 (2.77)	0.3	4.71	10.0	
		Week 11	CR845	29	22 (75.9)	3.82 (2.97)	0.0	2.71	10.0	
			Placebo	31	27 (87.1)	4.74 (2.68)	0.1	4.57	10.0	
		Week 12	CR845	29	20 (69.0)	3.51 (2.91)	0.0	2.64	9.7	
			Placebo	31	24 (77.4)	4.97 (2.66)	0.0	5.18	10.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	29	27 (93.1)	-0.80 (1.12)	-3.4	-0.77	1.0	-0.08 [-0.60, 0.43]
			Placebo	31	31 (100.0)	-0.69 (1.32)	-4.8	-0.63	1.7	
		Week 2	CR845	29	25 (86.2)	-2.34 (1.81)	-5.4	-2.20	1.0	-0.54 [-1.08, -0.00]
			Placebo	31	31 (100.0)	-1.40 (1.71)	-5.6	-1.04	1.1	
		Week 3	CR845	29	23 (79.3)	-2.87 (2.35)	-7.1	-3.43	1.0	-0.55 [-1.10, 0.01]
			Placebo	31	29 (93.5)	-1.66 (2.12)	-7.1	-1.33	0.9	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISHG: Change from baseline in weekly WI-NRS by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 4	CR845	29	22 (75.9)	-3.12 (2.39)	-7.6	-3.14	1.0	-0.56 [-1.12, 0.00]
			Placebo	31	30 (96.8)	-1.88 (2.09)	-8.0	-1.59	1.3	
		Week 5	CR845	29	22 (75.9)	-2.83 (2.74)	-8.0	-3.17	2.9	-0.21 [-0.77, 0.35]
			Placebo	31	29 (93.5)	-2.31 (2.23)	-8.1	-2.25	1.1	
		Week 6	CR845	29	23 (79.3)	-2.71 (2.72)	-7.8	-2.45	3.8	-0.13 [-0.67, 0.42]
			Placebo	31	30 (96.8)	-2.38 (2.45)	-8.1	-1.91	1.6	
		Week 7	CR845	29	23 (79.3)	-2.92 (2.43)	-7.4	-2.02	1.0	-0.40 [-0.95, 0.16]
			Placebo	31	29 (93.5)	-1.97 (2.33)	-7.0	-2.08	1.4	
		Week 8	CR845	29	23 (79.3)	-3.09 (2.59)	-8.3	-2.48	1.1	-0.29 [-0.85, 0.26]
			Placebo	31	27 (87.1)	-2.37 (2.29)	-6.1	-2.50	1.5	
		Week 9	CR845	29	21 (72.4)	-3.35 (2.74)	-8.3	-3.43	1.4	-0.40 [-0.97, 0.17]
			Placebo	31	28 (90.3)	-2.33 (2.45)	-6.4	-2.63	1.5	
		Week 10	CR845	29	22 (75.9)	-3.25 (2.79)	-8.8	-3.52	1.3	-0.40 [-0.97, 0.16]
			Placebo	31	27 (87.1)	-2.18 (2.56)	-6.7	-2.50	1.7	
		Week 11	CR845	29	22 (75.9)	-3.24 (2.84)	-8.8	-3.59	2.1	-0.27 [-0.83, 0.30]
			Placebo	31	27 (87.1)	-2.51 (2.62)	-6.9	-2.96	1.7	
		Week 12	CR845	29	20 (69.0)	-3.46 (2.87)	-8.8	-3.28	2.0	-0.47 [-1.08, 0.13]
			Placebo	31	24 (77.4)	-2.16 (2.62)	-7.0	-2.53	2.7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISHH: Change from baseline in weekly WI-NRS by dialysis method
ITT

H: Dialysis method	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Hemodialysis (HD)	Weekly WI-NRS	Baseline	CR845	222	222 (100.0)	7.27 (1.37)	4.5	7.13	10.0	
			Placebo	199	199 (100.0)	7.11 (1.39)	4.8	7.00	10.0	
		Week 1	CR845	222	216 (97.3)	6.48 (1.80)	0.9	6.43	10.0	
			Placebo	199	195 (98.0)	6.71 (1.58)	2.0	6.71	10.0	
		Week 2	CR845	222	211 (95.0)	5.71 (2.29)	0.0	5.86	10.0	
			Placebo	199	195 (98.0)	6.20 (1.90)	0.8	6.29	10.0	
		Week 3	CR845	222	208 (93.7)	5.38 (2.46)	0.0	5.43	10.0	
			Placebo	199	191 (96.0)	5.92 (2.01)	1.0	6.00	10.0	
		Week 4	CR845	222	202 (91.0)	4.96 (2.48)	0.0	5.14	10.0	
			Placebo	199	189 (95.0)	5.70 (2.18)	0.1	5.71	10.0	
		Week 5	CR845	222	204 (91.9)	4.80 (2.59)	0.0	5.00	10.0	
			Placebo	199	190 (95.5)	5.37 (2.29)	0.0	5.50	10.0	
		Week 6	CR845	222	199 (89.6)	4.60 (2.59)	0.0	4.71	10.0	
			Placebo	199	188 (94.5)	5.33 (2.40)	0.0	5.57	10.0	
		Week 7	CR845	222	200 (90.1)	4.52 (2.65)	0.0	4.86	10.0	
			Placebo	199	188 (94.5)	5.24 (2.33)	0.0	5.36	10.0	
		Week 8	CR845	222	196 (88.3)	4.47 (2.61)	0.0	4.43	10.0	
			Placebo	199	185 (93.0)	5.13 (2.37)	0.0	5.43	10.0	
		Week 9	CR845	222	195 (87.8)	4.45 (2.66)	0.0	4.43	10.0	
			Placebo	199	187 (94.0)	4.93 (2.39)	0.0	4.86	10.0	
		Week 10	CR845	222	194 (87.4)	4.40 (2.69)	0.0	4.29	10.0	
			Placebo	199	185 (93.0)	4.93 (2.40)	0.0	5.00	10.0	
		Week 11	CR845	222	189 (85.1)	4.28 (2.71)	0.0	4.14	10.0	
			Placebo	199	186 (93.5)	4.88 (2.45)	0.0	4.79	10.0	
		Week 12	CR845	222	179 (80.6)	4.20 (2.71)	0.0	3.86	10.0	
			Placebo	199	175 (87.9)	4.73 (2.48)	0.0	4.57	10.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	222	216 (97.3)	-0.79 (1.30)	-5.6	-0.61	2.4	-0.29 [-0.49, -0.10]
			Placebo	199	195 (98.0)	-0.42 (1.21)	-4.8	-0.38	2.9	
		Week 2	CR845	222	211 (95.0)	-1.55 (1.94)	-10.0	-1.09	2.0	-0.35 [-0.54, -0.15]
			Placebo	199	195 (98.0)	-0.93 (1.58)	-6.5	-0.79	3.5	
		Week 3	CR845	222	208 (93.7)	-1.88 (2.11)	-10.0	-1.43	2.1	-0.35 [-0.55, -0.15]
			Placebo	199	191 (96.0)	-1.21 (1.74)	-6.1	-1.07	3.3	
		Week 4	CR845	222	202 (91.0)	-2.30 (2.20)	-10.0	-1.99	1.5	-0.42 [-0.62, -0.22]
			Placebo	199	189 (95.0)	-1.42 (1.99)	-7.2	-1.14	3.5	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISHH: Change from baseline in weekly WI-NRS by dialysis method
ITT

H: Dialysis method	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 5	CR845	222	204 (91.9)	-2.45 (2.42)	-10.0	-2.00	2.9	-0.31 [-0.51, -0.12]
			Placebo	199	190 (95.5)	-1.74 (2.10)	-7.8	-1.56	3.5	
		Week 6	CR845	222	199 (89.6)	-2.65 (2.49)	-10.0	-2.05	3.8	-0.37 [-0.57, -0.17]
			Placebo	199	188 (94.5)	-1.79 (2.19)	-7.1	-1.60	3.1	
		Week 7	CR845	222	200 (90.1)	-2.73 (2.55)	-10.0	-2.19	1.6	-0.36 [-0.56, -0.16]
			Placebo	199	188 (94.5)	-1.87 (2.18)	-7.2	-1.57	3.3	
		Week 8	CR845	222	196 (88.3)	-2.78 (2.42)	-10.0	-2.56	1.9	-0.34 [-0.54, -0.14]
			Placebo	199	185 (93.0)	-1.98 (2.25)	-7.6	-1.54	3.5	
		Week 9	CR845	222	195 (87.8)	-2.81 (2.49)	-10.0	-2.57	1.6	-0.26 [-0.46, -0.06]
			Placebo	199	187 (94.0)	-2.19 (2.24)	-7.9	-1.93	3.5	
		Week 10	CR845	222	194 (87.4)	-2.85 (2.51)	-10.0	-2.72	3.0	-0.29 [-0.49, -0.08]
			Placebo	199	185 (93.0)	-2.17 (2.24)	-8.0	-2.00	3.5	
		Week 11	CR845	222	189 (85.1)	-2.98 (2.54)	-10.0	-2.75	2.4	-0.31 [-0.52, -0.11]
			Placebo	199	186 (93.5)	-2.22 (2.28)	-7.9	-2.10	3.6	
		Week 12	CR845	222	179 (80.6)	-3.06 (2.58)	-10.0	-2.88	3.0	-0.29 [-0.50, -0.08]
			Placebo	199	175 (87.9)	-2.35 (2.30)	-8.6	-2.17	3.6	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISHH: Change from baseline in weekly WI-NRS by dialysis method
ITT

H: Dialysis method	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Hemodiafiltration (HDF)	Weekly WI-NRS	Baseline	CR845	15	15 (100.0)	7.21 (1.15)	5.1	7.25	9.7	
			Placebo	37	37 (100.0)	7.16 (1.22)	5.3	7.00	10.0	
		Week 1	CR845	15	15 (100.0)	6.49 (1.97)	2.7	6.57	10.0	
			Placebo	37	37 (100.0)	6.17 (1.89)	0.0	6.29	9.9	
		Week 2	CR845	15	14 (93.3)	5.94 (2.07)	2.7	5.36	10.0	
			Placebo	37	37 (100.0)	5.52 (2.31)	0.0	5.57	9.9	
		Week 3	CR845	15	13 (86.7)	4.91 (2.78)	1.4	3.86	10.0	
			Placebo	37	36 (97.3)	5.08 (2.49)	0.0	5.00	10.0	
		Week 4	CR845	15	12 (80.0)	5.11 (2.87)	1.3	4.43	10.0	
			Placebo	37	36 (97.3)	4.78 (2.40)	0.0	4.64	9.0	
		Week 5	CR845	15	12 (80.0)	4.90 (2.31)	1.3	4.79	9.0	
			Placebo	37	36 (97.3)	4.64 (2.45)	0.0	5.00	9.7	
		Week 6	CR845	15	13 (86.7)	4.95 (2.53)	1.3	5.43	9.0	
			Placebo	37	36 (97.3)	4.54 (2.58)	0.0	4.29	9.3	
		Week 7	CR845	15	13 (86.7)	4.67 (2.57)	1.0	5.57	9.0	
			Placebo	37	36 (97.3)	4.84 (2.51)	0.0	4.66	10.0	
		Week 8	CR845	15	13 (86.7)	4.66 (2.71)	0.6	4.43	9.0	
			Placebo	37	36 (97.3)	4.69 (2.36)	0.0	4.50	9.7	
		Week 9	CR845	15	12 (80.0)	4.55 (2.69)	0.9	4.50	9.0	
			Placebo	37	35 (94.6)	4.74 (2.50)	0.0	5.00	9.4	
		Week 10	CR845	15	13 (86.7)	4.13 (2.95)	0.0	3.57	9.1	
			Placebo	37	35 (94.6)	4.64 (2.59)	0.0	4.43	9.9	
		Week 11	CR845	15	13 (86.7)	3.89 (3.09)	0.0	3.29	9.7	
			Placebo	37	33 (89.2)	4.57 (2.54)	0.0	4.57	9.3	
		Week 12	CR845	15	12 (80.0)	3.39 (2.71)	0.0	2.49	9.0	
			Placebo	37	32 (86.5)	4.52 (2.56)	0.0	4.50	9.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	15	15 (100.0)	-0.72 (1.43)	-3.8	-0.77	1.3	0.19 [-0.41, 0.79]
			Placebo	37	37 (100.0)	-1.00 (1.44)	-6.3	-0.64	0.7	
		Week 2	CR845	15	14 (93.3)	-1.24 (1.68)	-4.6	-1.21	1.3	0.23 [-0.39, 0.85]
			Placebo	37	37 (100.0)	-1.64 (1.80)	-6.3	-1.38	1.5	
		Week 3	CR845	15	13 (86.7)	-2.27 (2.72)	-6.2	-2.77	1.1	-0.08 [-0.71, 0.56]
			Placebo	37	36 (97.3)	-2.09 (2.02)	-7.1	-1.75	1.4	
		Week 4	CR845	15	12 (80.0)	-2.03 (2.82)	-7.5	-2.01	1.3	0.14 [-0.52, 0.79]
			Placebo	37	36 (97.3)	-2.35 (2.11)	-8.0	-1.83	1.4	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISHH: Change from baseline in weekly WI-NRS by dialysis method
ITT

H: Dialysis method	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 5	CR845	15	12 (80.0)	-2.24 (2.38)	-7.5	-2.26	1.3	0.09 [-0.56, 0.75]
			Placebo	37	36 (97.3)	-2.45 (2.26)	-8.1	-2.08	1.5	
		Week 6	CR845	15	13 (86.7)	-2.24 (2.46)	-5.8	-2.57	1.3	0.18 [-0.46, 0.81]
			Placebo	37	36 (97.3)	-2.66 (2.31)	-8.1	-2.46	1.4	
		Week 7	CR845	15	13 (86.7)	-2.52 (2.63)	-7.0	-1.71	1.3	-0.08 [-0.71, 0.56]
			Placebo	37	36 (97.3)	-2.33 (2.30)	-7.0	-2.12	1.4	
		Week 8	CR845	15	13 (86.7)	-2.53 (2.82)	-7.5	-2.91	1.8	-0.02 [-0.65, 0.62]
			Placebo	37	36 (97.3)	-2.49 (2.18)	-6.3	-2.50	1.8	
		Week 9	CR845	15	12 (80.0)	-2.59 (2.74)	-7.9	-2.84	2.0	-0.05 [-0.71, 0.61]
			Placebo	37	35 (94.6)	-2.47 (2.34)	-6.9	-2.50	1.9	
		Week 10	CR845	15	13 (86.7)	-3.06 (3.13)	-8.8	-3.67	2.4	-0.19 [-0.82, 0.45]
			Placebo	37	35 (94.6)	-2.57 (2.42)	-6.7	-2.73	3.1	
		Week 11	CR845	15	13 (86.7)	-3.30 (3.16)	-8.8	-3.81	3.0	-0.27 [-0.91, 0.38]
			Placebo	37	33 (89.2)	-2.57 (2.55)	-7.0	-2.59	2.9	
		Week 12	CR845	15	12 (80.0)	-3.83 (2.72)	-8.8	-4.45	1.3	-0.49 [-1.17, 0.18]
			Placebo	37	32 (86.5)	-2.56 (2.52)	-7.0	-2.63	2.7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISCA: Change from baseline in weekly WI-NRS - MMRM results by age
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
A: Age									0.159
< 65 years	Week 1	CR845	147	144 (98.0)	-0.58 (0.12)	(-0.82, -0.35)	-0.10 (0.14)	(-0.37, 0.17)	0.465
		Placebo	153	150 (98.0)	-0.48 (0.12)	(-0.72, -0.25)			
>= 65 years	Week 1	CR845	90	87 (96.7)	-0.93 (0.17)	(-1.27, -0.59)	-0.49 (0.22)	(-0.92, -0.06)	0.025 *
		Placebo	83	82 (98.8)	-0.44 (0.18)	(-0.79, -0.09)			
< 65 years	Week 2	CR845	147	138 (93.9)	-1.34 (0.16)	(-1.65, -1.04)	-0.32 (0.20)	(-0.71, 0.06)	0.099
		Placebo	153	151 (98.7)	-1.02 (0.15)	(-1.32, -0.72)			
>= 65 years	Week 2	CR845	90	87 (96.7)	-1.64 (0.22)	(-2.08, -1.20)	-0.67 (0.30)	(-1.26, -0.08)	0.026 *
		Placebo	83	81 (97.6)	-0.97 (0.23)	(-1.42, -0.52)			
< 65 years	Week 3	CR845	147	138 (93.9)	-1.78 (0.17)	(-2.13, -1.44)	-0.42 (0.22)	(-0.85, 0.02)	0.064
		Placebo	153	146 (95.4)	-1.37 (0.17)	(-1.71, -1.03)			
>= 65 years	Week 3	CR845	90	83 (92.2)	-1.93 (0.24)	(-2.40, -1.45)	-0.78 (0.32)	(-1.42, -0.14)	0.017 *
		Placebo	83	81 (97.6)	-1.15 (0.25)	(-1.64, -0.66)			
< 65 years	Week 4	CR845	147	134 (91.2)	-2.23 (0.19)	(-2.60, -1.85)	-0.63 (0.25)	(-1.11, -0.14)	0.011 *
		Placebo	153	146 (95.4)	-1.60 (0.19)	(-1.97, -1.24)			
>= 65 years	Week 4	CR845	90	80 (88.9)	-2.18 (0.25)	(-2.67, -1.69)	-0.81 (0.33)	(-1.47, -0.15)	0.017 *
		Placebo	83	79 (95.2)	-1.37 (0.25)	(-1.87, -0.87)			
< 65 years	Week 5	CR845	147	136 (92.5)	-2.36 (0.20)	(-2.76, -1.96)	-0.59 (0.26)	(-1.11, -0.07)	0.027 *
		Placebo	153	146 (95.4)	-1.77 (0.20)	(-2.16, -1.39)			
>= 65 years	Week 5	CR845	90	80 (88.9)	-2.44 (0.26)	(-2.95, -1.92)	-0.65 (0.35)	(-1.35, 0.04)	0.066
		Placebo	83	80 (96.4)	-1.79 (0.26)	(-2.31, -1.26)			
< 65 years	Week 6	CR845	147	132 (89.8)	-2.54 (0.21)	(-2.95, -2.12)	-0.68 (0.28)	(-1.23, -0.14)	0.014 *
		Placebo	153	146 (95.4)	-1.86 (0.21)	(-2.26, -1.45)			
>= 65 years	Week 6	CR845	90	80 (88.9)	-2.64 (0.26)	(-3.16, -2.12)	-0.73 (0.36)	(-1.44, -0.02)	0.044 *
		Placebo	83	78 (94.0)	-1.91 (0.27)	(-2.44, -1.38)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISCA: Change from baseline in weekly WI-NRS - MMRM results by age
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
< 65 years	Week 7	CR845	147	133 (90.5)	-2.59 (0.21)	(-3.01, -2.18)	-0.64 (0.28)	(-1.18, -0.09)	0.023 *
		Placebo	153	145 (94.8)	-1.96 (0.21)	(-2.36, -1.55)			
>= 65 years	Week 7	CR845	90	80 (88.9)	-2.76 (0.27)	(-3.28, -2.23)	-1.00 (0.36)	(-1.71, -0.29)	0.006 *
		Placebo	83	79 (95.2)	-1.76 (0.27)	(-2.29, -1.22)			
< 65 years	Week 8	CR845	147	131 (89.1)	-2.72 (0.21)	(-3.13, -2.30)	-0.59 (0.28)	(-1.14, -0.05)	0.033 *
		Placebo	153	144 (94.1)	-2.12 (0.21)	(-2.53, -1.72)			
>= 65 years	Week 8	CR845	90	78 (86.7)	-2.74 (0.27)	(-3.27, -2.22)	-0.82 (0.36)	(-1.53, -0.11)	0.023 *
		Placebo	83	77 (92.8)	-1.92 (0.27)	(-2.45, -1.39)			
< 65 years	Week 9	CR845	147	131 (89.1)	-2.77 (0.21)	(-3.19, -2.35)	-0.51 (0.28)	(-1.06, 0.04)	0.068
		Placebo	153	144 (94.1)	-2.26 (0.21)	(-2.67, -1.85)			
>= 65 years	Week 9	CR845	90	76 (84.4)	-2.68 (0.28)	(-3.22, -2.13)	-0.58 (0.37)	(-1.31, 0.16)	0.123
		Placebo	83	78 (94.0)	-2.10 (0.28)	(-2.65, -1.55)			
< 65 years	Week 10	CR845	147	133 (90.5)	-2.81 (0.22)	(-3.24, -2.39)	-0.60 (0.28)	(-1.16, -0.04)	0.036 *
		Placebo	153	143 (93.5)	-2.21 (0.21)	(-2.63, -1.80)			
>= 65 years	Week 10	CR845	90	74 (82.2)	-2.79 (0.28)	(-3.34, -2.24)	-0.53 (0.38)	(-1.27, 0.22)	0.166
		Placebo	83	77 (92.8)	-2.27 (0.28)	(-2.82, -1.71)			
< 65 years	Week 11	CR845	147	129 (87.8)	-2.95 (0.22)	(-3.38, -2.52)	-0.64 (0.29)	(-1.21, -0.07)	0.027 *
		Placebo	153	144 (94.1)	-2.31 (0.21)	(-2.73, -1.89)			
>= 65 years	Week 11	CR845	90	73 (81.1)	-2.83 (0.29)	(-3.39, -2.26)	-0.68 (0.39)	(-1.45, 0.09)	0.081
		Placebo	83	75 (90.4)	-2.15 (0.29)	(-2.71, -1.58)			
< 65 years	Week 12	CR845	147	122 (83.0)	-3.05 (0.22)	(-3.49, -2.61)	-0.66 (0.29)	(-1.24, -0.08)	0.025 *
		Placebo	153	137 (89.5)	-2.39 (0.22)	(-2.82, -1.97)			
>= 65 years	Week 12	CR845	90	69 (76.7)	-2.82 (0.29)	(-3.38, -2.25)	-0.47 (0.39)	(-1.25, 0.30)	0.228
		Placebo	83	70 (84.3)	-2.34 (0.29)	(-2.91, -1.77)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISCB: Change from baseline in weekly WI-NRS - MMRM results by sex
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
B: Sex									0.014 i
Male	Week 1	CR845	137	132 (96.4)	-0.56 (0.13)	(-0.82, -0.30)	-0.05 (0.15)	(-0.34, 0.24)	0.736
		Placebo	139	138 (99.3)	-0.51 (0.13)	(-0.76, -0.26)			
Female	Week 1	CR845	100	99 (99.0)	-0.92 (0.15)	(-1.22, -0.62)	-0.53 (0.19)	(-0.91, -0.15)	0.007 *
		Placebo	97	94 (96.9)	-0.39 (0.16)	(-0.71, -0.07)			
Male	Week 2	CR845	137	129 (94.2)	-1.29 (0.17)	(-1.62, -0.96)	-0.23 (0.21)	(-0.64, 0.18)	0.263
		Placebo	139	138 (99.3)	-1.05 (0.16)	(-1.37, -0.73)			
Female	Week 2	CR845	100	96 (96.0)	-1.68 (0.20)	(-2.08, -1.29)	-0.77 (0.27)	(-1.30, -0.24)	0.004 *
		Placebo	97	94 (96.9)	-0.91 (0.21)	(-1.33, -0.50)			
Male	Week 3	CR845	137	128 (93.4)	-1.55 (0.18)	(-1.91, -1.19)	-0.28 (0.23)	(-0.73, 0.18)	0.229
		Placebo	139	134 (96.4)	-1.27 (0.18)	(-1.62, -0.93)			
Female	Week 3	CR845	100	93 (93.0)	-2.22 (0.22)	(-2.66, -1.78)	-0.91 (0.30)	(-1.51, -0.32)	0.003 *
		Placebo	97	93 (95.9)	-1.31 (0.23)	(-1.76, -0.86)			
Male	Week 4	CR845	137	125 (91.2)	-1.88 (0.19)	(-2.26, -1.51)	-0.33 (0.24)	(-0.81, 0.15)	0.182
		Placebo	139	134 (96.4)	-1.56 (0.19)	(-1.92, -1.19)			
Female	Week 4	CR845	100	89 (89.0)	-2.66 (0.24)	(-3.13, -2.18)	-1.20 (0.33)	(-1.85, -0.56)	<0.001 *
		Placebo	97	91 (93.8)	-1.45 (0.25)	(-1.94, -0.97)			
Male	Week 5	CR845	137	126 (92.0)	-1.97 (0.20)	(-2.37, -1.57)	-0.19 (0.26)	(-0.71, 0.33)	0.471
		Placebo	139	133 (95.7)	-1.78 (0.20)	(-2.17, -1.39)			
Female	Week 5	CR845	100	90 (90.0)	-2.98 (0.25)	(-3.48, -2.48)	-1.21 (0.34)	(-1.89, -0.54)	<0.001 *
		Placebo	97	93 (95.9)	-1.77 (0.26)	(-2.27, -1.26)			
Male	Week 6	CR845	137	125 (91.2)	-2.02 (0.20)	(-2.42, -1.62)	-0.23 (0.26)	(-0.75, 0.29)	0.393
		Placebo	139	131 (94.2)	-1.79 (0.20)	(-2.19, -1.40)			
Female	Week 6	CR845	100	87 (87.0)	-3.35 (0.27)	(-3.87, -2.82)	-1.37 (0.36)	(-2.08, -0.66)	<0.001 *
		Placebo	97	93 (95.9)	-1.98 (0.27)	(-2.51, -1.45)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISCB: Change from baseline in weekly WI-NRS - MMRM results by sex
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Male	Week 7	CR845	137	125 (91.2)	-2.05 (0.21)	(-2.46, -1.65)	-0.26 (0.27)	(-0.79, 0.26)	0.325
		Placebo	139	131 (94.2)	-1.79 (0.20)	(-2.19, -1.39)			
Female	Week 7	CR845	100	88 (88.0)	-3.49 (0.26)	(-4.01, -2.97)	-1.48 (0.36)	(-2.19, -0.77)	<0.001 *
		Placebo	97	93 (95.9)	-2.01 (0.27)	(-2.54, -1.49)			
Male	Week 8	CR845	137	123 (89.8)	-2.08 (0.21)	(-2.48, -1.67)	-0.12 (0.27)	(-0.65, 0.41)	0.659
		Placebo	139	131 (94.2)	-1.96 (0.20)	(-2.35, -1.56)			
Female	Week 8	CR845	100	86 (86.0)	-3.64 (0.26)	(-4.16, -3.13)	-1.47 (0.35)	(-2.17, -0.78)	<0.001 *
		Placebo	97	90 (92.8)	-2.17 (0.26)	(-2.69, -1.65)			
Male	Week 9	CR845	137	120 (87.6)	-2.13 (0.21)	(-2.54, -1.73)	0.02 (0.27)	(-0.50, 0.55)	0.928
		Placebo	139	131 (94.2)	-2.16 (0.20)	(-2.55, -1.76)			
Female	Week 9	CR845	100	87 (87.0)	-3.58 (0.27)	(-4.12, -3.04)	-1.31 (0.37)	(-2.04, -0.58)	<0.001 *
		Placebo	97	91 (93.8)	-2.27 (0.27)	(-2.81, -1.72)			
Male	Week 10	CR845	137	120 (87.6)	-2.23 (0.21)	(-2.64, -1.81)	0.03 (0.27)	(-0.51, 0.56)	0.925
		Placebo	139	130 (93.5)	-2.25 (0.20)	(-2.66, -1.85)			
Female	Week 10	CR845	100	87 (87.0)	-3.61 (0.28)	(-4.15, -3.07)	-1.41 (0.37)	(-2.14, -0.67)	<0.001 *
		Placebo	97	90 (92.8)	-2.20 (0.28)	(-2.75, -1.66)			
Male	Week 11	CR845	137	117 (85.4)	-2.28 (0.22)	(-2.71, -1.86)	-0.01 (0.28)	(-0.56, 0.55)	0.981
		Placebo	139	129 (92.8)	-2.28 (0.21)	(-2.69, -1.86)			
Female	Week 11	CR845	100	85 (85.0)	-3.77 (0.28)	(-4.31, -3.22)	-1.55 (0.37)	(-2.29, -0.81)	<0.001 *
		Placebo	97	90 (92.8)	-2.21 (0.28)	(-2.76, -1.67)			
Male	Week 12	CR845	137	110 (80.3)	-2.32 (0.22)	(-2.75, -1.90)	0.02 (0.28)	(-0.53, 0.58)	0.931
		Placebo	139	125 (89.9)	-2.35 (0.21)	(-2.76, -1.93)			
Female	Week 12	CR845	100	81 (81.0)	-3.86 (0.28)	(-4.42, -3.31)	-1.46 (0.38)	(-2.21, -0.71)	<0.001 *
		Placebo	97	82 (84.5)	-2.40 (0.28)	(-2.96, -1.85)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISCC: Change from baseline in weekly WI-NRS - MMRM results by race
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
C: Race									1.000
Black/African American	Week 1	CR845	53	52 (98.1)	-0.74 (0.19)	(-1.11, -0.37)	-0.19 (0.27)	(-0.72, 0.34)	0.472
		Placebo	38	38 (100.0)	-0.55 (0.21)	(-0.97, -0.14)			
White	Week 1	CR845	164	159 (97.0)	-0.71 (0.12)	(-0.96, -0.47)	-0.26 (0.14)	(-0.53, 0.01)	0.062
		Placebo	169	166 (98.2)	-0.45 (0.12)	(-0.70, -0.21)			
Other	Week 1	CR845	20	20 (100.0)	-0.59 (0.44)	(-1.47, 0.28)	-0.35 (0.44)	(-1.24, 0.54)	0.430
		Placebo	29	28 (96.6)	-0.24 (0.39)	(-1.03, 0.55)			
Black/African American	Week 2	CR845	53	49 (92.5)	-1.06 (0.26)	(-1.58, -0.55)	0.08 (0.38)	(-0.69, 0.84)	0.841
		Placebo	38	37 (97.4)	-1.14 (0.30)	(-1.73, -0.55)			
White	Week 2	CR845	164	158 (96.3)	-1.57 (0.16)	(-1.88, -1.26)	-0.57 (0.19)	(-0.95, -0.18)	0.004 *
		Placebo	169	167 (98.8)	-1.00 (0.16)	(-1.31, -0.69)			
Other	Week 2	CR845	20	18 (90.0)	-1.47 (0.51)	(-2.50, -0.45)	-0.83 (0.56)	(-1.95, 0.30)	0.147
		Placebo	29	28 (96.6)	-0.65 (0.45)	(-1.55, 0.25)			
Black/African American	Week 3	CR845	53	49 (92.5)	-1.51 (0.29)	(-2.09, -0.94)	-0.12 (0.43)	(-0.98, 0.74)	0.782
		Placebo	38	37 (97.4)	-1.39 (0.33)	(-2.05, -0.73)			
White	Week 3	CR845	164	155 (94.5)	-1.95 (0.17)	(-2.29, -1.61)	-0.67 (0.22)	(-1.11, -0.24)	0.002 *
		Placebo	169	163 (96.4)	-1.28 (0.17)	(-1.61, -0.94)			
Other	Week 3	CR845	20	17 (85.0)	-1.64 (0.51)	(-2.66, -0.61)	-0.59 (0.56)	(-1.72, 0.54)	0.294
		Placebo	29	27 (93.1)	-1.04 (0.45)	(-1.94, -0.15)			
Black/African American	Week 4	CR845	53	47 (88.7)	-1.97 (0.31)	(-2.58, -1.35)	-0.30 (0.47)	(-1.23, 0.62)	0.516
		Placebo	38	35 (92.1)	-1.66 (0.36)	(-2.37, -0.95)			
White	Week 4	CR845	164	150 (91.5)	-2.29 (0.19)	(-2.65, -1.92)	-0.77 (0.24)	(-1.23, -0.30)	0.001 *
		Placebo	169	162 (95.9)	-1.52 (0.18)	(-1.88, -1.16)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISCC: Change from baseline in weekly WI-NRS - MMRM results by race
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Other	Week 4	CR845	20	17 (85.0)	-2.17 (0.51)	(-3.20, -1.14)	-1.02 (0.56)	(-2.14, 0.10)	0.074
		Placebo	29	28 (96.6)	-1.15 (0.45)	(-2.04, -0.25)			
Black/African American	Week 5	CR845	53	49 (92.5)	-2.00 (0.33)	(-2.66, -1.35)	-0.14 (0.49)	(-1.12, 0.85)	0.781
		Placebo	38	36 (94.7)	-1.87 (0.38)	(-2.62, -1.11)			
White	Week 5	CR845	164	151 (92.1)	-2.51 (0.20)	(-2.90, -2.12)	-0.73 (0.26)	(-1.23, -0.22)	0.005 *
		Placebo	169	162 (95.9)	-1.78 (0.20)	(-2.17, -1.40)			
Other	Week 5	CR845	20	16 (80.0)	-2.39 (0.51)	(-3.41, -1.36)	-0.94 (0.55)	(-2.05, 0.18)	0.096
		Placebo	29	28 (96.6)	-1.45 (0.44)	(-2.33, -0.56)			
Black/African American	Week 6	CR845	53	45 (84.9)	-2.26 (0.34)	(-2.93, -1.58)	-0.38 (0.51)	(-1.38, 0.63)	0.459
		Placebo	38	37 (97.4)	-1.88 (0.39)	(-2.65, -1.12)			
White	Week 6	CR845	164	150 (91.5)	-2.65 (0.20)	(-3.05, -2.25)	-0.78 (0.27)	(-1.30, -0.25)	0.004 *
		Placebo	169	160 (94.7)	-1.87 (0.20)	(-2.27, -1.48)			
Other	Week 6	CR845	20	17 (85.0)	-2.76 (0.57)	(-3.89, -1.62)	-1.07 (0.64)	(-2.35, 0.21)	0.100
		Placebo	29	27 (93.1)	-1.69 (0.48)	(-2.66, -0.72)			
Black/African American	Week 7	CR845	53	46 (86.8)	-2.57 (0.35)	(-3.28, -1.87)	-0.60 (0.53)	(-1.65, 0.45)	0.260
		Placebo	38	36 (94.7)	-1.97 (0.40)	(-2.77, -1.18)			
White	Week 7	CR845	164	150 (91.5)	-2.66 (0.20)	(-3.06, -2.26)	-0.78 (0.26)	(-1.30, -0.26)	0.003 *
		Placebo	169	161 (95.3)	-1.88 (0.20)	(-2.27, -1.49)			
Other	Week 7	CR845	20	17 (85.0)	-2.85 (0.59)	(-4.03, -1.66)	-1.24 (0.67)	(-2.59, 0.11)	0.072
		Placebo	29	27 (93.1)	-1.61 (0.50)	(-2.62, -0.61)			
Black/African American	Week 8	CR845	53	45 (84.9)	-2.70 (0.37)	(-3.44, -1.97)	-0.48 (0.55)	(-1.58, 0.62)	0.391
		Placebo	38	36 (94.7)	-2.23 (0.42)	(-3.06, -1.39)			
White	Week 8	CR845	164	147 (89.6)	-2.71 (0.20)	(-3.10, -2.31)	-0.71 (0.26)	(-1.23, -0.19)	0.007 *
		Placebo	169	158 (93.5)	-1.99 (0.20)	(-2.38, -1.61)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISCC: Change from baseline in weekly WI-NRS - MMRM results by race
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Other	Week 8	CR845	20	17 (85.0)	-2.92 (0.56)	(-4.04, -1.81)	-0.94 (0.62)	(-2.19, 0.32)	0.139
		Placebo	29	27 (93.1)	-1.99 (0.47)	(-2.94, -1.04)			
Black/African American	Week 9	CR845	53	45 (84.9)	-2.67 (0.37)	(-3.40, -1.94)	-0.39 (0.55)	(-1.48, 0.69)	0.472
		Placebo	38	37 (97.4)	-2.28 (0.41)	(-3.10, -1.45)			
White	Week 9	CR845	164	147 (89.6)	-2.75 (0.21)	(-3.15, -2.34)	-0.61 (0.27)	(-1.14, -0.08)	0.023 *
		Placebo	169	159 (94.1)	-2.13 (0.20)	(-2.53, -1.73)			
Other	Week 9	CR845	20	15 (75.0)	-2.70 (0.55)	(-3.80, -1.60)	-0.38 (0.61)	(-1.61, 0.84)	0.530
		Placebo	29	26 (89.7)	-2.32 (0.46)	(-3.24, -1.39)			
Black/African American	Week 10	CR845	53	45 (84.9)	-2.92 (0.36)	(-3.63, -2.22)	-0.63 (0.53)	(-1.68, 0.43)	0.240
		Placebo	38	37 (97.4)	-2.30 (0.40)	(-3.09, -1.50)			
White	Week 10	CR845	164	146 (89.0)	-2.74 (0.21)	(-3.16, -2.33)	-0.55 (0.28)	(-1.09, -0.00)	0.049 *
		Placebo	169	158 (93.5)	-2.20 (0.21)	(-2.60, -1.79)			
Other	Week 10	CR845	20	16 (80.0)	-2.79 (0.58)	(-3.96, -1.62)	-0.61 (0.66)	(-1.93, 0.72)	0.362
		Placebo	29	25 (86.2)	-2.18 (0.49)	(-3.17, -1.20)			
Black/African American	Week 11	CR845	53	43 (81.1)	-2.99 (0.37)	(-3.72, -2.26)	-0.70 (0.55)	(-1.79, 0.38)	0.201
		Placebo	38	36 (94.7)	-2.28 (0.41)	(-3.10, -1.46)			
White	Week 11	CR845	164	143 (87.2)	-2.88 (0.21)	(-3.30, -2.46)	-0.70 (0.28)	(-1.25, -0.15)	0.013 *
		Placebo	169	158 (93.5)	-2.18 (0.21)	(-2.59, -1.77)			
Other	Week 11	CR845	20	16 (80.0)	-2.92 (0.60)	(-4.12, -1.72)	-0.44 (0.68)	(-1.82, 0.94)	0.521
		Placebo	29	25 (86.2)	-2.48 (0.50)	(-3.49, -1.47)			
Black/African American	Week 12	CR845	53	39 (73.6)	-3.22 (0.37)	(-3.96, -2.49)	-0.69 (0.55)	(-1.79, 0.40)	0.211
		Placebo	38	35 (92.1)	-2.53 (0.42)	(-3.35, -1.70)			
White	Week 12	CR845	164	136 (82.9)	-2.90 (0.22)	(-3.33, -2.48)	-0.64 (0.28)	(-1.20, -0.08)	0.024 *
		Placebo	169	150 (88.8)	-2.26 (0.21)	(-2.68, -1.85)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISCC: Change from baseline in weekly WI-NRS - MMRM results by race
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Other	Week 12	CR845	20	16 (80.0)	-2.72 (0.57)	(-3.87, -1.57)	-0.05 (0.64)	(-1.35, 1.25)	0.936
		Placebo	29	22 (75.9)	-2.67 (0.48)	(-3.64, -1.69)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISCD: Change from baseline in weekly WI-NRS - MMRM results by baseline WI-NRS
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
D: Baseline worst itching NRS score (WI-NRS)									0.039 i
>= 4 to < 7	Week 1	CR845	102	100 (98.0)	-0.58 (0.17)	(-0.91, -0.25)	-0.48 (0.18)	(-0.84, -0.12)	0.010 *
		Placebo	113	111 (98.2)	-0.10 (0.17)	(-0.43, 0.23)			
>= 7	Week 1	CR845	135	131 (97.0)	-0.78 (0.12)	(-1.02, -0.55)	-0.07 (0.15)	(-0.37, 0.24)	0.666
		Placebo	123	121 (98.4)	-0.72 (0.13)	(-0.97, -0.47)			
>= 4 to < 7	Week 2	CR845	102	99 (97.1)	-1.27 (0.20)	(-1.66, -0.87)	-0.60 (0.24)	(-1.07, -0.14)	0.012 *
		Placebo	113	110 (97.3)	-0.66 (0.19)	(-1.05, -0.28)			
>= 7	Week 2	CR845	135	126 (93.3)	-1.57 (0.17)	(-1.91, -1.23)	-0.35 (0.23)	(-0.80, 0.11)	0.137
		Placebo	123	122 (99.2)	-1.23 (0.18)	(-1.57, -0.88)			
>= 4 to < 7	Week 3	CR845	102	97 (95.1)	-1.63 (0.21)	(-2.05, -1.21)	-0.73 (0.25)	(-1.24, -0.23)	0.004 *
		Placebo	113	108 (95.6)	-0.90 (0.21)	(-1.30, -0.49)			
>= 7	Week 3	CR845	135	124 (91.9)	-1.96 (0.19)	(-2.34, -1.58)	-0.40 (0.26)	(-0.92, 0.12)	0.136
		Placebo	123	119 (96.7)	-1.57 (0.20)	(-1.96, -1.18)			
>= 4 to < 7	Week 4	CR845	102	96 (94.1)	-1.88 (0.22)	(-2.31, -1.45)	-0.85 (0.26)	(-1.37, -0.34)	0.001 *
		Placebo	113	108 (95.6)	-1.03 (0.21)	(-1.44, -0.61)			
>= 7	Week 4	CR845	135	118 (87.4)	-2.43 (0.21)	(-2.85, -2.01)	-0.54 (0.29)	(-1.11, 0.03)	0.065
		Placebo	123	117 (95.1)	-1.89 (0.22)	(-2.32, -1.47)			
>= 4 to < 7	Week 5	CR845	102	98 (96.1)	-1.95 (0.23)	(-2.40, -1.50)	-0.66 (0.28)	(-1.21, -0.11)	0.019 *
		Placebo	113	108 (95.6)	-1.29 (0.22)	(-1.73, -0.86)			
>= 7	Week 5	CR845	135	118 (87.4)	-2.70 (0.23)	(-3.15, -2.26)	-0.56 (0.31)	(-1.18, 0.05)	0.072
		Placebo	123	118 (95.9)	-2.14 (0.23)	(-2.59, -1.68)			
>= 4 to < 7	Week 6	CR845	102	96 (94.1)	-2.06 (0.23)	(-2.52, -1.60)	-0.66 (0.29)	(-1.23, -0.10)	0.022 *
		Placebo	113	106 (93.8)	-1.40 (0.22)	(-1.84, -0.96)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISCD: Change from baseline in weekly WI-NRS - MMRM results by baseline WI-NRS
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
>= 7	Week 6	CR845	135	116 (85.9)	-2.95 (0.23)	(-3.41, -2.48)	-0.73 (0.32)	(-1.37, -0.09)	0.025 *
		Placebo	123	118 (95.9)	-2.22 (0.24)	(-2.68, -1.75)			
>= 4 to < 7	Week 7	CR845	102	97 (95.1)	-2.15 (0.24)	(-2.61, -1.68)	-0.83 (0.29)	(-1.40, -0.26)	0.005 *
		Placebo	113	107 (94.7)	-1.32 (0.23)	(-1.76, -0.87)			
>= 7	Week 7	CR845	135	116 (85.9)	-3.02 (0.23)	(-3.48, -2.56)	-0.69 (0.32)	(-1.33, -0.06)	0.032 *
		Placebo	123	117 (95.1)	-2.32 (0.24)	(-2.79, -1.86)			
>= 4 to < 7	Week 8	CR845	102	94 (92.2)	-2.27 (0.23)	(-2.73, -1.80)	-0.85 (0.29)	(-1.42, -0.28)	0.004 *
		Placebo	113	106 (93.8)	-1.42 (0.23)	(-1.86, -0.97)			
>= 7	Week 8	CR845	135	115 (85.2)	-3.07 (0.23)	(-3.53, -2.61)	-0.52 (0.32)	(-1.15, 0.12)	0.111
		Placebo	123	115 (93.5)	-2.55 (0.24)	(-3.02, -2.08)			
>= 4 to < 7	Week 9	CR845	102	93 (91.2)	-2.30 (0.24)	(-2.76, -1.83)	-0.71 (0.29)	(-1.28, -0.14)	0.016 *
		Placebo	113	105 (92.9)	-1.59 (0.23)	(-2.03, -1.14)			
>= 7	Week 9	CR845	135	114 (84.4)	-3.05 (0.24)	(-3.52, -2.58)	-0.36 (0.33)	(-1.01, 0.29)	0.274
		Placebo	123	117 (95.1)	-2.69 (0.24)	(-3.17, -2.22)			
>= 4 to < 7	Week 10	CR845	102	93 (91.2)	-2.32 (0.25)	(-2.80, -1.83)	-0.65 (0.30)	(-1.25, -0.05)	0.033 *
		Placebo	113	105 (92.9)	-1.67 (0.23)	(-2.13, -1.20)			
>= 7	Week 10	CR845	135	114 (84.4)	-3.14 (0.24)	(-3.61, -2.67)	-0.48 (0.33)	(-1.13, 0.17)	0.150
		Placebo	123	115 (93.5)	-2.66 (0.24)	(-3.14, -2.19)			
>= 4 to < 7	Week 11	CR845	102	90 (88.2)	-2.42 (0.25)	(-2.91, -1.93)	-0.67 (0.31)	(-1.28, -0.06)	0.032 *
		Placebo	113	104 (92.0)	-1.75 (0.24)	(-2.22, -1.28)			
>= 7	Week 11	CR845	135	112 (83.0)	-3.25 (0.24)	(-3.73, -2.77)	-0.62 (0.34)	(-1.28, 0.04)	0.067
		Placebo	123	115 (93.5)	-2.63 (0.25)	(-3.11, -2.14)			
>= 4 to < 7	Week 12	CR845	102	84 (82.4)	-2.50 (0.25)	(-2.99, -2.00)	-0.66 (0.31)	(-1.28, -0.04)	0.037 *
		Placebo	113	101 (89.4)	-1.84 (0.24)	(-2.31, -1.36)			
>= 7	Week 12	CR845	135	107 (79.3)	-3.31 (0.25)	(-3.80, -2.83)	-0.54 (0.34)	(-1.21, 0.13)	0.111
		Placebo	123	106 (86.2)	-2.77 (0.25)	(-3.26, -2.28)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISCE: Change from baseline in weekly WI-NRS - MMRM results by specific medical condition
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
E: Presence of specific medical conditions									0.926
No	Week 1	CR845	195	191 (97.9)	-0.79 (0.10)	(-0.98, -0.61)	-0.24 (0.13)	(-0.50, 0.02)	0.068
		Placebo	199	195 (98.0)	-0.56 (0.09)	(-0.74, -0.37)			
Yes	Week 1	CR845	42	40 (95.2)	-0.71 (0.19)	(-1.10, -0.33)	-0.31 (0.28)	(-0.87, 0.25)	0.275
		Placebo	37	37 (100.0)	-0.40 (0.20)	(-0.81, 0.00)			
No	Week 2	CR845	195	187 (95.9)	-1.46 (0.13)	(-1.71, -1.21)	-0.42 (0.17)	(-0.77, -0.08)	0.015 *
		Placebo	199	195 (98.0)	-1.03 (0.12)	(-1.28, -0.79)			
Yes	Week 2	CR845	42	38 (90.5)	-1.83 (0.33)	(-2.48, -1.18)	-0.60 (0.47)	(-1.55, 0.34)	0.206
		Placebo	37	37 (100.0)	-1.23 (0.34)	(-1.91, -0.54)			
No	Week 3	CR845	195	183 (93.8)	-1.83 (0.14)	(-2.10, -1.55)	-0.48 (0.19)	(-0.86, -0.10)	0.013 *
		Placebo	199	190 (95.5)	-1.35 (0.14)	(-1.62, -1.08)			
Yes	Week 3	CR845	42	38 (90.5)	-2.27 (0.37)	(-3.01, -1.53)	-0.87 (0.53)	(-1.94, 0.19)	0.107
		Placebo	37	37 (100.0)	-1.40 (0.39)	(-2.17, -0.63)			
No	Week 4	CR845	195	176 (90.3)	-2.22 (0.15)	(-2.52, -1.93)	-0.68 (0.21)	(-1.09, -0.27)	0.001 *
		Placebo	199	190 (95.5)	-1.55 (0.15)	(-1.84, -1.26)			
Yes	Week 4	CR845	42	38 (90.5)	-2.54 (0.39)	(-3.32, -1.76)	-0.72 (0.56)	(-1.84, 0.40)	0.207
		Placebo	37	35 (94.6)	-1.82 (0.41)	(-2.63, -1.01)			
No	Week 5	CR845	195	178 (91.3)	-2.38 (0.16)	(-2.69, -2.06)	-0.60 (0.22)	(-1.04, -0.17)	0.007 *
		Placebo	199	191 (96.0)	-1.77 (0.16)	(-2.08, -1.47)			
Yes	Week 5	CR845	42	38 (90.5)	-2.83 (0.42)	(-3.68, -1.98)	-0.60 (0.61)	(-1.82, 0.62)	0.330
		Placebo	37	35 (94.6)	-2.23 (0.44)	(-3.11, -1.35)			
No	Week 6	CR845	195	177 (90.8)	-2.58 (0.17)	(-2.91, -2.25)	-0.69 (0.23)	(-1.15, -0.23)	0.003 *
		Placebo	199	189 (95.0)	-1.89 (0.16)	(-2.21, -1.57)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor previous use of anti-itch medication is also included in the model.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISCE: Change from baseline in weekly WI-NRS - MMRM results by specific medical condition
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Yes	Week 6	CR845	42	35 (83.3)	-2.91 (0.44)	(-3.78, -2.04)	-0.72 (0.63)	(-1.97, 0.53)	0.252
		Placebo	37	35 (94.6)	-2.19 (0.45)	(-3.08, -1.29)			
No	Week 7	CR845	195	177 (90.8)	-2.66 (0.17)	(-2.99, -2.33)	-0.77 (0.23)	(-1.23, -0.31)	0.001 *
		Placebo	199	188 (94.5)	-1.89 (0.16)	(-2.22, -1.57)			
Yes	Week 7	CR845	42	36 (85.7)	-3.00 (0.43)	(-3.86, -2.14)	-0.75 (0.62)	(-1.98, 0.49)	0.231
		Placebo	37	36 (97.3)	-2.25 (0.44)	(-3.14, -1.37)			
No	Week 8	CR845	195	173 (88.7)	-2.76 (0.17)	(-3.10, -2.43)	-0.69 (0.23)	(-1.16, -0.23)	0.003 *
		Placebo	199	186 (93.5)	-2.07 (0.16)	(-2.39, -1.75)			
Yes	Week 8	CR845	42	36 (85.7)	-2.94 (0.43)	(-3.80, -2.08)	-0.59 (0.62)	(-1.82, 0.64)	0.343
		Placebo	37	35 (94.6)	-2.35 (0.44)	(-3.23, -1.46)			
No	Week 9	CR845	195	173 (88.7)	-2.77 (0.17)	(-3.11, -2.43)	-0.56 (0.24)	(-1.04, -0.09)	0.020 *
		Placebo	199	186 (93.5)	-2.21 (0.17)	(-2.54, -1.88)			
Yes	Week 9	CR845	42	34 (81.0)	-2.96 (0.42)	(-3.80, -2.12)	-0.37 (0.60)	(-1.57, 0.83)	0.542
		Placebo	37	36 (97.3)	-2.59 (0.43)	(-3.45, -1.73)			
No	Week 10	CR845	195	172 (88.2)	-2.80 (0.18)	(-3.14, -2.45)	-0.56 (0.25)	(-1.04, -0.08)	0.023 *
		Placebo	199	184 (92.5)	-2.24 (0.17)	(-2.58, -1.90)			
Yes	Week 10	CR845	42	35 (83.3)	-3.21 (0.41)	(-4.02, -2.40)	-0.61 (0.58)	(-1.77, 0.55)	0.297
		Placebo	37	36 (97.3)	-2.60 (0.42)	(-3.43, -1.77)			
No	Week 11	CR845	195	169 (86.7)	-2.92 (0.18)	(-3.27, -2.56)	-0.70 (0.25)	(-1.19, -0.20)	0.006 *
		Placebo	199	183 (92.0)	-2.22 (0.18)	(-2.57, -1.87)			
Yes	Week 11	CR845	42	33 (78.6)	-3.24 (0.41)	(-4.04, -2.43)	-0.44 (0.58)	(-1.59, 0.71)	0.447
		Placebo	37	36 (97.3)	-2.79 (0.41)	(-3.62, -1.97)			
No	Week 12	CR845	195	160 (82.1)	-2.98 (0.18)	(-3.34, -2.62)	-0.62 (0.25)	(-1.12, -0.13)	0.014 *
		Placebo	199	175 (87.9)	-2.35 (0.18)	(-2.70, -2.00)			
Yes	Week 12	CR845	42	31 (73.8)	-3.29 (0.42)	(-4.12, -2.46)	-0.45 (0.59)	(-1.64, 0.73)	0.449
		Placebo	37	32 (86.5)	-2.84 (0.43)	(-3.69, -1.99)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor previous use of anti-itch medication is also included in the model.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISCF: Change from baseline in weekly WI-NRS - MMRM results by use of concomitant itch medication
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis					
					Change from Baseline		Treatment Difference			
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value	
F: Use of concomitant itch medication									0.025	i
No	Week 1	CR845	150	146 (97.3)	-0.56 (0.13)	(-0.83, -0.30)	-0.07 (0.15)	(-0.36, 0.23)	0.659	
		Placebo	151	150 (99.3)	-0.50 (0.13)	(-0.76, -0.23)				
Yes	Week 1	CR845	87	85 (97.7)	-0.95 (0.14)	(-1.24, -0.67)	-0.59 (0.19)	(-0.95, -0.22)	0.002	*
		Placebo	85	82 (96.5)	-0.37 (0.15)	(-0.66, -0.08)				
No	Week 2	CR845	150	142 (94.7)	-1.31 (0.16)	(-1.64, -0.99)	-0.29 (0.20)	(-0.69, 0.10)	0.144	
		Placebo	151	149 (98.7)	-1.02 (0.16)	(-1.34, -0.70)				
Yes	Week 2	CR845	87	83 (95.4)	-1.69 (0.21)	(-2.11, -1.27)	-0.77 (0.29)	(-1.34, -0.19)	0.009	*
		Placebo	85	83 (97.6)	-0.92 (0.21)	(-1.35, -0.50)				
No	Week 3	CR845	150	140 (93.3)	-1.67 (0.18)	(-2.02, -1.31)	-0.42 (0.23)	(-0.87, 0.03)	0.068	
		Placebo	151	146 (96.7)	-1.25 (0.18)	(-1.60, -0.89)				
Yes	Week 3	CR845	87	81 (93.1)	-2.12 (0.23)	(-2.57, -1.67)	-0.79 (0.31)	(-1.40, -0.17)	0.012	*
		Placebo	85	81 (95.3)	-1.33 (0.23)	(-1.78, -0.88)				
No	Week 4	CR845	150	138 (92.0)	-1.96 (0.19)	(-2.33, -1.59)	-0.43 (0.24)	(-0.90, 0.05)	0.080	
		Placebo	151	145 (96.0)	-1.53 (0.19)	(-1.90, -1.16)				
Yes	Week 4	CR845	87	76 (87.4)	-2.64 (0.25)	(-3.13, -2.15)	-1.18 (0.34)	(-1.85, -0.51)	<0.001	*
		Placebo	85	80 (94.1)	-1.46 (0.25)	(-1.95, -0.97)				
No	Week 5	CR845	150	140 (93.3)	-2.13 (0.20)	(-2.53, -1.74)	-0.38 (0.26)	(-0.88, 0.13)	0.142	
		Placebo	151	145 (96.0)	-1.76 (0.20)	(-2.14, -1.37)				
Yes	Week 5	CR845	87	76 (87.4)	-2.84 (0.27)	(-3.37, -2.31)	-1.07 (0.37)	(-1.80, -0.34)	0.004	*
		Placebo	85	81 (95.3)	-1.78 (0.27)	(-2.30, -1.25)				
No	Week 6	CR845	150	139 (92.7)	-2.34 (0.21)	(-2.75, -1.93)	-0.53 (0.27)	(-1.07, 0.00)	0.052	
		Placebo	151	143 (94.7)	-1.81 (0.21)	(-2.22, -1.40)				

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor presence of medical condition is also included in the model.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISCF: Change from baseline in weekly WI-NRS - MMRM results by use of concomitant itch medication
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Yes	Week 6	CR845	87	73 (83.9)	-3.00 (0.27)	(-3.54, -2.47)	-1.06 (0.37)	(-1.80, -0.33)	0.005 *
		Placebo	85	81 (95.3)	-1.94 (0.27)	(-2.47, -1.41)			
No	Week 7	CR845	150	139 (92.7)	-2.44 (0.21)	(-2.85, -2.03)	-0.56 (0.27)	(-1.09, -0.03)	0.039 *
		Placebo	151	143 (94.7)	-1.88 (0.21)	(-2.29, -1.48)			
Yes	Week 7	CR845	87	74 (85.1)	-3.02 (0.28)	(-3.56, -2.47)	-1.16 (0.38)	(-1.91, -0.41)	0.003 *
		Placebo	85	81 (95.3)	-1.85 (0.27)	(-2.39, -1.31)			
No	Week 8	CR845	150	138 (92.0)	-2.59 (0.21)	(-3.00, -2.19)	-0.54 (0.27)	(-1.06, -0.01)	0.044 *
		Placebo	151	142 (94.0)	-2.06 (0.20)	(-2.46, -1.66)			
Yes	Week 8	CR845	87	71 (81.6)	-2.92 (0.29)	(-3.49, -2.36)	-0.91 (0.39)	(-1.68, -0.14)	0.021 *
		Placebo	85	79 (92.9)	-2.01 (0.28)	(-2.56, -1.46)			
No	Week 9	CR845	150	134 (89.3)	-2.56 (0.21)	(-2.98, -2.15)	-0.37 (0.27)	(-0.91, 0.17)	0.176
		Placebo	151	144 (95.4)	-2.19 (0.21)	(-2.60, -1.78)			
Yes	Week 9	CR845	87	73 (83.9)	-3.03 (0.28)	(-3.58, -2.47)	-0.84 (0.39)	(-1.60, -0.08)	0.031 *
		Placebo	85	78 (91.8)	-2.19 (0.28)	(-2.73, -1.64)			
No	Week 10	CR845	150	133 (88.7)	-2.62 (0.22)	(-3.05, -2.20)	-0.41 (0.28)	(-0.97, 0.14)	0.146
		Placebo	151	143 (94.7)	-2.21 (0.21)	(-2.63, -1.79)			
Yes	Week 10	CR845	87	74 (85.1)	-3.07 (0.28)	(-3.62, -2.52)	-0.85 (0.38)	(-1.61, -0.10)	0.026 *
		Placebo	85	77 (90.6)	-2.22 (0.27)	(-2.76, -1.68)			
No	Week 11	CR845	150	133 (88.7)	-2.76 (0.22)	(-3.19, -2.33)	-0.54 (0.28)	(-1.10, 0.02)	0.061
		Placebo	151	141 (93.4)	-2.22 (0.22)	(-2.65, -1.80)			
Yes	Week 11	CR845	87	69 (79.3)	-3.11 (0.29)	(-3.69, -2.54)	-0.86 (0.40)	(-1.64, -0.08)	0.031 *
		Placebo	85	78 (91.8)	-2.25 (0.28)	(-2.81, -1.70)			
No	Week 12	CR845	150	125 (83.3)	-2.78 (0.23)	(-3.22, -2.34)	-0.49 (0.30)	(-1.07, 0.09)	0.100
		Placebo	151	133 (88.1)	-2.29 (0.22)	(-2.73, -1.86)			
Yes	Week 12	CR845	87	66 (75.9)	-3.25 (0.28)	(-3.80, -2.70)	-0.77 (0.38)	(-1.53, -0.02)	0.045 *
		Placebo	85	74 (87.1)	-2.48 (0.27)	(-3.02, -1.93)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor presence of medical condition is also included in the model.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISCG: Change from baseline in weekly WI-NRS - MMRM results by region
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
G: Region									0.512
USA	Week 1	CR845	146	142 (97.3)	-0.63 (0.12)	(-0.86, -0.39)	-0.19 (0.15)	(-0.49, 0.10)	0.199
		Placebo	133	129 (97.0)	-0.43 (0.13)	(-0.69, -0.18)			
Asia	Week 1	CR845	8	8 (100.0)	-1.55 (0.58)	(-2.80, -0.31)	-1.76 (0.75)	(-3.37, -0.15)	0.034 *
		Placebo	12	12 (100.0)	0.21 (0.48)	(-0.81, 1.23)			
Eastern Europe	Week 1	CR845	54	54 (100.0)	-1.04 (0.27)	(-1.58, -0.51)	-0.35 (0.27)	(-0.88, 0.18)	0.190
		Placebo	60	60 (100.0)	-0.69 (0.25)	(-1.19, -0.19)			
Western Europe/European origin	Week 1	CR845	29	27 (93.1)	-0.63 (0.26)	(-1.16, -0.11)	-0.08 (0.33)	(-0.74, 0.57)	0.803
		Placebo	31	31 (100.0)	-0.55 (0.25)	(-1.04, -0.06)			
USA	Week 2	CR845	146	138 (94.5)	-1.09 (0.15)	(-1.39, -0.80)	-0.15 (0.20)	(-0.55, 0.25)	0.454
		Placebo	133	129 (97.0)	-0.94 (0.16)	(-1.26, -0.63)			
Asia	Week 2	CR845	8	8 (100.0)	-2.52 (0.66)	(-3.91, -1.12)	-2.15 (0.85)	(-3.96, -0.35)	0.022 *
		Placebo	12	12 (100.0)	-0.36 (0.54)	(-1.50, 0.78)			
Eastern Europe	Week 2	CR845	54	54 (100.0)	-2.14 (0.32)	(-2.78, -1.50)	-0.94 (0.36)	(-1.66, -0.22)	0.011 *
		Placebo	60	60 (100.0)	-1.19 (0.30)	(-1.79, -0.60)			
Western Europe/European origin	Week 2	CR845	29	25 (86.2)	-2.08 (0.37)	(-2.81, -1.35)	-0.83 (0.47)	(-1.78, 0.12)	0.087
		Placebo	31	31 (100.0)	-1.25 (0.34)	(-1.93, -0.58)			
USA	Week 3	CR845	146	137 (93.8)	-1.44 (0.17)	(-1.77, -1.12)	-0.30 (0.22)	(-0.74, 0.14)	0.187
		Placebo	133	126 (94.7)	-1.15 (0.18)	(-1.49, -0.80)			
Asia	Week 3	CR845	8	8 (100.0)	-2.82 (0.54)	(-3.97, -1.67)	-1.91 (0.70)	(-3.40, -0.42)	0.015 *
		Placebo	12	12 (100.0)	-0.91 (0.44)	(-1.85, 0.03)			
Eastern Europe	Week 3	CR845	54	53 (98.1)	-2.50 (0.34)	(-3.17, -1.83)	-0.85 (0.39)	(-1.63, -0.08)	0.031 *
		Placebo	60	60 (100.0)	-1.64 (0.32)	(-2.27, -1.02)			

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N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISCG: Change from baseline in weekly WI-NRS - MMRM results by region
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Western Europe/European origin	Week 3	CR845	29	23 (79.3)	-2.76 (0.46)	(-3.68, -1.83)	-1.26 (0.61)	(-2.48, -0.05)	0.042 *
		Placebo	31	29 (93.5)	-1.49 (0.42)	(-2.33, -0.65)			
USA	Week 4	CR845	146	133 (91.1)	-1.86 (0.18)	(-2.21, -1.51)	-0.41 (0.25)	(-0.89, 0.07)	0.096
		Placebo	133	123 (92.5)	-1.45 (0.19)	(-1.82, -1.08)			
Asia	Week 4	CR845	8	8 (100.0)	-3.12 (0.65)	(-4.51, -1.74)	-2.18 (0.85)	(-3.97, -0.39)	0.020 *
		Placebo	12	12 (100.0)	-0.95 (0.54)	(-2.08, 0.19)			
Eastern Europe	Week 4	CR845	54	51 (94.4)	-2.77 (0.37)	(-3.49, -2.05)	-1.01 (0.43)	(-1.86, -0.16)	0.021 *
		Placebo	60	60 (100.0)	-1.76 (0.34)	(-2.43, -1.09)			
Western Europe/European origin	Week 4	CR845	29	22 (75.9)	-3.10 (0.47)	(-4.05, -2.15)	-1.32 (0.62)	(-2.56, -0.08)	0.037 *
		Placebo	31	30 (96.8)	-1.78 (0.42)	(-2.63, -0.93)			
USA	Week 5	CR845	146	136 (93.2)	-2.03 (0.19)	(-2.41, -1.64)	-0.35 (0.27)	(-0.88, 0.18)	0.192
		Placebo	133	125 (94.0)	-1.68 (0.21)	(-2.08, -1.27)			
Asia	Week 5	CR845	8	7 (87.5)	-3.19 (0.75)	(-4.76, -1.61)	-1.86 (0.96)	(-3.90, 0.17)	0.070
		Placebo	12	12 (100.0)	-1.33 (0.61)	(-2.61, -0.04)			
Eastern Europe	Week 5	CR845	54	51 (94.4)	-3.23 (0.37)	(-3.96, -2.51)	-1.22 (0.43)	(-2.08, -0.37)	0.006 *
		Placebo	60	60 (100.0)	-2.01 (0.34)	(-2.68, -1.34)			
Western Europe/European origin	Week 5	CR845	29	22 (75.9)	-2.72 (0.53)	(-3.80, -1.65)	-0.65 (0.70)	(-2.06, 0.75)	0.356
		Placebo	31	29 (93.5)	-2.07 (0.47)	(-3.02, -1.12)			
USA	Week 6	CR845	146	131 (89.7)	-2.23 (0.20)	(-2.64, -1.83)	-0.57 (0.28)	(-1.13, -0.01)	0.045 *
		Placebo	133	123 (92.5)	-1.66 (0.21)	(-2.09, -1.24)			
Asia	Week 6	CR845	8	7 (87.5)	-3.44 (0.81)	(-5.15, -1.72)	-1.71 (1.05)	(-3.92, 0.51)	0.122
		Placebo	12	11 (91.7)	-1.73 (0.66)	(-3.12, -0.33)			

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LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISCG: Change from baseline in weekly WI-NRS - MMRM results by region
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Eastern Europe	Week 6	CR845	54	51 (94.4)	-3.42 (0.36)	(-4.14, -2.70)	-1.18 (0.43)	(-2.03, -0.33)	0.007 *
		Placebo	60	60 (100.0)	-2.24 (0.34)	(-2.91, -1.57)			
Western Europe/European origin	Week 6	CR845	29	23 (79.3)	-2.71 (0.55)	(-3.83, -1.60)	-0.48 (0.73)	(-1.94, 0.97)	0.508
		Placebo	31	30 (96.8)	-2.23 (0.49)	(-3.21, -1.25)			
USA	Week 7	CR845	146	132 (90.4)	-2.31 (0.20)	(-2.71, -1.90)	-0.48 (0.28)	(-1.04, 0.07)	0.089
		Placebo	133	124 (93.2)	-1.82 (0.21)	(-2.25, -1.40)			
Asia	Week 7	CR845	8	7 (87.5)	-3.61 (0.88)	(-5.47, -1.76)	-2.21 (1.13)	(-4.59, 0.18)	0.068
		Placebo	12	12 (100.0)	-1.41 (0.71)	(-2.91, 0.09)			
Eastern Europe	Week 7	CR845	54	51 (94.4)	-3.47 (0.38)	(-4.22, -2.71)	-1.29 (0.46)	(-2.20, -0.39)	0.006 *
		Placebo	60	59 (98.3)	-2.18 (0.36)	(-2.88, -1.47)			
Western Europe/European origin	Week 7	CR845	29	23 (79.3)	-2.95 (0.52)	(-3.99, -1.91)	-1.05 (0.68)	(-2.41, 0.31)	0.128
		Placebo	31	29 (93.5)	-1.90 (0.46)	(-2.83, -0.97)			
USA	Week 8	CR845	146	129 (88.4)	-2.39 (0.21)	(-2.80, -1.98)	-0.40 (0.29)	(-0.96, 0.17)	0.171
		Placebo	133	123 (92.5)	-1.99 (0.22)	(-2.42, -1.56)			
Asia	Week 8	CR845	8	7 (87.5)	-3.84 (0.74)	(-5.41, -2.26)	-2.13 (0.95)	(-4.15, -0.10)	0.041 *
		Placebo	12	12 (100.0)	-1.71 (0.60)	(-2.98, -0.44)			
Eastern Europe	Week 8	CR845	54	50 (92.6)	-3.46 (0.37)	(-4.20, -2.72)	-1.29 (0.44)	(-2.17, -0.41)	0.004 *
		Placebo	60	59 (98.3)	-2.17 (0.35)	(-2.86, -1.49)			
Western Europe/European origin	Week 8	CR845	29	23 (79.3)	-3.11 (0.52)	(-4.14, -2.07)	-0.74 (0.68)	(-2.10, 0.62)	0.277
		Placebo	31	27 (87.1)	-2.36 (0.46)	(-3.29, -1.43)			
USA	Week 9	CR845	146	130 (89.0)	-2.40 (0.21)	(-2.81, -1.98)	-0.21 (0.29)	(-0.79, 0.36)	0.466
		Placebo	133	124 (93.2)	-2.19 (0.22)	(-2.62, -1.75)			

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LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
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A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISCG: Change from baseline in weekly WI-NRS - MMRM results by region
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Asia	Week 9	CR845	8	7 (87.5)	-3.37 (0.73)	(-4.92, -1.82)	-1.01 (0.94)	(-3.01, 0.99)	0.301
		Placebo	12	11 (91.7)	-2.36 (0.59)	(-3.62, -1.11)			
Eastern Europe	Week 9	CR845	54	49 (90.7)	-3.52 (0.38)	(-4.26, -2.77)	-1.24 (0.45)	(-2.13, -0.36)	0.006 *
		Placebo	60	59 (98.3)	-2.27 (0.35)	(-2.96, -1.58)			
Western Europe/European origin	Week 9	CR845	29	21 (72.4)	-3.19 (0.55)	(-4.30, -2.09)	-0.94 (0.72)	(-2.39, 0.51)	0.200
		Placebo	31	28 (90.3)	-2.26 (0.49)	(-3.24, -1.27)			
USA	Week 10	CR845	146	130 (89.0)	-2.46 (0.21)	(-2.88, -2.04)	-0.23 (0.29)	(-0.81, 0.35)	0.433
		Placebo	133	123 (92.5)	-2.23 (0.22)	(-2.67, -1.79)			
Asia	Week 10	CR845	8	7 (87.5)	-3.47 (0.71)	(-4.97, -1.97)	-1.17 (0.91)	(-3.10, 0.76)	0.217
		Placebo	12	11 (91.7)	-2.30 (0.57)	(-3.51, -1.09)			
Eastern Europe	Week 10	CR845	54	48 (88.9)	-3.60 (0.38)	(-4.35, -2.84)	-1.30 (0.45)	(-2.19, -0.40)	0.005 *
		Placebo	60	59 (98.3)	-2.30 (0.35)	(-3.00, -1.61)			
Western Europe/European origin	Week 10	CR845	29	22 (75.9)	-3.10 (0.59)	(-4.28, -1.92)	-0.94 (0.78)	(-2.50, 0.62)	0.231
		Placebo	31	27 (87.1)	-2.16 (0.53)	(-3.22, -1.10)			
USA	Week 11	CR845	146	126 (86.3)	-2.59 (0.21)	(-3.00, -2.17)	-0.41 (0.29)	(-0.99, 0.16)	0.157
		Placebo	133	124 (93.2)	-2.17 (0.22)	(-2.61, -1.74)			
Asia	Week 11	CR845	8	7 (87.5)	-3.61 (0.71)	(-5.12, -2.10)	-1.11 (0.92)	(-3.06, 0.83)	0.243
		Placebo	12	11 (91.7)	-2.50 (0.58)	(-3.72, -1.27)			
Eastern Europe	Week 11	CR845	54	47 (87.0)	-3.71 (0.40)	(-4.51, -2.91)	-1.31 (0.49)	(-2.27, -0.34)	0.009 *
		Placebo	60	57 (95.0)	-2.40 (0.37)	(-3.14, -1.67)			
Western Europe/European origin	Week 11	CR845	29	22 (75.9)	-3.09 (0.59)	(-4.27, -1.91)	-0.76 (0.78)	(-2.32, 0.80)	0.333
		Placebo	31	27 (87.1)	-2.33 (0.53)	(-3.39, -1.27)			

Note: ITT = Intent-to-treat Set.
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LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISCG: Change from baseline in weekly WI-NRS - MMRM results by region
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
USA	Week 12	CR845	146	118 (80.8)	-2.68 (0.22)	(-3.10, -2.25)	-0.40 (0.30)	(-0.98, 0.19)	0.185
		Placebo	133	115 (86.5)	-2.28 (0.22)	(-2.72, -1.84)			
Asia	Week 12	CR845	8	7 (87.5)	-3.43 (0.64)	(-4.79, -2.07)	-0.75 (0.83)	(-2.51, 1.00)	0.376
		Placebo	12	11 (91.7)	-2.68 (0.52)	(-3.78, -1.57)			
Eastern Europe	Week 12	CR845	54	46 (85.2)	-3.71 (0.41)	(-4.51, -2.91)	-1.13 (0.49)	(-2.10, -0.16)	0.023 *
		Placebo	60	57 (95.0)	-2.58 (0.37)	(-3.32, -1.84)			
Western Europe/European origin	Week 12	CR845	29	20 (69.0)	-3.18 (0.60)	(-4.38, -1.98)	-0.77 (0.79)	(-2.35, 0.82)	0.336
		Placebo	31	24 (77.4)	-2.41 (0.54)	(-3.49, -1.33)			

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N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISCH: Change from baseline in weekly WI-NRS - MMRM results by dialysis method
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis					
					Change from Baseline		Treatment Difference			
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value	
H: Dialysis method									0.159	
Hemodialysis (HD)	Week 1	CR845	222	216 (97.3)	-0.72 (0.10)	(-0.91, -0.53)	-0.35 (0.12)	(-0.59, -0.11)	0.005	*
		Placebo	199	195 (98.0)	-0.37 (0.10)	(-0.58, -0.17)				
Hemodiafiltration (HDF)	Week 1	CR845	15	15 (100.0)	-0.99 (0.71)	(-2.42, 0.44)	0.27 (0.47)	(-0.67, 1.21)	0.560	
		Placebo	37	37 (100.0)	-1.26 (0.54)	(-2.34, -0.19)				
Hemodialysis (HD)	Week 2	CR845	222	211 (95.0)	-1.49 (0.13)	(-1.74, -1.23)	-0.60 (0.17)	(-0.94, -0.25)	<0.001	*
		Placebo	199	195 (98.0)	-0.89 (0.14)	(-1.16, -0.62)				
Hemodiafiltration (HDF)	Week 2	CR845	15	14 (93.3)	-1.36 (0.76)	(-2.87, 0.16)	0.55 (0.56)	(-0.58, 1.68)	0.330	
		Placebo	37	37 (100.0)	-1.91 (0.56)	(-3.03, -0.79)				
Hemodialysis (HD)	Week 3	CR845	222	208 (93.7)	-1.83 (0.14)	(-2.11, -1.55)	-0.69 (0.19)	(-1.07, -0.32)	<0.001	*
		Placebo	199	191 (96.0)	-1.14 (0.15)	(-1.43, -0.85)				
Hemodiafiltration (HDF)	Week 3	CR845	15	13 (86.7)	-2.36 (0.84)	(-4.03, -0.69)	0.06 (0.70)	(-1.35, 1.46)	0.937	
		Placebo	37	36 (97.3)	-2.41 (0.60)	(-3.61, -1.22)				
Hemodialysis (HD)	Week 4	CR845	222	202 (91.0)	-2.22 (0.15)	(-2.52, -1.92)	-0.85 (0.21)	(-1.25, -0.44)	<0.001	*
		Placebo	199	189 (95.0)	-1.38 (0.16)	(-1.68, -1.07)				
Hemodiafiltration (HDF)	Week 4	CR845	15	12 (80.0)	-2.41 (0.87)	(-4.14, -0.68)	0.22 (0.75)	(-1.28, 1.72)	0.769	
		Placebo	37	36 (97.3)	-2.63 (0.62)	(-3.85, -1.40)				
Hemodialysis (HD)	Week 5	CR845	222	204 (91.9)	-2.40 (0.16)	(-2.72, -2.09)	-0.74 (0.22)	(-1.17, -0.30)	0.001	*
		Placebo	199	190 (95.5)	-1.67 (0.17)	(-2.00, -1.34)				

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISCH: Change from baseline in weekly WI-NRS - MMRM results by dialysis method
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Hemodiafiltration (HDF)	Week 5	CR845	15	12 (80.0)	-2.49 (0.87)	(-4.22, -0.76)	0.18 (0.74)	(-1.31, 1.67)	0.808
		Placebo	37	36 (97.3)	-2.67 (0.61)	(-3.89, -1.45)			
Hemodialysis (HD)	Week 6	CR845	222	199 (89.6)	-2.59 (0.17)	(-2.92, -2.26)	-0.85 (0.23)	(-1.30, -0.39)	<0.001 *
		Placebo	199	188 (94.5)	-1.74 (0.17)	(-2.08, -1.40)			
Hemodiafiltration (HDF)	Week 6	CR845	15	13 (86.7)	-2.65 (0.88)	(-4.40, -0.89)	0.24 (0.77)	(-1.29, 1.78)	0.753
		Placebo	37	36 (97.3)	-2.89 (0.62)	(-4.13, -1.65)			
Hemodialysis (HD)	Week 7	CR845	222	200 (90.1)	-2.66 (0.17)	(-2.99, -2.32)	-0.85 (0.23)	(-1.31, -0.40)	<0.001 *
		Placebo	199	188 (94.5)	-1.80 (0.18)	(-2.15, -1.46)			
Hemodiafiltration (HDF)	Week 7	CR845	15	13 (86.7)	-3.00 (0.90)	(-4.79, -1.21)	-0.37 (0.79)	(-1.96, 1.22)	0.642
		Placebo	37	36 (97.3)	-2.63 (0.63)	(-3.89, -1.38)			
Hemodialysis (HD)	Week 8	CR845	222	196 (88.3)	-2.73 (0.17)	(-3.06, -2.40)	-0.76 (0.23)	(-1.22, -0.30)	0.001 *
		Placebo	199	185 (93.0)	-1.97 (0.18)	(-2.31, -1.62)			
Hemodiafiltration (HDF)	Week 8	CR845	15	13 (86.7)	-2.96 (0.89)	(-4.74, -1.18)	-0.17 (0.78)	(-1.74, 1.40)	0.830
		Placebo	37	36 (97.3)	-2.79 (0.63)	(-4.04, -1.54)			
Hemodialysis (HD)	Week 9	CR845	222	195 (87.8)	-2.75 (0.17)	(-3.09, -2.41)	-0.59 (0.24)	(-1.06, -0.13)	0.013 *
		Placebo	199	187 (94.0)	-2.16 (0.18)	(-2.51, -1.81)			
Hemodiafiltration (HDF)	Week 9	CR845	15	12 (80.0)	-2.86 (0.90)	(-4.66, -1.06)	-0.12 (0.80)	(-1.72, 1.48)	0.881
		Placebo	37	35 (94.6)	-2.74 (0.63)	(-4.00, -1.48)			
Hemodialysis (HD)	Week 10	CR845	222	194 (87.4)	-2.78 (0.17)	(-3.12, -2.44)	-0.61 (0.24)	(-1.08, -0.14)	0.010 *
		Placebo	199	185 (93.0)	-2.17 (0.18)	(-2.52, -1.81)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: aweek, created on: 17FEB2022

Table BT2WIC_ISCH: Change from baseline in weekly WI-NRS - MMRM results by dialysis method
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis					
					Change from Baseline		Treatment Difference			
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value	
Hemodiafiltration (HDF)	Week 10	CR845	15	13 (86.7)	-3.50 (0.94)	(-5.38, -1.63)	-0.66 (0.86)	(-2.39, 1.07)	0.446	
		Placebo	37	35 (94.6)	-2.84 (0.65)	(-4.14, -1.54)				
Hemodialysis (HD)	Week 11	CR845	222	189 (85.1)	-2.87 (0.18)	(-3.22, -2.53)	-0.68 (0.24)	(-1.16, -0.21)	0.005	*
		Placebo	199	186 (93.5)	-2.19 (0.18)	(-2.55, -1.84)				
Hemodiafiltration (HDF)	Week 11	CR845	15	13 (86.7)	-3.76 (0.96)	(-5.67, -1.84)	-0.92 (0.89)	(-2.71, 0.87)	0.306	
		Placebo	37	33 (89.2)	-2.84 (0.66)	(-4.16, -1.51)				
Hemodialysis (HD)	Week 12	CR845	222	179 (80.6)	-2.94 (0.18)	(-3.28, -2.59)	-0.62 (0.24)	(-1.10, -0.14)	0.012	*
		Placebo	199	175 (87.9)	-2.31 (0.18)	(-2.67, -1.95)				
Hemodiafiltration (HDF)	Week 12	CR845	15	12 (80.0)	-3.77 (0.97)	(-5.71, -1.84)	-0.82 (0.90)	(-2.63, 0.99)	0.369	
		Placebo	37	32 (86.5)	-2.95 (0.67)	(-4.29, -1.62)				

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: aweek, created on: 17FEB2022

Table BT2WICD3_ISPA: Decrease of WI-NRS of at least 3 points by age
ITT

		CR845			Placebo						
Decrease of WI-NRS of at least 3 points		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	A: Age										0.878
	< 65 years	147	122 (83.0)	62 (42.2) [34.1, 50.6]	153	137 (89.5)	53 (34.6) [27.1, 42.7]	1.218 [0.912, 1.625]	1.376 [0.863, 2.195]	7.5 [-4.1, 19.2]	0.180
	>= 65 years	90	69 (76.7)	33 (36.7) [26.8, 47.5]	83	70 (84.3)	24 (28.9) [19.5, 39.9]	1.268 [0.822, 1.955]	1.423 [0.751, 2.698]	7.8 [-7.3, 22.8]	0.280

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table BT2WICD3_ISPB: Decrease of WI-NRS of at least 3 points by sex
ITT

		CR845			Placebo						
Decrease of WI-NRS of at least 3 points		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	B: Sex										0.198
	Male	137	110 (80.3)	47 (34.3) [26.4, 42.9]	139	125 (89.9)	45 (32.4) [24.7, 40.8]	1.060 [0.759, 1.480]	1.091 [0.661, 1.800]	1.9 [-9.9, 13.8]	0.734
	Female	100	81 (81.0)	48 (48.0) [37.9, 58.2]	97	82 (84.5)	32 (33.0) [23.8, 43.3]	1.455 [1.026, 2.063]	1.875 [1.053, 3.339]	15.0 [0.5, 29.6]	0.032 *

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table BT2WICD3_ISPC: Decrease of WI-NRS of at least 3 points by race
ITT

		CR845			Placebo						
Decrease of WI-NRS of at least 3 points		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	C: Race										0.521
	Black/African American	53	39 (73.6)	23 (43.4) [29.8, 57.7]	38	35 (92.1)	12 (31.6) [17.5, 48.7]	1.374 [0.785, 2.406]	1.661 [0.694, 3.979]	11.8 [-10.4, 34.0]	0.256
	White	164	136 (82.9)	66 (40.2) [32.7, 48.2]	169	150 (88.8)	54 (32.0) [25.0, 39.6]	1.259 [0.944, 1.681]	1.434 [0.915, 2.248]	8.3 [-2.6, 19.2]	0.116
	Other	20	16 (80.0)	6 (30.0) [11.9, 54.3]	29	22 (75.9)	11 (37.9) [20.7, 57.7]	0.791 [0.350, 1.788]	0.701 [0.208, 2.365]	-7.9 [-38.9, 23.0]	0.570

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table BT2WICD3_ISPD: Decrease of WI-NRS of at least 3 points by baseline WI-NRS
ITT

		CR845			Placebo							
Decrease of WI-NRS of at least 3 points		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.187	
	>= 4 to < 7	102	84 (82.4)	45 (44.1) [34.3, 54.3]	113	101 (89.4)	34 (30.1) [21.8, 39.4]	1.466 [1.027, 2.093]	1.834 [1.047, 3.214]	14.0 [0.3, 27.8]	0.034	*
	>= 7	135	107 (79.3)	50 (37.0) [28.9, 45.8]	123	106 (86.2)	43 (35.0) [26.6, 44.1]	1.059 [0.764, 1.468]	1.094 [0.658, 1.821]	2.1 [-10.4, 14.6]	0.729	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table BT2WICD3_ISPE: Decrease of WI-NRS of at least 3 points by specific medical condition
ITT

		CR845			Placebo						
Decrease of WI-NRS of at least 3 points		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	E: Presence of specific medical conditions										0.890
	No	195	160 (82.1)	79 (40.5) [33.6, 47.8]	199	175 (87.9)	66 (33.2) [26.7, 40.2]	1.222 [0.941, 1.585]	1.372 [0.910, 2.070]	7.3 [-2.7, 17.4]	0.131
	Yes	42	31 (73.8)	16 (38.1) [23.6, 54.4]	37	32 (86.5)	11 (29.7) [15.9, 47.0]	1.281 [0.684, 2.400]	1.455 [0.568, 3.726]	8.4 [-15.0, 31.7]	0.437

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table BT2WICD3_ISPF: Decrease of WI-NRS of at least 3 points by use of concomitant itch medication
ITT

		CR845			Placebo						
Decrease of WI-NRS of at least 3 points		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	F: Use of concomitant itch medication										0.685
	No	150	125 (83.3)	60 (40.0) [32.1, 48.3]	151	133 (88.1)	51 (33.8) [26.3, 41.9]	1.184 [0.880, 1.594]	1.307 [0.817, 2.090]	6.2 [-5.3, 17.8]	0.264
	Yes	87	66 (75.9)	35 (40.2) [29.9, 51.3]	85	74 (87.1)	26 (30.6) [21.0, 41.5]	1.315 [0.873, 1.982]	1.527 [0.814, 2.867]	9.6 [-5.7, 25.0]	0.188

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table BT2WICD3_ISPG: Decrease of WI-NRS of at least 3 points by region
ITT

		CR845			Placebo							
Decrease of WI-NRS of at least 3 points		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	G: Region										0.351	
	USA	146	118 (80.8)	51 (34.9) [27.2, 43.3]	133	115 (86.5)	43 (32.3) [24.5, 41.0]	1.080 [0.776, 1.504]	1.124 [0.683, 1.848]	2.6 [-9.2, 14.4]	0.647	
	Asia	8	7 (87.5)	3 (37.5) [8.5, 75.5]	12	11 (91.7)	5 (41.7) [15.2, 72.3]	0.900 [0.294, 2.751]	0.840 [0.134, 5.261]	-4.2 [-58.2, 49.9]	1.000	#
	Eastern Europe	54	46 (85.2)	31 (57.4) [43.2, 70.8]	60	57 (95.0)	20 (33.3) [21.7, 46.7]	1.722 [1.126, 2.635]	2.696 [1.259, 5.770]	24.1 [4.5, 43.6]	0.010	*
	Western Europe/European origin	29	20 (69.0)	10 (34.5) [17.9, 54.3]	31	24 (77.4)	9 (29.0) [14.2, 48.0]	1.188 [0.564, 2.501]	1.287 [0.433, 3.826]	5.5 [-21.4, 32.3]	0.653	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table BT2WICD3_ISPH: Decrease of WI-NRS of at least 3 points by dialysis method
ITT

		CR845			Placebo						
Decrease of WI-NRS of at least 3 points		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	H: Dialysis method										0.708
	Hemodialysis (HD)	222	179 (80.6)	87 (39.2) [32.7, 45.9]	199	175 (87.9)	63 (31.7) [25.3, 38.6]	1.238 [0.953, 1.608]	1.391 [0.930, 2.080]	7.5 [-2.1, 17.1]	0.108
	Hemodiafiltration (HDF)	15	12 (80.0)	8 (53.3) [26.6, 78.7]	37	32 (86.5)	14 (37.8) [22.5, 55.2]	1.410 [0.752, 2.642]	1.878 [0.558, 6.313]	15.5 [-18.9, 49.9]	0.310

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table BT2WICD4_ISPA: Decrease of WI-NRS of at least 4 points by age
ITT

		CR845			Placebo						
Decrease of WI-NRS of at least 4 points		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	A: Age										0.724
	< 65 years	147	122 (83.0)	46 (31.3) [23.9, 39.5]	153	137 (89.5)	36 (23.5) [17.1, 31.1]	1.330 [0.916, 1.931]	1.480 [0.888, 2.467]	7.8 [-3.0, 18.5]	0.132
	>= 65 years	90	69 (76.7)	26 (28.9) [19.8, 39.4]	83	70 (84.3)	16 (19.3) [11.4, 29.4]	1.499 [0.867, 2.589]	1.701 [0.836, 3.463]	9.6 [-4.2, 23.4]	0.142

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table BT2WICD4_ISPB: Decrease of WI-NRS of at least 4 points by sex
ITT

		CR845			Placebo						
Decrease of WI-NRS of at least 4 points		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	B: Sex										0.242
	Male	137	110 (80.3)	30 (21.9) [15.3, 29.8]	139	125 (89.9)	27 (19.4) [13.2, 27.0]	1.127 [0.709, 1.792]	1.163 [0.649, 2.085]	2.5 [-7.8, 12.7]	0.612
	Female	100	81 (81.0)	42 (42.0) [32.2, 52.3]	97	82 (84.5)	25 (25.8) [17.4, 35.7]	1.630 [1.083, 2.453]	2.086 [1.140, 3.815]	16.2 [2.2, 30.3]	0.017 *

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table BT2WICD4_ISPC: Decrease of WI-NRS of at least 4 points by race
ITT

Decrease of WI-NRS of at least 4 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	C: Race										0.950	
	Black/African American	53	39 (73.6)	17 (32.1) [19.9, 46.3]	38	35 (92.1)	9 (23.7) [11.4, 40.2]	1.354 [0.678, 2.706]	1.522 [0.592, 3.913]	8.4 [-12.3, 29.1]	0.385	
	White	164	136 (82.9)	52 (31.7) [24.7, 39.4]	169	150 (88.8)	39 (23.1) [17.0, 30.2]	1.374 [0.963, 1.960]	1.548 [0.952, 2.516]	8.6 [-1.5, 18.8]	0.078	
	Other	20	16 (80.0)	3 (15.0) [3.2, 37.9]	29	22 (75.9)	4 (13.8) [3.9, 31.7]	1.088 [0.272, 4.341]	1.103 [0.219, 5.567]	1.2 [-23.1, 25.5]	1.000	#

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table BT2WICD4_ISPD: Decrease of WI-NRS of at least 4 points by baseline WI-NRS
ITT

		CR845			Placebo							
Decrease of WI-NRS of at least 4 points		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.308	
	>= 4 to < 7	102	84 (82.4)	30 (29.4) [20.8, 39.3]	113	101 (89.4)	20 (17.7) [11.2, 26.0]	1.662 [1.009, 2.736]	1.938 [1.018, 3.689]	11.7 [-0.5, 23.9]	0.043	*
	>= 7	135	107 (79.3)	42 (31.1) [23.4, 39.6]	123	106 (86.2)	32 (26.0) [18.5, 34.7]	1.196 [0.810, 1.766]	1.284 [0.746, 2.211]	5.1 [-6.7, 16.9]	0.367	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table BT2WICD4_ISPE: Decrease of WI-NRS of at least 4 points by specific medical condition
ITT

Decrease of WI-NRS of at least 4 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	E: Presence of specific medical conditions										0.486	
	No	195	160 (82.1)	61 (31.3) [24.8, 38.3]	199	175 (87.9)	43 (21.6) [16.1, 28.0]	1.448 [1.034, 2.027]	1.652 [1.049, 2.599]	9.7 [0.5, 18.8]	0.030	*
	Yes	42	31 (73.8)	11 (26.2) [13.9, 42.0]	37	32 (86.5)	9 (24.3) [11.8, 41.2]	1.077 [0.502, 2.307]	1.104 [0.399, 3.057]	1.9 [-19.9, 23.6]	0.850	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table BT2WICD4_ISPF: Decrease of WI-NRS of at least 4 points by use of concomitant itch medication
ITT

		CR845			Placebo						
Decrease of WI-NRS of at least 4 points		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	F: Use of concomitant itch medication										0.158
	No	150	125 (83.3)	43 (28.7) [21.6, 36.6]	151	133 (88.1)	37 (24.5) [17.9, 32.2]	1.170 [0.802, 1.706]	1.238 [0.742, 2.067]	4.2 [-6.5, 14.8]	0.414
	Yes	87	66 (75.9)	29 (33.3) [23.6, 44.3]	85	74 (87.1)	15 (17.6) [10.2, 27.4]	1.889 [1.093, 3.264]	2.333 [1.143, 4.765]	15.7 [1.7, 29.6]	0.019 *

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table BT2WICD4_ISPG: Decrease of WI-NRS of at least 4 points by region
ITT

		CR845			Placebo							
Decrease of WI-NRS of at least 4 points		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	G: Region										0.676	
	USA	146	118 (80.8)	39 (26.7) [19.7, 34.7]	133	115 (86.5)	28 (21.1) [14.5, 29.0]	1.269 [0.830, 1.941]	1.367 [0.785, 2.381]	5.7 [-5.0, 16.4]	0.270	
	Asia	8	7 (87.5)	1 (12.5) [0.3, 52.7]	12	11 (91.7)	2 (16.7) [2.1, 48.4]	0.750 [0.081, 6.958]	0.714 [0.054, 9.497]	-4.2 [-45.7, 37.4]	1.000	#
	Eastern Europe	54	46 (85.2)	23 (42.6) [29.2, 56.8]	60	57 (95.0)	14 (23.3) [13.4, 36.0]	1.825 [1.050, 3.175]	2.438 [1.089, 5.455]	19.3 [0.5, 38.0]	0.029	*
	Western Europe/European origin	29	20 (69.0)	9 (31.0) [15.3, 50.8]	31	24 (77.4)	8 (25.8) [11.9, 44.6]	1.203 [0.537, 2.694]	1.294 [0.420, 3.986]	5.2 [-20.9, 31.4]	0.656	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table BT2WICD4_ISPH: Decrease of WI-NRS of at least 4 points by dialysis method
ITT

		CR845			Placebo							
Decrease of WI-NRS of at least 4 points		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	H: Dialysis method										0.913	
	Hemodialysis (HD)	222	179 (80.6)	66 (29.7) [23.8, 36.2]	199	175 (87.9)	42 (21.1) [15.7, 27.4]	1.409 [1.006, 1.972]	1.582 [1.013, 2.470]	8.6 [-0.1, 17.4]	0.043	*
	Hemodiafiltration (HDF)	15	12 (80.0)	6 (40.0) [16.3, 67.7]	37	32 (86.5)	10 (27.0) [13.8, 44.1]	1.480 [0.655, 3.344]	1.800 [0.509, 6.361]	13.0 [-20.3, 46.3]	0.508	#

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table BT2WIR_ISPA: Complete WI-NRS responder by age
ITT

		CR845			Placebo						
Complete WI-NRS responder		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	A: Age										0.435
	< 65 years	147	147 (100.0)	20 (13.6) [8.5, 20.2]	153	153 (100.0)	11 (7.2) [3.6, 12.5]	1.892 [0.940, 3.811]	2.033 [0.938, 4.407]	6.4 [-1.1, 14.0]	0.068
	>= 65 years	90	90 (100.0)	9 (10.0) [4.7, 18.1]	83	83 (100.0)	7 (8.4) [3.5, 16.6]	1.186 [0.462, 3.040]	1.206 [0.428, 3.400]	1.6 [-8.2, 11.3]	0.723

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table BT2WIR_ISPB: Complete WI-NRS responder by sex
ITT

		CR845			Placebo						
Complete WI-NRS responder		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	B: Sex										0.024 i
	Male	137	137 (100.0)	8 (5.8) [2.6, 11.2]	139	139 (100.0)	11 (7.9) [4.0, 13.7]	0.738 [0.306, 1.778]	0.722 [0.281, 1.853]	-2.1 [-8.8, 4.6]	0.497
	Female	100	100 (100.0)	21 (21.0) [13.5, 30.3]	97	97 (100.0)	7 (7.2) [3.0, 14.3]	2.910 [1.296, 6.532]	3.418 [1.380, 8.467]	13.8 [3.3, 24.3]	0.006 *

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table BT2WIR_ISPC: Complete WI-NRS responder by race
ITT

		CR845			Placebo						
Complete WI-NRS responder		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	C: Race										0.875
	Black/African American	53	53 (100.0)	4 (7.5) [2.1, 18.2]	38	38 (100.0)	2 (5.3) [0.6, 17.7]	1.434 [0.277, 7.433]	1.469 [0.255, 8.465]	2.3 [-10.0, 14.6]	1.000 #
	White	164	164 (100.0)	23 (14.0) [9.1, 20.3]	169	169 (100.0)	15 (8.9) [5.1, 14.2]	1.580 [0.855, 2.920]	1.675 [0.840, 3.337]	5.1 [-2.3, 12.6]	0.140
	Other	20	20 (100.0)	2 (10.0) [1.2, 31.7]	29	29 (100.0)	1 (3.4) [0.1, 17.8]	2.900 [0.282, 29.862]	3.111 [0.263, 36.870]	6.6 [-12.4, 25.5]	0.559 #

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table BT2WIR_ISPD: Complete WI-NRS responder by baseline WI-NRS
ITT

		CR845			Placebo						
Complete WI-NRS responder		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.341
	>= 4 to < 7	102	102 (100.0)	14 (13.7) [7.7, 22.0]	113	113 (100.0)	12 (10.6) [5.6, 17.8]	1.292 [0.627, 2.664]	1.339 [0.588, 3.047]	3.1 [-6.6, 12.8]	0.487
	>= 7	135	135 (100.0)	15 (11.1) [6.4, 17.7]	123	123 (100.0)	6 (4.9) [1.8, 10.3]	2.278 [0.913, 5.685]	2.438 [0.914, 6.497]	6.2 [-1.1, 13.5]	0.068

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table BT2WIR_ISPE: Complete WI-NRS responder by specific medical condition
ITT

Complete WI-NRS responder		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	E: Presence of specific medical conditions										0.485	
	No	195	195 (100.0)	23 (11.8) [7.6, 17.2]	199	199 (100.0)	16 (8.0) [4.7, 12.7]	1.467 [0.800, 2.691]	1.529 [0.782, 2.992]	3.8 [-2.6, 10.2]	0.213	
	Yes	42	42 (100.0)	6 (14.3) [5.4, 28.5]	37	37 (100.0)	2 (5.4) [0.7, 18.2]	2.643 [0.568, 12.304]	2.917 [0.551, 15.441]	8.9 [-6.5, 24.3]	0.271	#

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table BT2WIR_ISPF: Complete WI-NRS responder by use of concomitant itch medication
ITT

Complete WI-NRS responder		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	F: Use of concomitant itch medication										0.181	
	No	150	150 (100.0)	17 (11.3) [6.7, 17.5]	151	151 (100.0)	14 (9.3) [5.2, 15.1]	1.222 [0.625, 2.390]	1.251 [0.593, 2.639]	2.1 [-5.5, 9.6]	0.557	
	Yes	87	87 (100.0)	12 (13.8) [7.3, 22.9]	85	85 (100.0)	4 (4.7) [1.3, 11.6]	2.931 [0.984, 8.730]	3.240 [1.001, 10.485]	9.1 [-0.6, 18.8]	0.041	*

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table BT2WIR_ISPG: Complete WI-NRS responder by region
ITT

		CR845			Placebo						
Complete WI-NRS responder		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	G: Region										0.254
	USA	146	146 (100.0)	11 (7.5) [3.8, 13.1]	133	133 (100.0)	11 (8.3) [4.2, 14.3]	0.911 [0.408, 2.031]	0.904 [0.378, 2.159]	-0.7 [-7.8, 6.3]	0.820
	Asia	8	8 (100.0)	1 (12.5) [0.3, 52.7]	12	12 (100.0)	1 (8.3) [0.2, 38.5]	1.500 [0.109, 20.675]	1.571 [0.084, 29.409]	4.2 [-34.0, 42.3]	1.000 #
	Eastern Europe	54	54 (100.0)	11 (20.4) [10.6, 33.5]	60	60 (100.0)	4 (6.7) [1.8, 16.2]	3.056 [1.034, 9.031]	3.581 [1.066, 12.027]	13.7 [-0.5, 27.9]	0.031 *
	Western Europe/European origin	29	29 (100.0)	6 (20.7) [8.0, 39.7]	31	31 (100.0)	2 (6.5) [0.8, 21.4]	3.207 [0.703, 14.635]	3.783 [0.697, 20.526]	14.2 [-6.2, 34.7]	0.140 #

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table BT2WIR_ISPH: Complete WI-NRS responder by dialysis method
ITT

		CR845			Placebo						
Complete WI-NRS responder		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	H: Dialysis method										0.983
	Hemodialysis (HD)	222	222 (100.0)	27 (12.2) [8.2, 17.2]	199	199 (100.0)	15 (7.5) [4.3, 12.1]	1.614 [0.884, 2.944]	1.698 [0.876, 3.295]	4.6 [-1.5, 10.8]	0.114
	Hemodiafiltration (HDF)	15	15 (100.0)	2 (13.3) [1.7, 40.5]	37	37 (100.0)	3 (8.1) [1.7, 21.9]	1.644 [0.305, 8.873]	1.744 [0.261, 11.657]	5.2 [-18.8, 29.2]	0.619 #

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek, created on: 17FEB2022

Table BT2DTC_ISHA: Change from baseline in 5-D total score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
< 65 years	5-D total score	Baseline	CR845	147	143 (97.3)	16.9 (3.5)	7	17.0	25	
			Placebo	153	153 (100.0)	16.3 (3.4)	7	16.0	24	
		Week 4	CR845	147	134 (91.2)	12.9 (3.7)	5	13.0	23	
			Placebo	153	144 (94.1)	13.9 (4.0)	8	13.0	25	
		Week 8	CR845	147	131 (89.1)	12.2 (4.0)	5	12.0	25	
			Placebo	153	143 (93.5)	12.8 (3.7)	5	13.0	23	
		Week 10	CR845	147	132 (89.8)	12.0 (4.0)	5	11.0	23	
			Placebo	153	141 (92.2)	12.8 (4.0)	5	12.0	25	
		Week 12	CR845	147	131 (89.1)	11.8 (4.2)	5	11.0	23	
			Placebo	153	142 (92.8)	12.7 (4.2)	5	12.0	23	
	Change from baseline in 5-D total score	Week 4	CR845	147	131 (89.1)	-4.0 (3.4)	-13	-4.0	3	-0.46 [-0.70, -0.22]
			Placebo	153	144 (94.1)	-2.3 (3.9)	-12	-2.0	9	
		Week 8	CR845	147	128 (87.1)	-4.8 (3.8)	-16	-5.0	2	-0.34 [-0.58, -0.10]
			Placebo	153	143 (93.5)	-3.5 (3.9)	-14	-3.0	6	
		Week 10	CR845	147	129 (87.8)	-5.0 (4.0)	-17	-5.0	4	-0.37 [-0.61, -0.12]
			Placebo	153	141 (92.2)	-3.5 (4.0)	-14	-3.0	10	
		Week 12	CR845	147	128 (87.1)	-5.2 (4.2)	-19	-5.0	4	-0.40 [-0.64, -0.16]
			Placebo	153	142 (92.8)	-3.5 (4.2)	-14	-3.0	8	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DTC_ISHA: Change from baseline in 5-D total score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 65 years	5-D total score	Baseline	CR845	90	89 (98.9)	16.4 (3.7)	7	16.0	24	
			Placebo	83	83 (100.0)	16.1 (3.2)	9	16.0	22	
		Week 4	CR845	90	79 (87.8)	12.7 (4.1)	5	13.0	22	
			Placebo	83	81 (97.6)	13.6 (3.6)	5	14.0	24	
		Week 8	CR845	90	78 (86.7)	12.3 (4.2)	5	12.0	22	
			Placebo	83	79 (95.2)	13.3 (3.8)	5	14.0	22	
		Week 10	CR845	90	74 (82.2)	12.0 (4.3)	5	11.0	23	
			Placebo	83	76 (91.6)	13.3 (3.6)	5	13.0	25	
		Week 12	CR845	90	73 (81.1)	12.0 (4.4)	5	11.0	23	
			Placebo	83	77 (92.8)	12.8 (3.8)	5	13.0	23	
	Change from baseline in 5-D total score	Week 4	CR845	90	79 (87.8)	-3.7 (4.0)	-14	-3.0	4	-0.36 [-0.67, -0.05]
			Placebo	83	81 (97.6)	-2.4 (3.4)	-11	-2.0	11	
		Week 8	CR845	90	78 (86.7)	-4.0 (3.8)	-16	-4.0	4	-0.34 [-0.66, -0.03]
			Placebo	83	79 (95.2)	-2.7 (3.8)	-12	-2.0	8	
		Week 10	CR845	90	74 (82.2)	-4.3 (4.3)	-16	-4.5	5	-0.41 [-0.73, -0.08]
			Placebo	83	76 (91.6)	-2.7 (3.8)	-11	-3.0	12	
		Week 12	CR845	90	73 (81.1)	-4.2 (4.6)	-16	-4.0	6	-0.22 [-0.54, 0.10]
			Placebo	83	77 (92.8)	-3.3 (3.7)	-11	-3.0	10	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DTC_ISHB: Change from baseline in 5-D total score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Male	5-D total score	Baseline	CR845	137	135 (98.5)	16.7 (3.4)	7	17.0	25	
			Placebo	139	139 (100.0)	15.9 (3.4)	7	16.0	24	
		Week 4	CR845	137	124 (90.5)	13.5 (3.7)	5	14.0	22	
			Placebo	139	131 (94.2)	13.2 (3.5)	5	13.0	22	
		Week 8	CR845	137	122 (89.1)	13.0 (3.9)	5	13.0	22	
			Placebo	139	132 (95.0)	12.6 (3.6)	5	13.0	22	
		Week 10	CR845	137	118 (86.1)	12.8 (4.1)	5	12.0	23	
			Placebo	139	127 (91.4)	12.5 (3.4)	5	12.0	22	
		Week 12	CR845	137	118 (86.1)	12.6 (4.3)	5	12.0	23	
			Placebo	139	127 (91.4)	12.5 (3.7)	5	13.0	22	
	Change from baseline in 5-D total score	Week 4	CR845	137	123 (89.8)	-3.2 (3.3)	-14	-3.0	4	-0.16 [-0.41, 0.09]
			Placebo	139	131 (94.2)	-2.6 (3.8)	-12	-2.0	9	
		Week 8	CR845	137	121 (88.3)	-3.7 (3.4)	-16	-4.0	3	-0.11 [-0.36, 0.14]
			Placebo	139	132 (95.0)	-3.3 (3.7)	-12	-3.0	6	
		Week 10	CR845	137	117 (85.4)	-3.9 (3.7)	-16	-4.0	5	-0.15 [-0.40, 0.10]
			Placebo	139	127 (91.4)	-3.4 (3.6)	-12	-3.0	10	
		Week 12	CR845	137	117 (85.4)	-4.2 (3.9)	-16	-4.0	4	-0.22 [-0.47, 0.03]
			Placebo	139	127 (91.4)	-3.4 (3.8)	-11	-3.0	8	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DTC_ISHB: Change from baseline in 5-D total score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Female	5-D total score	Baseline	CR845	100	97 (97.0)	16.7 (3.7)	7	17.0	24	
			Placebo	97	97 (100.0)	16.6 (3.1)	10	16.0	24	
		Week 4	CR845	100	89 (89.0)	11.9 (3.8)	5	12.0	23	
			Placebo	97	94 (96.9)	14.6 (4.1)	8	14.0	25	
		Week 8	CR845	100	87 (87.0)	11.1 (4.1)	5	11.0	25	
			Placebo	97	90 (92.8)	13.5 (4.0)	5	13.0	23	
		Week 10	CR845	100	88 (88.0)	11.0 (3.8)	5	10.0	22	
			Placebo	97	90 (92.8)	13.7 (4.3)	5	13.0	25	
		Week 12	CR845	100	86 (86.0)	11.0 (4.1)	5	10.0	23	
			Placebo	97	92 (94.8)	13.1 (4.5)	5	12.0	23	
	Change from baseline in 5-D total score	Week 4	CR845	100	87 (87.0)	-4.9 (3.9)	-14	-5.0	3	-0.79 [-1.09, -0.48]
			Placebo	97	94 (96.9)	-2.0 (3.6)	-10	-2.0	11	
		Week 8	CR845	100	85 (85.0)	-5.7 (4.2)	-16	-6.0	4	-0.61 [-0.92, -0.31]
			Placebo	97	90 (92.8)	-3.1 (4.2)	-14	-3.0	8	
		Week 10	CR845	100	86 (86.0)	-5.8 (4.4)	-17	-6.0	4	-0.64 [-0.95, -0.34]
			Placebo	97	90 (92.8)	-3.0 (4.5)	-14	-3.0	12	
		Week 12	CR845	100	84 (84.0)	-5.7 (4.8)	-19	-5.0	6	-0.48 [-0.78, -0.18]
			Placebo	97	92 (94.8)	-3.5 (4.4)	-14	-3.5	10	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DTC_ISHC: Change from baseline in 5-D total score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Black/African American	5-D total score	Baseline	CR845	53	50 (94.3)	16.9 (3.5)	9	16.5	25	
			Placebo	38	38 (100.0)	16.6 (3.6)	10	16.0	24	
		Week 4	CR845	53	47 (88.7)	13.6 (3.9)	7	14.0	22	
			Placebo	38	35 (92.1)	13.9 (4.1)	8	13.0	25	
		Week 8	CR845	53	47 (88.7)	12.7 (4.3)	5	12.0	22	
			Placebo	38	37 (97.4)	13.5 (3.7)	5	13.0	22	
		Week 10	CR845	53	44 (83.0)	12.4 (4.4)	5	11.0	23	
			Placebo	38	36 (94.7)	13.6 (4.7)	5	13.5	25	
		Week 12	CR845	53	44 (83.0)	12.1 (4.4)	5	10.0	22	
			Placebo	38	37 (97.4)	13.2 (4.3)	5	13.0	23	
	Change from baseline in 5-D total score	Week 4	CR845	53	45 (84.9)	-3.3 (3.6)	-14	-3.0	1	-0.19 [-0.64, 0.25]
			Placebo	38	35 (92.1)	-2.5 (4.6)	-12	-2.0	11	
		Week 8	CR845	53	45 (84.9)	-4.4 (3.9)	-16	-5.0	2	-0.26 [-0.69, 0.18]
			Placebo	38	37 (97.4)	-3.2 (4.8)	-14	-3.0	8	
		Week 10	CR845	53	42 (79.2)	-4.7 (4.2)	-16	-4.5	4	-0.31 [-0.76, 0.14]
			Placebo	38	36 (94.7)	-3.2 (5.4)	-14	-4.0	12	
		Week 12	CR845	53	42 (79.2)	-5.0 (4.3)	-16	-5.0	3	-0.32 [-0.76, 0.13]
			Placebo	38	37 (97.4)	-3.6 (4.9)	-14	-3.0	10	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DTC_ISHC: Change from baseline in 5-D total score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
White	5-D total score	Baseline	CR845	164	162 (98.8)	16.7 (3.6)	7	17.0	24	
			Placebo	169	169 (100.0)	16.1 (3.1)	7	16.0	24	
		Week 4	CR845	164	149 (90.9)	12.6 (3.8)	5	12.0	23	
			Placebo	169	162 (95.9)	13.9 (3.8)	5	14.0	24	
		Week 8	CR845	164	145 (88.4)	12.2 (4.1)	5	12.0	25	
			Placebo	169	159 (94.1)	12.9 (3.8)	5	13.0	23	
		Week 10	CR845	164	146 (89.0)	12.0 (4.1)	5	11.0	23	
			Placebo	169	156 (92.3)	12.9 (3.6)	5	12.5	22	
		Week 12	CR845	164	144 (87.8)	11.8 (4.3)	5	11.0	23	
			Placebo	169	159 (94.1)	12.8 (4.0)	5	12.0	22	
	Change from baseline in 5-D total score	Week 4	CR845	164	148 (90.2)	-4.1 (3.8)	-13	-4.0	4	-0.52 [-0.74, -0.29]
			Placebo	169	162 (95.9)	-2.2 (3.5)	-10	-2.0	9	
		Week 8	CR845	164	144 (87.8)	-4.6 (3.9)	-16	-4.0	4	-0.37 [-0.60, -0.14]
			Placebo	169	159 (94.1)	-3.1 (3.7)	-12	-3.0	7	
		Week 10	CR845	164	145 (88.4)	-4.7 (4.1)	-16	-5.0	5	-0.42 [-0.65, -0.19]
			Placebo	169	156 (92.3)	-3.1 (3.6)	-11	-3.0	10	
		Week 12	CR845	164	143 (87.2)	-4.9 (4.3)	-19	-5.0	6	-0.42 [-0.65, -0.19]
			Placebo	169	159 (94.1)	-3.2 (3.7)	-14	-3.0	8	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DTC_ISHC: Change from baseline in 5-D total score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Other	5-D total score	Baseline	CR845	20	20 (100.0)	16.1 (3.1)	9	16.0	24	
			Placebo	29	29 (100.0)	16.3 (4.0)	9	16.0	23	
		Week 4	CR845	20	17 (85.0)	12.1 (4.2)	5	11.0	22	
			Placebo	29	28 (96.6)	13.3 (3.8)	8	13.0	20	
		Week 8	CR845	20	17 (85.0)	11.3 (2.8)	7	11.0	17	
			Placebo	29	26 (89.7)	12.6 (3.5)	7	13.0	19	
		Week 10	CR845	20	16 (80.0)	11.1 (3.8)	7	10.0	18	
			Placebo	29	25 (86.2)	12.5 (4.2)	7	12.0	22	
		Week 12	CR845	20	16 (80.0)	12.1 (3.9)	6	12.0	19	
			Placebo	29	23 (79.3)	11.8 (4.4)	5	11.0	20	
	Change from baseline in 5-D total score	Week 4	CR845	20	17 (85.0)	-4.0 (2.6)	-10	-4.0	0	-0.31 [-0.91, 0.30]
			Placebo	29	28 (96.6)	-3.0 (3.7)	-10	-2.0	2	
		Week 8	CR845	20	17 (85.0)	-4.8 (3.3)	-13	-4.0	0	-0.27 [-0.88, 0.35]
			Placebo	29	26 (89.7)	-3.8 (3.8)	-12	-4.0	4	
		Week 10	CR845	20	16 (80.0)	-4.9 (4.3)	-17	-4.5	0	-0.26 [-0.89, 0.37]
			Placebo	29	25 (86.2)	-3.8 (4.0)	-12	-4.0	3	
		Week 12	CR845	20	16 (80.0)	-3.8 (4.8)	-14	-4.0	4	0.18 [-0.46, 0.82]
			Placebo	29	23 (79.3)	-4.6 (4.6)	-13	-5.0	5	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DTC_ISHD: Change from baseline in 5-D total score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 4 to < 7	5-D total score	Baseline	CR845	102	100 (98.0)	15.0 (3.0)	7	15.0	21	
			Placebo	113	113 (100.0)	14.6 (2.9)	7	14.0	22	
		Week 4	CR845	102	95 (93.1)	11.7 (3.2)	5	11.0	23	
			Placebo	113	109 (96.5)	12.7 (3.5)	5	13.0	23	
		Week 8	CR845	102	95 (93.1)	11.0 (3.1)	5	11.0	22	
			Placebo	113	105 (92.9)	12.3 (3.5)	5	12.0	22	
		Week 10	CR845	102	92 (90.2)	10.7 (3.3)	5	10.0	23	
			Placebo	113	102 (90.3)	12.1 (3.7)	5	11.0	22	
		Week 12	CR845	102	91 (89.2)	10.7 (3.6)	5	10.0	23	
			Placebo	113	103 (91.2)	11.8 (3.7)	5	11.0	21	
	Change from baseline in 5-D total score	Week 4	CR845	102	93 (91.2)	-3.3 (3.3)	-13	-3.0	3	-0.43 [-0.71, -0.15]
			Placebo	113	109 (96.5)	-1.9 (3.5)	-10	-2.0	9	
		Week 8	CR845	102	93 (91.2)	-4.0 (3.2)	-13	-4.0	4	-0.50 [-0.79, -0.22]
			Placebo	113	105 (92.9)	-2.4 (3.4)	-12	-2.0	7	
		Week 10	CR845	102	90 (88.2)	-4.3 (3.1)	-13	-5.0	5	-0.55 [-0.84, -0.26]
			Placebo	113	102 (90.3)	-2.4 (3.6)	-12	-3.0	10	
		Week 12	CR845	102	89 (87.3)	-4.4 (4.0)	-13	-4.0	6	-0.43 [-0.71, -0.14]
			Placebo	113	103 (91.2)	-2.8 (3.5)	-12	-3.0	8	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DTC_ISHD: Change from baseline in 5-D total score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 7	5-D total score	Baseline	CR845	135	132 (97.8)	18.0 (3.4)	7	18.0	25	
			Placebo	123	123 (100.0)	17.7 (2.9)	10	18.0	24	
		Week 4	CR845	135	118 (87.4)	13.7 (4.1)	5	14.0	22	
			Placebo	123	116 (94.3)	14.8 (3.9)	8	14.0	25	
		Week 8	CR845	135	114 (84.4)	13.2 (4.5)	5	13.0	25	
			Placebo	123	117 (95.1)	13.6 (3.9)	5	14.0	23	
		Week 10	CR845	135	114 (84.4)	13.1 (4.4)	5	13.0	23	
			Placebo	123	115 (93.5)	13.7 (3.9)	5	14.0	25	
		Week 12	CR845	135	113 (83.7)	12.9 (4.5)	5	13.0	23	
			Placebo	123	116 (94.3)	13.6 (4.2)	5	13.0	23	
	Change from baseline in 5-D total score	Week 4	CR845	135	117 (86.7)	-4.3 (3.9)	-14	-4.0	4	-0.41 [-0.67, -0.15]
			Placebo	123	116 (94.3)	-2.8 (3.9)	-12	-3.0	11	
		Week 8	CR845	135	113 (83.7)	-5.0 (4.3)	-16	-5.0	3	-0.22 [-0.48, 0.04]
			Placebo	123	117 (95.1)	-4.0 (4.2)	-14	-4.0	8	
		Week 10	CR845	135	113 (83.7)	-5.1 (4.8)	-17	-5.0	4	-0.27 [-0.53, -0.00]
			Placebo	123	115 (93.5)	-3.9 (4.1)	-14	-4.0	12	
		Week 12	CR845	135	112 (83.0)	-5.2 (4.6)	-19	-5.0	3	-0.27 [-0.53, -0.01]
			Placebo	123	116 (94.3)	-4.0 (4.4)	-14	-4.0	10	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DTC_ISHE: Change from baseline in 5-D total score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	5-D total score	Baseline	CR845	195	190 (97.4)	16.7 (3.6)	7	17.0	25	
			Placebo	199	199 (100.0)	16.0 (3.3)	7	16.0	24	
		Week 4	CR845	195	175 (89.7)	12.8 (3.8)	5	13.0	23	
			Placebo	199	191 (96.0)	13.8 (3.9)	5	13.0	25	
		Week 8	CR845	195	173 (88.7)	12.3 (4.1)	5	12.0	25	
			Placebo	199	185 (93.0)	12.8 (3.8)	5	13.0	23	
		Week 10	CR845	195	171 (87.7)	12.0 (3.9)	5	11.0	23	
			Placebo	199	180 (90.5)	12.9 (4.0)	5	12.5	25	
		Week 12	CR845	195	170 (87.2)	11.9 (4.2)	5	11.0	23	
			Placebo	199	183 (92.0)	12.8 (4.1)	5	12.0	23	
	Change from baseline in 5-D total score	Week 4	CR845	195	172 (88.2)	-3.9 (3.6)	-14	-4.0	4	-0.45 [-0.66, -0.24]
			Placebo	199	191 (96.0)	-2.2 (3.8)	-12	-2.0	11	
		Week 8	CR845	195	170 (87.2)	-4.4 (3.6)	-16	-5.0	4	-0.32 [-0.53, -0.11]
			Placebo	199	185 (93.0)	-3.2 (4.0)	-14	-3.0	8	
		Week 10	CR845	195	168 (86.2)	-4.7 (3.8)	-16	-5.0	5	-0.42 [-0.64, -0.21]
			Placebo	199	180 (90.5)	-3.0 (4.1)	-14	-3.0	12	
		Week 12	CR845	195	167 (85.6)	-4.8 (4.2)	-19	-5.0	6	-0.39 [-0.60, -0.17]
			Placebo	199	183 (92.0)	-3.2 (4.1)	-14	-3.0	10	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DTC_ISHE: Change from baseline in 5-D total score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	5-D total score	Baseline	CR845	42	42 (100.0)	16.7 (3.3)	11	17.0	24	
			Placebo	37	37 (100.0)	17.3 (3.1)	10	18.0	22	
		Week 4	CR845	42	38 (90.5)	12.7 (4.0)	5	12.5	22	
			Placebo	37	34 (91.9)	14.0 (3.7)	7	14.0	21	
		Week 8	CR845	42	36 (85.7)	11.7 (4.3)	5	12.0	21	
			Placebo	37	37 (100.0)	13.8 (3.5)	7	14.0	21	
		Week 10	CR845	42	35 (83.3)	12.1 (4.9)	5	12.0	23	
			Placebo	37	37 (100.0)	13.3 (3.3)	7	14.0	20	
		Week 12	CR845	42	34 (81.0)	11.9 (4.6)	5	11.0	23	
			Placebo	37	36 (97.3)	12.7 (3.7)	5	12.5	20	
	Change from baseline in 5-D total score	Week 4	CR845	42	38 (90.5)	-4.1 (3.9)	-14	-3.0	1	-0.26 [-0.73, 0.20]
			Placebo	37	34 (91.9)	-3.1 (3.2)	-11	-3.0	3	
		Week 8	CR845	42	36 (85.7)	-5.1 (4.9)	-16	-4.0	1	-0.37 [-0.83, 0.09]
			Placebo	37	37 (100.0)	-3.5 (3.5)	-12	-4.0	6	
		Week 10	CR845	42	35 (83.3)	-4.8 (5.5)	-17	-4.0	4	-0.18 [-0.64, 0.29]
			Placebo	37	37 (100.0)	-4.0 (3.3)	-12	-4.0	3	
		Week 12	CR845	42	34 (81.0)	-4.9 (5.3)	-16	-4.5	3	-0.10 [-0.57, 0.36]
			Placebo	37	36 (97.3)	-4.5 (3.5)	-12	-5.0	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DTC_ISHF: Change from baseline in 5-D total score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	5-D total score	Baseline	CR845	150	146 (97.3)	16.5 (3.5)	7	17.0	25	
			Placebo	151	151 (100.0)	16.1 (3.3)	7	16.0	24	
		Week 4	CR845	150	139 (92.7)	12.6 (3.8)	5	12.0	23	
			Placebo	151	146 (96.7)	13.8 (3.6)	5	14.0	24	
		Week 8	CR845	150	137 (91.3)	12.1 (4.0)	5	11.0	22	
			Placebo	151	142 (94.0)	12.8 (3.6)	5	13.0	22	
		Week 10	CR845	150	133 (88.7)	12.1 (4.1)	5	11.0	23	
			Placebo	151	140 (92.7)	12.7 (3.6)	5	12.0	22	
		Week 12	CR845	150	134 (89.3)	11.9 (4.3)	5	11.0	23	
			Placebo	151	141 (93.4)	12.7 (3.8)	5	12.0	22	
	Change from baseline in 5-D total score	Week 4	CR845	150	136 (90.7)	-3.9 (3.7)	-14	-3.0	4	-0.41 [-0.65, -0.18]
			Placebo	151	146 (96.7)	-2.3 (3.8)	-12	-2.0	9	
		Week 8	CR845	150	134 (89.3)	-4.4 (3.5)	-14	-4.0	4	-0.30 [-0.53, -0.06]
			Placebo	151	142 (94.0)	-3.3 (3.9)	-14	-3.0	7	
		Week 10	CR845	150	130 (86.7)	-4.4 (3.7)	-14	-5.0	4	-0.27 [-0.51, -0.03]
			Placebo	151	140 (92.7)	-3.4 (4.0)	-14	-3.0	10	
		Week 12	CR845	150	131 (87.3)	-4.6 (4.1)	-16	-5.0	6	-0.27 [-0.51, -0.03]
			Placebo	151	141 (93.4)	-3.5 (4.1)	-14	-3.0	8	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DTC_ISHF: Change from baseline in 5-D total score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	5-D total score	Baseline	CR845	87	86 (98.9)	17.0 (3.5)	9	17.0	24	
			Placebo	85	85 (100.0)	16.3 (3.4)	9	16.0	24	
		Week 4	CR845	87	74 (85.1)	13.1 (3.9)	5	13.0	22	
			Placebo	85	79 (92.9)	13.8 (4.3)	7	13.0	25	
		Week 8	CR845	87	72 (82.8)	12.4 (4.3)	5	12.0	25	
			Placebo	85	80 (94.1)	13.3 (4.1)	7	13.0	23	
		Week 10	CR845	87	73 (83.9)	11.9 (4.2)	5	11.0	21	
			Placebo	85	77 (90.6)	13.4 (4.3)	6	13.0	25	
		Week 12	CR845	87	70 (80.5)	12.0 (4.2)	5	11.5	20	
			Placebo	85	78 (91.8)	12.9 (4.5)	5	13.0	23	
	Change from baseline in 5-D total score	Week 4	CR845	87	74 (85.1)	-3.9 (3.6)	-14	-4.0	3	-0.44 [-0.76, -0.12]
			Placebo	85	79 (92.9)	-2.3 (3.7)	-10	-2.0	11	
		Week 8	CR845	87	72 (82.8)	-4.7 (4.4)	-16	-4.5	3	-0.39 [-0.71, -0.07]
			Placebo	85	80 (94.1)	-3.1 (4.0)	-12	-3.0	8	
		Week 10	CR845	87	73 (83.9)	-5.3 (4.8)	-17	-4.0	5	-0.55 [-0.87, -0.22]
			Placebo	85	77 (90.6)	-2.9 (4.0)	-12	-3.0	12	
		Week 12	CR845	87	70 (80.5)	-5.3 (4.7)	-19	-4.5	4	-0.45 [-0.78, -0.13]
			Placebo	85	78 (91.8)	-3.3 (4.0)	-12	-3.0	10	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DTC_ISHG: Change from baseline in 5-D total score by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
USA	5-D total score	Baseline	CR845	146	141 (96.6)	17.0 (3.6)	7	17.0	25	
			Placebo	133	133 (100.0)	16.1 (3.4)	7	16.0	24	
		Week 4	CR845	146	133 (91.1)	13.3 (3.6)	5	13.0	23	
			Placebo	133	123 (92.5)	14.0 (3.8)	8	14.0	25	
		Week 8	CR845	146	131 (89.7)	12.6 (3.9)	5	12.0	22	
			Placebo	133	125 (94.0)	12.8 (3.8)	5	13.0	22	
		Week 10	CR845	146	129 (88.4)	12.5 (3.9)	5	12.0	23	
			Placebo	133	122 (91.7)	12.7 (3.9)	5	12.0	25	
		Week 12	CR845	146	128 (87.7)	12.1 (4.0)	5	11.0	23	
			Placebo	133	125 (94.0)	12.6 (3.9)	5	12.0	23	
	Change from baseline in 5-D total score	Week 4	CR845	146	130 (89.0)	-3.6 (3.6)	-14	-3.0	4	-0.44 [-0.69, -0.19]
			Placebo	133	123 (92.5)	-1.9 (3.8)	-12	-2.0	9	
		Week 8	CR845	146	128 (87.7)	-4.3 (3.8)	-16	-4.0	4	-0.27 [-0.52, -0.03]
			Placebo	133	125 (94.0)	-3.3 (4.0)	-14	-3.0	7	
		Week 10	CR845	146	126 (86.3)	-4.5 (3.9)	-16	-4.0	5	-0.27 [-0.52, -0.02]
			Placebo	133	122 (91.7)	-3.4 (4.0)	-14	-3.0	10	
		Week 12	CR845	146	125 (85.6)	-4.9 (4.2)	-16	-5.0	6	-0.35 [-0.60, -0.10]
			Placebo	133	125 (94.0)	-3.5 (4.1)	-14	-3.0	8	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DTC_ISHG: Change from baseline in 5-D total score by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Asia	5-D total score	Baseline	CR845	8	8 (100.0)	14.3 (2.9)	9	14.5	18	
			Placebo	12	12 (100.0)	16.7 (3.2)	10	17.0	21	
		Week 4	CR845	8	8 (100.0)	9.8 (3.2)	5	10.0	15	
			Placebo	12	12 (100.0)	13.1 (3.4)	8	13.0	20	
		Week 8	CR845	8	7 (87.5)	9.7 (2.3)	7	9.0	14	
			Placebo	12	12 (100.0)	12.3 (3.3)	7	11.5	18	
		Week 10	CR845	8	7 (87.5)	9.4 (3.0)	7	8.0	15	
			Placebo	12	11 (91.7)	12.2 (4.0)	7	13.0	19	
		Week 12	CR845	8	7 (87.5)	10.0 (2.3)	8	9.0	13	
			Placebo	12	11 (91.7)	11.6 (5.1)	5	10.0	20	
	Change from baseline in 5-D total score	Week 4	CR845	8	8 (100.0)	-4.5 (1.8)	-6	-5.0	-1	-0.30 [-1.20, 0.60]
			Placebo	12	12 (100.0)	-3.6 (3.6)	-8	-3.5	1	
		Week 8	CR845	8	7 (87.5)	-4.1 (2.2)	-8	-4.0	-2	0.05 [-0.88, 0.98]
			Placebo	12	12 (100.0)	-4.3 (4.7)	-12	-4.0	4	
		Week 10	CR845	8	7 (87.5)	-4.4 (2.5)	-8	-5.0	-1	0.05 [-0.90, 1.00]
			Placebo	12	11 (91.7)	-4.6 (5.2)	-12	-4.0	3	
		Week 12	CR845	8	7 (87.5)	-3.9 (3.9)	-8	-4.0	4	0.26 [-0.69, 1.21]
			Placebo	12	11 (91.7)	-5.2 (5.8)	-13	-5.0	5	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DTC_ISHG: Change from baseline in 5-D total score by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Eastern Europe	5-D total score	Baseline	CR845	54	54 (100.0)	16.3 (3.8)	7	16.0	24	
			Placebo	60	60 (100.0)	15.8 (3.1)	9	15.5	24	
		Week 4	CR845	54	50 (92.6)	12.2 (3.7)	5	11.5	21	
			Placebo	60	59 (98.3)	13.0 (3.7)	5	13.0	23	
		Week 8	CR845	54	48 (88.9)	11.5 (4.7)	5	11.0	25	
			Placebo	60	59 (98.3)	12.7 (3.7)	5	12.0	23	
		Week 10	CR845	54	48 (88.9)	11.0 (4.2)	5	10.0	23	
			Placebo	60	59 (98.3)	13.2 (3.3)	5	13.0	22	
		Week 12	CR845	54	47 (87.0)	11.0 (4.7)	5	10.0	23	
			Placebo	60	58 (96.7)	12.9 (3.8)	5	12.0	21	
	Change from baseline in 5-D total score	Week 4	CR845	54	50 (92.6)	-4.2 (3.8)	-13	-4.0	2	-0.43 [-0.81, -0.05]
			Placebo	60	59 (98.3)	-2.7 (3.3)	-10	-2.0	6	
		Week 8	CR845	54	48 (88.9)	-4.9 (4.1)	-15	-5.0	3	-0.47 [-0.85, -0.08]
			Placebo	60	59 (98.3)	-3.1 (3.5)	-11	-2.0	6	
		Week 10	CR845	54	48 (88.9)	-5.1 (4.4)	-15	-5.0	4	-0.68 [-1.08, -0.29]
			Placebo	60	59 (98.3)	-2.6 (2.9)	-8	-3.0	6	
		Week 12	CR845	54	47 (87.0)	-5.0 (4.8)	-19	-5.0	4	-0.52 [-0.91, -0.13]
			Placebo	60	58 (96.7)	-3.0 (3.0)	-9	-3.0	6	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DTC_ISHG: Change from baseline in 5-D total score by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Western Europe/European origin	5-D total score	Baseline	CR845	29	29 (100.0)	17.1 (2.7)	13	17.0	24	
			Placebo	31	31 (100.0)	17.5 (3.4)	9	18.0	23	
		Week 4	CR845	29	22 (75.9)	12.3 (5.1)	5	11.0	22	
			Placebo	31	31 (100.0)	14.7 (4.4)	8	14.0	24	
		Week 8	CR845	29	23 (79.3)	12.2 (4.2)	5	11.0	20	
			Placebo	31	26 (83.9)	14.6 (4.0)	7	14.0	21	
		Week 10	CR845	29	22 (75.9)	12.0 (4.9)	5	11.5	23	
			Placebo	31	25 (80.6)	14.3 (4.7)	6	13.0	25	
		Week 12	CR845	29	22 (75.9)	13.0 (4.9)	5	12.0	22	
			Placebo	31	25 (80.6)	14.0 (4.8)	5	14.0	23	
	Change from baseline in 5-D total score	Week 4	CR845	29	22 (75.9)	-5.0 (4.2)	-13	-4.0	2	-0.56 [-1.11, 0.00]
			Placebo	31	31 (100.0)	-2.7 (4.2)	-11	-2.0	11	
		Week 8	CR845	29	23 (79.3)	-5.1 (4.1)	-14	-5.0	0	-0.51 [-1.08, 0.06]
			Placebo	31	26 (83.9)	-3.0 (4.2)	-9	-3.0	8	
		Week 10	CR845	29	22 (75.9)	-5.3 (5.0)	-17	-4.0	3	-0.48 [-1.06, 0.10]
			Placebo	31	25 (80.6)	-2.9 (5.0)	-11	-4.0	12	
		Week 12	CR845	29	22 (75.9)	-4.2 (4.6)	-14	-3.5	3	-0.18 [-0.76, 0.39]
			Placebo	31	25 (80.6)	-3.3 (4.7)	-10	-3.0	10	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DTC_ISHH: Change from baseline in 5-D total score by dialysis method
ITT

H: Dialysis method	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Hemodialysis (HD)	5-D total score	Baseline	CR845	222	217 (97.7)	16.7 (3.5)	7	17.0	25	
			Placebo	199	199 (100.0)	16.2 (3.4)	7	16.0	24	
		Week 4	CR845	222	200 (90.1)	12.8 (3.8)	5	13.0	23	
			Placebo	199	188 (94.5)	13.8 (3.8)	7	13.0	25	
		Week 8	CR845	222	196 (88.3)	12.2 (4.0)	5	12.0	25	
			Placebo	199	187 (94.0)	13.0 (3.8)	5	13.0	23	
		Week 10	CR845	222	194 (87.4)	12.1 (4.0)	5	11.0	23	
			Placebo	199	185 (93.0)	12.9 (3.8)	5	13.0	25	
		Week 12	CR845	222	191 (86.0)	11.8 (4.2)	5	11.0	23	
			Placebo	199	185 (93.0)	12.6 (4.0)	5	12.0	23	
	Change from baseline in 5-D total score	Week 4	CR845	222	197 (88.7)	-3.9 (3.7)	-14	-4.0	4	-0.44 [-0.64, -0.24]
			Placebo	199	188 (94.5)	-2.3 (3.7)	-12	-2.0	9	
		Week 8	CR845	222	193 (86.9)	-4.6 (3.9)	-16	-4.0	4	-0.34 [-0.55, -0.14]
			Placebo	199	187 (94.0)	-3.2 (3.9)	-14	-3.0	7	
		Week 10	CR845	222	191 (86.0)	-4.7 (4.2)	-17	-5.0	5	-0.34 [-0.55, -0.14]
			Placebo	199	185 (93.0)	-3.3 (3.9)	-14	-3.0	10	
		Week 12	CR845	222	188 (84.7)	-4.9 (4.4)	-19	-5.0	6	-0.32 [-0.52, -0.12]
			Placebo	199	185 (93.0)	-3.6 (4.0)	-14	-3.0	8	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DTC_ISHH: Change from baseline in 5-D total score by dialysis method
ITT

H: Dialysis method	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Hemodiafiltration (HDF)	5-D total score	Baseline	CR845	15	15 (100.0)	16.4 (3.6)	12	16.0	24	
			Placebo	37	37 (100.0)	16.4 (3.1)	9	16.0	23	
		Week 4	CR845	15	13 (86.7)	13.0 (4.7)	5	12.0	20	
			Placebo	37	37 (100.0)	13.8 (4.2)	5	14.0	24	
		Week 8	CR845	15	13 (86.7)	12.6 (4.8)	7	12.0	22	
			Placebo	37	35 (94.6)	12.9 (3.8)	5	13.0	21	
		Week 10	CR845	15	12 (80.0)	11.5 (5.3)	5	10.5	23	
			Placebo	37	32 (86.5)	13.6 (4.1)	5	13.5	25	
		Week 12	CR845	15	13 (86.7)	12.8 (5.4)	5	11.0	23	
			Placebo	37	34 (91.9)	13.8 (4.5)	5	14.0	23	
	Change from baseline in 5-D total score	Week 4	CR845	15	13 (86.7)	-3.7 (3.1)	-9	-3.0	0	-0.28 [-0.92, 0.35]
			Placebo	37	37 (100.0)	-2.6 (4.2)	-11	-2.0	11	
		Week 8	CR845	15	13 (86.7)	-4.1 (3.3)	-9	-5.0	1	-0.18 [-0.82, 0.45]
			Placebo	37	35 (94.6)	-3.4 (4.0)	-10	-4.0	8	
		Week 10	CR845	15	12 (80.0)	-5.2 (3.5)	-9	-6.0	2	-0.63 [-1.31, 0.05]
			Placebo	37	32 (86.5)	-2.5 (4.4)	-11	-3.0	12	
		Week 12	CR845	15	13 (86.7)	-3.9 (2.8)	-9	-5.0	2	-0.30 [-0.94, 0.34]
			Placebo	37	34 (91.9)	-2.7 (4.3)	-9	-3.5	10	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DDC_ISHA: Change from baseline in 5-D degree score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
< 65 years	5-D degree score	Baseline	CR845	147	144 (98.0)	3.5 (0.8)	1	4.0	5	
			Placebo	153	153 (100.0)	3.5 (0.7)	2	3.0	5	
		Week 4	CR845	147	134 (91.2)	2.8 (0.8)	1	3.0	5	
			Placebo	153	144 (94.1)	3.0 (0.8)	1	3.0	5	
		Week 8	CR845	147	132 (89.8)	2.7 (0.8)	1	3.0	5	
			Placebo	153	143 (93.5)	2.8 (0.7)	1	3.0	5	
		Week 10	CR845	147	132 (89.8)	2.6 (0.9)	1	2.0	5	
			Placebo	153	141 (92.2)	2.8 (0.8)	1	3.0	5	
		Week 12	CR845	147	131 (89.1)	2.6 (0.9)	1	2.0	5	
			Placebo	153	142 (92.8)	2.7 (0.8)	1	3.0	4	
	Change from baseline in 5-D degree score	Week 4	CR845	147	132 (89.8)	-0.7 (1.0)	-3	-1.0	3	-0.25 [-0.49, -0.02]
			Placebo	153	144 (94.1)	-0.5 (0.8)	-3	0.0	2	
		Week 8	CR845	147	130 (88.4)	-0.9 (1.1)	-4	-1.0	3	-0.16 [-0.40, 0.08]
			Placebo	153	143 (93.5)	-0.7 (0.9)	-3	-1.0	1	
		Week 10	CR845	147	130 (88.4)	-0.9 (1.1)	-4	-1.0	3	-0.20 [-0.44, 0.04]
			Placebo	153	141 (92.2)	-0.7 (0.9)	-3	-1.0	2	
		Week 12	CR845	147	129 (87.8)	-1.0 (1.1)	-4	-1.0	3	-0.15 [-0.39, 0.08]
			Placebo	153	142 (92.8)	-0.8 (0.9)	-3	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DDC_ISHA: Change from baseline in 5-D degree score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 65 years	5-D degree score	Baseline	CR845	90	90 (100.0)	3.5 (0.7)	2	3.0	5	
			Placebo	83	83 (100.0)	3.4 (0.7)	2	3.0	5	
		Week 4	CR845	90	80 (88.9)	2.7 (0.8)	1	3.0	4	
			Placebo	83	81 (97.6)	3.0 (0.8)	1	3.0	5	
		Week 8	CR845	90	78 (86.7)	2.7 (0.9)	1	3.0	5	
			Placebo	83	79 (95.2)	3.0 (0.8)	1	3.0	5	
		Week 10	CR845	90	74 (82.2)	2.6 (0.9)	1	3.0	5	
			Placebo	83	76 (91.6)	2.9 (0.7)	1	3.0	5	
		Week 12	CR845	90	74 (82.2)	2.6 (0.9)	1	3.0	5	
			Placebo	83	77 (92.8)	2.8 (0.8)	1	3.0	5	
	Change from baseline in 5-D degree score	Week 4	CR845	90	80 (88.9)	-0.8 (1.0)	-4	-1.0	1	-0.36 [-0.67, -0.04]
			Placebo	83	81 (97.6)	-0.5 (0.8)	-3	0.0	1	
		Week 8	CR845	90	78 (86.7)	-0.7 (1.1)	-4	-1.0	2	-0.26 [-0.58, 0.05]
			Placebo	83	79 (95.2)	-0.5 (0.8)	-3	0.0	1	
		Week 10	CR845	90	74 (82.2)	-0.8 (1.0)	-4	-1.0	1	-0.34 [-0.66, -0.02]
			Placebo	83	76 (91.6)	-0.5 (0.8)	-3	0.0	1	
		Week 12	CR845	90	74 (82.2)	-0.9 (1.2)	-4	-1.0	2	-0.20 [-0.52, 0.12]
			Placebo	83	77 (92.8)	-0.7 (0.9)	-3	-1.0	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DDC_ISHB: Change from baseline in 5-D degree score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Male	5-D degree score	Baseline	CR845	137	135 (98.5)	3.5 (0.7)	1	3.0	5	
			Placebo	139	139 (100.0)	3.4 (0.7)	2	3.0	5	
		Week 4	CR845	137	124 (90.5)	2.9 (0.8)	1	3.0	5	
			Placebo	139	131 (94.2)	2.9 (0.7)	1	3.0	5	
		Week 8	CR845	137	123 (89.8)	2.8 (0.8)	1	3.0	5	
			Placebo	139	132 (95.0)	2.8 (0.7)	1	3.0	4	
		Week 10	CR845	137	118 (86.1)	2.7 (0.9)	1	3.0	5	
			Placebo	139	127 (91.4)	2.7 (0.7)	1	3.0	5	
		Week 12	CR845	137	118 (86.1)	2.7 (0.9)	1	3.0	5	
			Placebo	139	127 (91.4)	2.7 (0.8)	1	3.0	4	
	Change from baseline in 5-D degree score	Week 4	CR845	137	123 (89.8)	-0.6 (0.8)	-2	-1.0	1	-0.02 [-0.27, 0.22]
			Placebo	139	131 (94.2)	-0.6 (0.9)	-3	0.0	2	
		Week 8	CR845	137	122 (89.1)	-0.6 (0.9)	-3	-1.0	2	0.01 [-0.24, 0.25]
			Placebo	139	132 (95.0)	-0.6 (0.9)	-3	0.0	1	
		Week 10	CR845	137	117 (85.4)	-0.7 (0.9)	-3	-1.0	1	0.03 [-0.22, 0.28]
			Placebo	139	127 (91.4)	-0.7 (0.9)	-3	-1.0	2	
		Week 12	CR845	137	117 (85.4)	-0.7 (0.9)	-3	-1.0	2	0.00 [-0.25, 0.26]
			Placebo	139	127 (91.4)	-0.7 (0.9)	-3	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DDC_ISHB: Change from baseline in 5-D degree score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Female	5-D degree score	Baseline	CR845	100	99 (99.0)	3.6 (0.8)	1	4.0	5	
			Placebo	97	97 (100.0)	3.6 (0.7)	2	3.0	5	
		Week 4	CR845	100	90 (90.0)	2.6 (0.8)	1	3.0	5	
			Placebo	97	94 (96.9)	3.2 (0.8)	2	3.0	5	
		Week 8	CR845	100	87 (87.0)	2.5 (0.9)	1	2.0	5	
			Placebo	97	90 (92.8)	2.9 (0.8)	1	3.0	5	
		Week 10	CR845	100	88 (88.0)	2.4 (0.9)	1	2.0	5	
			Placebo	97	90 (92.8)	3.0 (0.8)	1	3.0	5	
		Week 12	CR845	100	87 (87.0)	2.4 (0.9)	1	2.0	5	
			Placebo	97	92 (94.8)	2.8 (0.9)	1	3.0	5	
	Change from baseline in 5-D degree score	Week 4	CR845	100	89 (89.0)	-1.0 (1.1)	-4	-1.0	3	-0.62 [-0.92, -0.33]
			Placebo	97	94 (96.9)	-0.4 (0.8)	-2	0.0	1	
		Week 8	CR845	100	86 (86.0)	-1.1 (1.2)	-4	-1.0	3	-0.43 [-0.73, -0.13]
			Placebo	97	90 (92.8)	-0.7 (0.9)	-3	-1.0	1	
		Week 10	CR845	100	87 (87.0)	-1.1 (1.3)	-4	-1.0	3	-0.56 [-0.86, -0.26]
			Placebo	97	90 (92.8)	-0.6 (0.8)	-3	-1.0	2	
		Week 12	CR845	100	86 (86.0)	-1.2 (1.3)	-4	-1.0	3	-0.37 [-0.66, -0.07]
			Placebo	97	92 (94.8)	-0.8 (0.9)	-3	-1.0	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DDC_ISHC: Change from baseline in 5-D degree score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Black/African American	5-D degree score	Baseline	CR845	53	51 (96.2)	3.6 (0.8)	1	4.0	5	
			Placebo	38	38 (100.0)	3.5 (0.7)	2	3.0	5	
		Week 4	CR845	53	47 (88.7)	2.9 (0.8)	1	3.0	4	
			Placebo	38	35 (92.1)	3.1 (0.8)	2	3.0	5	
		Week 8	CR845	53	47 (88.7)	2.9 (1.1)	1	3.0	5	
			Placebo	38	37 (97.4)	2.9 (0.8)	1	3.0	4	
		Week 10	CR845	53	44 (83.0)	2.7 (0.9)	1	3.0	5	
			Placebo	38	36 (94.7)	2.9 (0.9)	1	3.0	5	
		Week 12	CR845	53	45 (84.9)	2.6 (0.8)	1	2.0	4	
			Placebo	38	37 (97.4)	2.8 (0.8)	1	3.0	4	
	Change from baseline in 5-D degree score	Week 4	CR845	53	45 (84.9)	-0.7 (1.0)	-4	-1.0	2	-0.29 [-0.74, 0.15]
			Placebo	38	35 (92.1)	-0.4 (0.9)	-3	0.0	1	
		Week 8	CR845	53	45 (84.9)	-0.8 (1.2)	-4	-1.0	2	-0.14 [-0.58, 0.30]
			Placebo	38	37 (97.4)	-0.6 (0.9)	-3	0.0	1	
		Week 10	CR845	53	42 (79.2)	-0.9 (1.1)	-4	-1.0	3	-0.25 [-0.69, 0.20]
			Placebo	38	36 (94.7)	-0.7 (1.0)	-2	-1.0	2	
		Week 12	CR845	53	43 (81.1)	-1.0 (1.0)	-4	-1.0	2	-0.28 [-0.72, 0.16]
			Placebo	38	37 (97.4)	-0.8 (0.8)	-3	-1.0	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DDC_ISHC: Change from baseline in 5-D degree score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
White	5-D degree score	Baseline	CR845	164	163 (99.4)	3.5 (0.8)	1	3.0	5	
			Placebo	169	169 (100.0)	3.5 (0.7)	2	3.0	5	
		Week 4	CR845	164	150 (91.5)	2.7 (0.8)	1	3.0	5	
			Placebo	169	162 (95.9)	3.0 (0.8)	1	3.0	5	
		Week 8	CR845	164	146 (89.0)	2.7 (0.8)	1	3.0	5	
			Placebo	169	159 (94.1)	2.9 (0.8)	1	3.0	5	
		Week 10	CR845	164	146 (89.0)	2.6 (0.9)	1	3.0	5	
			Placebo	169	156 (92.3)	2.9 (0.8)	1	3.0	5	
		Week 12	CR845	164	144 (87.8)	2.6 (0.9)	1	3.0	5	
			Placebo	169	159 (94.1)	2.8 (0.8)	1	3.0	5	
	Change from baseline in 5-D degree score	Week 4	CR845	164	150 (91.5)	-0.7 (1.0)	-3	-1.0	3	-0.27 [-0.49, -0.04]
			Placebo	169	162 (95.9)	-0.5 (0.8)	-3	0.0	2	
		Week 8	CR845	164	146 (89.0)	-0.8 (1.1)	-4	-1.0	3	-0.17 [-0.39, 0.06]
			Placebo	169	159 (94.1)	-0.6 (0.8)	-3	0.0	1	
		Week 10	CR845	164	146 (89.0)	-0.9 (1.1)	-4	-1.0	3	-0.24 [-0.47, -0.02]
			Placebo	169	156 (92.3)	-0.6 (0.8)	-3	-1.0	2	
		Week 12	CR845	164	144 (87.8)	-0.9 (1.1)	-4	-1.0	3	-0.17 [-0.40, 0.06]
			Placebo	169	159 (94.1)	-0.7 (0.9)	-3	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DDC_ISHC: Change from baseline in 5-D degree score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Other	5-D degree score	Baseline	CR845	20	20 (100.0)	3.7 (0.6)	3	4.0	5	
			Placebo	29	29 (100.0)	3.3 (0.8)	2	3.0	5	
		Week 4	CR845	20	17 (85.0)	2.6 (0.9)	1	3.0	5	
			Placebo	29	28 (96.6)	2.8 (0.7)	2	3.0	5	
		Week 8	CR845	20	17 (85.0)	2.4 (0.5)	2	2.0	3	
			Placebo	29	26 (89.7)	2.7 (0.8)	1	3.0	5	
		Week 10	CR845	20	16 (80.0)	2.6 (1.0)	1	2.0	5	
			Placebo	29	25 (86.2)	2.7 (0.7)	2	3.0	5	
		Week 12	CR845	20	16 (80.0)	2.7 (0.9)	1	3.0	4	
			Placebo	29	23 (79.3)	2.3 (0.8)	1	2.0	4	
	Change from baseline in 5-D degree score	Week 4	CR845	20	17 (85.0)	-1.1 (0.7)	-2	-1.0	0	-0.66 [-1.27, -0.04]
			Placebo	29	28 (96.6)	-0.6 (0.7)	-2	-0.5	1	
		Week 8	CR845	20	17 (85.0)	-1.2 (0.8)	-3	-1.0	0	-0.63 [-1.25, -0.00]
			Placebo	29	26 (89.7)	-0.7 (0.9)	-3	-0.5	1	
		Week 10	CR845	20	16 (80.0)	-1.0 (1.2)	-3	-1.0	1	-0.27 [-0.90, 0.36]
			Placebo	29	25 (86.2)	-0.7 (0.9)	-3	-1.0	1	
		Week 12	CR845	20	16 (80.0)	-1.0 (1.2)	-3	-1.0	1	0.04 [-0.60, 0.68]
			Placebo	29	23 (79.3)	-1.0 (0.9)	-3	-1.0	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DDC_ISHD: Change from baseline in 5-D degree score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 4 to < 7	5-D degree score	Baseline	CR845	102	101 (99.0)	3.2 (0.7)	2	3.0	5	
			Placebo	113	113 (100.0)	3.2 (0.6)	2	3.0	5	
		Week 4	CR845	102	95 (93.1)	2.6 (0.7)	1	3.0	5	
			Placebo	113	109 (96.5)	2.8 (0.7)	1	3.0	5	
		Week 8	CR845	102	95 (93.1)	2.5 (0.7)	1	2.0	5	
			Placebo	113	105 (92.9)	2.7 (0.7)	1	3.0	4	
		Week 10	CR845	102	92 (90.2)	2.4 (0.8)	1	2.0	5	
			Placebo	113	102 (90.3)	2.7 (0.7)	1	3.0	5	
		Week 12	CR845	102	91 (89.2)	2.4 (0.8)	1	2.0	5	
			Placebo	113	103 (91.2)	2.6 (0.8)	1	3.0	4	
	Change from baseline in 5-D degree score	Week 4	CR845	102	94 (92.2)	-0.5 (0.9)	-2	-1.0	3	-0.15 [-0.43, 0.13]
			Placebo	113	109 (96.5)	-0.4 (0.8)	-2	0.0	2	
		Week 8	CR845	102	94 (92.2)	-0.7 (1.0)	-3	-1.0	3	-0.25 [-0.52, 0.03]
			Placebo	113	105 (92.9)	-0.5 (0.7)	-3	0.0	1	
		Week 10	CR845	102	91 (89.2)	-0.8 (1.0)	-3	-1.0	3	-0.35 [-0.63, -0.06]
			Placebo	113	102 (90.3)	-0.5 (0.7)	-2	0.0	2	
		Week 12	CR845	102	90 (88.2)	-0.8 (1.0)	-3	-1.0	3	-0.28 [-0.56, 0.01]
			Placebo	113	103 (91.2)	-0.6 (0.8)	-2	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DDC_ISHD: Change from baseline in 5-D degree score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 7	5-D degree score	Baseline	CR845	135	133 (98.5)	3.7 (0.8)	1	4.0	5	
			Placebo	123	123 (100.0)	3.7 (0.7)	2	4.0	5	
		Week 4	CR845	135	119 (88.1)	2.8 (0.9)	1	3.0	5	
			Placebo	123	116 (94.3)	3.2 (0.8)	2	3.0	5	
		Week 8	CR845	135	115 (85.2)	2.8 (0.9)	1	3.0	5	
			Placebo	123	117 (95.1)	3.0 (0.8)	1	3.0	5	
		Week 10	CR845	135	114 (84.4)	2.8 (0.9)	1	3.0	5	
			Placebo	123	115 (93.5)	3.0 (0.9)	1	3.0	5	
		Week 12	CR845	135	114 (84.4)	2.7 (0.9)	1	3.0	5	
			Placebo	123	116 (94.3)	2.8 (0.8)	1	3.0	5	
	Change from baseline in 5-D degree score	Week 4	CR845	135	118 (87.4)	-0.9 (1.0)	-4	-1.0	2	-0.38 [-0.64, -0.12]
			Placebo	123	116 (94.3)	-0.6 (0.9)	-3	0.0	1	
		Week 8	CR845	135	114 (84.4)	-0.9 (1.1)	-4	-1.0	2	-0.15 [-0.41, 0.11]
			Placebo	123	117 (95.1)	-0.8 (0.9)	-3	-1.0	1	
		Week 10	CR845	135	113 (83.7)	-1.0 (1.1)	-4	-1.0	3	-0.17 [-0.43, 0.09]
			Placebo	123	115 (93.5)	-0.8 (0.9)	-3	-1.0	2	
		Week 12	CR845	135	113 (83.7)	-1.0 (1.2)	-4	-1.0	2	-0.08 [-0.34, 0.18]
			Placebo	123	116 (94.3)	-0.9 (0.9)	-3	-1.0	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DDC_ISHE: Change from baseline in 5-D degree score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	5-D degree score	Baseline	CR845	195	192 (98.5)	3.5 (0.8)	1	4.0	5	
			Placebo	199	199 (100.0)	3.5 (0.7)	2	3.0	5	
		Week 4	CR845	195	176 (90.3)	2.8 (0.8)	1	3.0	5	
			Placebo	199	191 (96.0)	3.0 (0.8)	1	3.0	5	
		Week 8	CR845	195	174 (89.2)	2.7 (0.8)	1	3.0	5	
			Placebo	199	185 (93.0)	2.8 (0.8)	1	3.0	5	
		Week 10	CR845	195	171 (87.7)	2.6 (0.9)	1	3.0	5	
			Placebo	199	180 (90.5)	2.8 (0.8)	1	3.0	5	
		Week 12	CR845	195	170 (87.2)	2.6 (0.9)	1	3.0	5	
			Placebo	199	183 (92.0)	2.7 (0.8)	1	3.0	5	
	Change from baseline in 5-D degree score	Week 4	CR845	195	174 (89.2)	-0.7 (0.9)	-3	-1.0	3	-0.25 [-0.45, -0.04]
			Placebo	199	191 (96.0)	-0.5 (0.8)	-3	0.0	2	
		Week 8	CR845	195	172 (88.2)	-0.8 (1.0)	-4	-1.0	3	-0.15 [-0.36, 0.05]
			Placebo	199	185 (93.0)	-0.6 (0.9)	-3	0.0	1	
		Week 10	CR845	195	169 (86.7)	-0.8 (1.1)	-4	-1.0	3	-0.21 [-0.42, 0.00]
			Placebo	199	180 (90.5)	-0.6 (0.9)	-3	-1.0	2	
		Week 12	CR845	195	168 (86.2)	-0.9 (1.1)	-4	-1.0	3	-0.16 [-0.37, 0.05]
			Placebo	199	183 (92.0)	-0.7 (0.9)	-3	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DDC_ISHE: Change from baseline in 5-D degree score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	5-D degree score	Baseline	CR845	42	42 (100.0)	3.5 (0.7)	2	4.0	5	
			Placebo	37	37 (100.0)	3.6 (0.6)	2	4.0	5	
		Week 4	CR845	42	38 (90.5)	2.6 (0.9)	1	2.5	5	
			Placebo	37	34 (91.9)	3.0 (0.6)	2	3.0	4	
		Week 8	CR845	42	36 (85.7)	2.6 (1.1)	1	2.0	5	
			Placebo	37	37 (100.0)	3.0 (0.8)	1	3.0	4	
		Week 10	CR845	42	35 (83.3)	2.5 (0.9)	1	2.0	4	
			Placebo	37	37 (100.0)	2.9 (0.7)	2	3.0	4	
		Week 12	CR845	42	35 (83.3)	2.6 (0.9)	1	3.0	5	
			Placebo	37	36 (97.3)	2.8 (0.7)	1	3.0	4	
	Change from baseline in 5-D degree score	Week 4	CR845	42	38 (90.5)	-1.0 (1.0)	-4	-1.0	1	-0.48 [-0.95, -0.01]
			Placebo	37	34 (91.9)	-0.5 (0.8)	-3	0.0	1	
		Week 8	CR845	42	36 (85.7)	-1.0 (1.3)	-4	-1.0	2	-0.37 [-0.83, 0.09]
			Placebo	37	37 (100.0)	-0.6 (0.7)	-2	-1.0	1	
		Week 10	CR845	42	35 (83.3)	-1.1 (1.1)	-4	-1.0	1	-0.43 [-0.90, 0.03]
			Placebo	37	37 (100.0)	-0.7 (0.7)	-2	-1.0	1	
		Week 12	CR845	42	35 (83.3)	-1.0 (1.2)	-4	-1.0	2	-0.19 [-0.65, 0.28]
			Placebo	37	36 (97.3)	-0.8 (0.8)	-2	-1.0	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DDC_ISHF: Change from baseline in 5-D degree score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	5-D degree score	Baseline	CR845	150	147 (98.0)	3.5 (0.8)	1	3.0	5	
			Placebo	151	151 (100.0)	3.5 (0.7)	2	3.0	5	
		Week 4	CR845	150	140 (93.3)	2.7 (0.8)	1	3.0	5	
			Placebo	151	146 (96.7)	3.0 (0.7)	1	3.0	5	
		Week 8	CR845	150	138 (92.0)	2.7 (0.8)	1	3.0	5	
			Placebo	151	142 (94.0)	2.8 (0.8)	1	3.0	5	
		Week 10	CR845	150	133 (88.7)	2.6 (0.9)	1	2.0	5	
			Placebo	151	140 (92.7)	2.8 (0.8)	1	3.0	5	
		Week 12	CR845	150	134 (89.3)	2.6 (0.9)	1	2.5	5	
			Placebo	151	141 (93.4)	2.7 (0.8)	1	3.0	5	
	Change from baseline in 5-D degree score	Week 4	CR845	150	138 (92.0)	-0.7 (0.9)	-3	-1.0	3	-0.21 [-0.44, 0.02]
			Placebo	151	146 (96.7)	-0.5 (0.9)	-3	0.0	2	
		Week 8	CR845	150	136 (90.7)	-0.8 (1.0)	-4	-1.0	3	-0.10 [-0.34, 0.14]
			Placebo	151	142 (94.0)	-0.7 (0.9)	-3	-1.0	1	
		Week 10	CR845	150	131 (87.3)	-0.8 (1.0)	-3	-1.0	3	-0.12 [-0.36, 0.12]
			Placebo	151	140 (92.7)	-0.7 (0.9)	-3	-1.0	2	
		Week 12	CR845	150	132 (88.0)	-0.8 (1.0)	-4	-1.0	3	-0.08 [-0.31, 0.16]
			Placebo	151	141 (93.4)	-0.8 (0.9)	-3	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DDC_ISHF: Change from baseline in 5-D degree score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	5-D degree score	Baseline	CR845	87	87 (100.0)	3.6 (0.8)	1	4.0	5	
			Placebo	85	85 (100.0)	3.5 (0.7)	2	3.0	5	
		Week 4	CR845	87	74 (85.1)	2.8 (0.8)	1	3.0	5	
			Placebo	85	79 (92.9)	3.1 (0.9)	1	3.0	5	
		Week 8	CR845	87	72 (82.8)	2.7 (1.0)	1	3.0	5	
			Placebo	85	80 (94.1)	2.9 (0.7)	1	3.0	5	
		Week 10	CR845	87	73 (83.9)	2.6 (0.9)	1	3.0	5	
			Placebo	85	77 (90.6)	2.9 (0.8)	1	3.0	5	
		Week 12	CR845	87	71 (81.6)	2.6 (0.9)	1	3.0	5	
			Placebo	85	78 (91.8)	2.7 (0.8)	1	3.0	4	
	Change from baseline in 5-D degree score	Week 4	CR845	87	74 (85.1)	-0.8 (1.0)	-4	-1.0	2	-0.44 [-0.76, -0.12]
			Placebo	85	79 (92.9)	-0.4 (0.8)	-2	0.0	1	
		Week 8	CR845	87	72 (82.8)	-0.9 (1.2)	-4	-1.0	2	-0.36 [-0.68, -0.04]
			Placebo	85	80 (94.1)	-0.6 (0.8)	-2	0.0	1	
		Week 10	CR845	87	73 (83.9)	-1.0 (1.2)	-4	-1.0	3	-0.46 [-0.78, -0.13]
			Placebo	85	77 (90.6)	-0.6 (0.8)	-3	-1.0	2	
		Week 12	CR845	87	71 (81.6)	-1.1 (1.2)	-4	-1.0	2	-0.33 [-0.65, -0.01]
			Placebo	85	78 (91.8)	-0.7 (0.8)	-3	-1.0	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DDC_ISHG: Change from baseline in 5-D degree score by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
USA	5-D degree score	Baseline	CR845	146	143 (97.9)	3.6 (0.8)	1	4.0	5	
			Placebo	133	133 (100.0)	3.4 (0.7)	2	3.0	5	
		Week 4	CR845	146	133 (91.1)	2.9 (0.8)	1	3.0	5	
			Placebo	133	123 (92.5)	3.0 (0.8)	2	3.0	5	
		Week 8	CR845	146	131 (89.7)	2.8 (0.9)	1	3.0	5	
			Placebo	133	125 (94.0)	2.8 (0.7)	1	3.0	4	
		Week 10	CR845	146	129 (88.4)	2.7 (0.9)	1	3.0	5	
			Placebo	133	122 (91.7)	2.7 (0.8)	1	3.0	5	
		Week 12	CR845	146	129 (88.4)	2.6 (0.8)	1	3.0	5	
			Placebo	133	125 (94.0)	2.7 (0.8)	1	3.0	4	
	Change from baseline in 5-D degree score	Week 4	CR845	146	131 (89.7)	-0.7 (1.0)	-4	-1.0	3	-0.38 [-0.63, -0.13]
			Placebo	133	123 (92.5)	-0.3 (0.8)	-3	0.0	2	
		Week 8	CR845	146	129 (88.4)	-0.8 (1.1)	-4	-1.0	3	-0.21 [-0.46, 0.04]
			Placebo	133	125 (94.0)	-0.6 (0.9)	-3	0.0	1	
		Week 10	CR845	146	127 (87.0)	-0.9 (1.1)	-4	-1.0	3	-0.17 [-0.42, 0.08]
			Placebo	133	122 (91.7)	-0.7 (0.9)	-3	-1.0	2	
		Week 12	CR845	146	127 (87.0)	-0.9 (1.1)	-4	-1.0	3	-0.18 [-0.43, 0.07]
			Placebo	133	125 (94.0)	-0.7 (0.9)	-3	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DDC_ISHG: Change from baseline in 5-D degree score by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Asia	5-D degree score	Baseline	CR845	8	8 (100.0)	3.6 (0.5)	3	4.0	4	
			Placebo	12	12 (100.0)	3.5 (0.7)	3	3.0	5	
		Week 4	CR845	8	8 (100.0)	2.3 (0.7)	1	2.0	3	
			Placebo	12	12 (100.0)	3.0 (0.6)	2	3.0	4	
		Week 8	CR845	8	7 (87.5)	2.3 (0.5)	2	2.0	3	
			Placebo	12	12 (100.0)	2.8 (0.5)	2	3.0	3	
		Week 10	CR845	8	7 (87.5)	2.6 (1.1)	2	2.0	5	
			Placebo	12	11 (91.7)	2.6 (0.7)	2	3.0	4	
		Week 12	CR845	8	7 (87.5)	2.3 (0.5)	2	2.0	3	
			Placebo	12	11 (91.7)	2.4 (0.9)	1	2.0	4	
	Change from baseline in 5-D degree score	Week 4	CR845	8	8 (100.0)	-1.4 (0.7)	-2	-1.5	0	-1.42 [-2.42, -0.41]
			Placebo	12	12 (100.0)	-0.5 (0.5)	-1	-0.5	0	
		Week 8	CR845	8	7 (87.5)	-1.3 (0.5)	-2	-1.0	-1	-0.65 [-1.60, 0.31]
			Placebo	12	12 (100.0)	-0.8 (1.0)	-3	-0.5	0	
		Week 10	CR845	8	7 (87.5)	-1.0 (1.0)	-2	-1.0	1	-0.08 [-1.03, 0.86]
			Placebo	12	11 (91.7)	-0.9 (1.1)	-3	-1.0	1	
		Week 12	CR845	8	7 (87.5)	-1.3 (0.8)	-2	-1.0	0	-0.11 [-1.06, 0.83]
			Placebo	12	11 (91.7)	-1.2 (1.0)	-3	-1.0	0	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DDC_ISHG: Change from baseline in 5-D degree score by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Eastern Europe	5-D degree score	Baseline	CR845	54	54 (100.0)	3.4 (0.8)	1	3.0	5	
			Placebo	60	60 (100.0)	3.5 (0.7)	2	3.0	5	
		Week 4	CR845	54	51 (94.4)	2.6 (0.8)	1	3.0	5	
			Placebo	60	59 (98.3)	2.8 (0.8)	1	3.0	5	
		Week 8	CR845	54	49 (90.7)	2.6 (0.9)	1	3.0	5	
			Placebo	60	59 (98.3)	2.8 (0.7)	1	3.0	4	
		Week 10	CR845	54	48 (88.9)	2.4 (0.9)	1	2.0	5	
			Placebo	60	59 (98.3)	3.0 (0.7)	1	3.0	4	
		Week 12	CR845	54	47 (87.0)	2.4 (1.0)	1	2.0	4	
			Placebo	60	58 (96.7)	2.9 (0.8)	1	3.0	4	
	Change from baseline in 5-D degree score	Week 4	CR845	54	51 (94.4)	-0.7 (1.0)	-3	-1.0	1	-0.11 [-0.48, 0.27]
			Placebo	60	59 (98.3)	-0.6 (0.8)	-3	0.0	1	
		Week 8	CR845	54	49 (90.7)	-0.7 (1.1)	-3	-1.0	2	-0.06 [-0.44, 0.32]
			Placebo	60	59 (98.3)	-0.7 (0.8)	-2	-1.0	1	
		Week 10	CR845	54	48 (88.9)	-0.9 (1.1)	-4	-1.0	1	-0.47 [-0.86, -0.09]
			Placebo	60	59 (98.3)	-0.5 (0.7)	-2	0.0	1	
		Week 12	CR845	54	47 (87.0)	-1.0 (1.2)	-4	-1.0	1	-0.32 [-0.71, 0.07]
			Placebo	60	58 (96.7)	-0.6 (0.8)	-2	-0.5	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DDC_ISHG: Change from baseline in 5-D degree score by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Western Europe/European origin	5-D degree score	Baseline	CR845	29	29 (100.0)	3.5 (0.6)	2	3.0	5	
			Placebo	31	31 (100.0)	3.8 (0.7)	2	4.0	5	
		Week 4	CR845	29	22 (75.9)	2.5 (1.0)	1	2.5	5	
			Placebo	31	31 (100.0)	3.1 (1.0)	2	3.0	5	
		Week 8	CR845	29	23 (79.3)	2.5 (0.8)	1	2.0	4	
			Placebo	31	26 (83.9)	3.2 (1.0)	1	3.0	5	
		Week 10	CR845	29	22 (75.9)	2.5 (0.9)	1	2.0	4	
			Placebo	31	25 (80.6)	3.1 (1.1)	1	3.0	5	
		Week 12	CR845	29	22 (75.9)	2.7 (0.9)	1	2.5	4	
			Placebo	31	25 (80.6)	2.9 (1.0)	1	3.0	5	
	Change from baseline in 5-D degree score	Week 4	CR845	29	22 (75.9)	-0.9 (0.8)	-2	-1.0	0	-0.17 [-0.71, 0.38]
			Placebo	31	31 (100.0)	-0.8 (0.8)	-3	-1.0	1	
		Week 8	CR845	29	23 (79.3)	-1.0 (1.0)	-3	-1.0	0	-0.29 [-0.86, 0.27]
			Placebo	31	26 (83.9)	-0.7 (0.8)	-2	-1.0	1	
		Week 10	CR845	29	22 (75.9)	-1.0 (1.1)	-3	-1.0	1	-0.24 [-0.81, 0.34]
			Placebo	31	25 (80.6)	-0.8 (0.9)	-3	-1.0	1	
		Week 12	CR845	29	22 (75.9)	-0.8 (1.2)	-3	-1.0	2	0.19 [-0.39, 0.76]
			Placebo	31	25 (80.6)	-1.0 (0.8)	-3	-1.0	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DDC_ISHH: Change from baseline in 5-D degree score by dialysis method
ITT

H: Dialysis method	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Hemodialysis (HD)	5-D degree score	Baseline	CR845	222	219 (98.6)	3.5 (0.8)	1	4.0	5	
			Placebo	199	199 (100.0)	3.4 (0.7)	2	3.0	5	
		Week 4	CR845	222	201 (90.5)	2.7 (0.8)	1	3.0	5	
			Placebo	199	188 (94.5)	3.0 (0.8)	1	3.0	5	
		Week 8	CR845	222	197 (88.7)	2.7 (0.9)	1	3.0	5	
			Placebo	199	187 (94.0)	2.9 (0.7)	1	3.0	5	
		Week 10	CR845	222	194 (87.4)	2.6 (0.9)	1	3.0	5	
			Placebo	199	185 (93.0)	2.8 (0.8)	1	3.0	5	
		Week 12	CR845	222	192 (86.5)	2.6 (0.9)	1	3.0	5	
			Placebo	199	185 (93.0)	2.7 (0.8)	1	3.0	4	
	Change from baseline in 5-D degree score	Week 4	CR845	222	199 (89.6)	-0.8 (1.0)	-4	-1.0	3	-0.38 [-0.58, -0.18]
			Placebo	199	188 (94.5)	-0.4 (0.8)	-3	0.0	2	
		Week 8	CR845	222	195 (87.8)	-0.9 (1.1)	-4	-1.0	3	-0.25 [-0.45, -0.05]
			Placebo	199	187 (94.0)	-0.6 (0.9)	-3	0.0	1	
		Week 10	CR845	222	192 (86.5)	-0.9 (1.1)	-4	-1.0	3	-0.24 [-0.44, -0.03]
			Placebo	199	185 (93.0)	-0.7 (0.9)	-3	-1.0	2	
		Week 12	CR845	222	190 (85.6)	-1.0 (1.1)	-4	-1.0	3	-0.19 [-0.40, 0.01]
			Placebo	199	185 (93.0)	-0.8 (0.9)	-3	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DDC_ISHH: Change from baseline in 5-D degree score by dialysis method
ITT

H: Dialysis method	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Hemodiafiltration (HDF)	5-D degree score	Baseline	CR845	15	15 (100.0)	3.3 (0.6)	2	3.0	4	
			Placebo	37	37 (100.0)	3.7 (0.6)	3	4.0	5	
		Week 4	CR845	15	13 (86.7)	2.8 (0.7)	1	3.0	4	
			Placebo	37	37 (100.0)	2.9 (0.8)	1	3.0	5	
		Week 8	CR845	15	13 (86.7)	2.8 (0.7)	2	3.0	4	
			Placebo	37	35 (94.6)	2.9 (0.9)	1	3.0	5	
		Week 10	CR845	15	12 (80.0)	2.4 (1.1)	1	2.0	5	
			Placebo	37	32 (86.5)	3.2 (0.9)	1	3.0	5	
		Week 12	CR845	15	13 (86.7)	2.6 (1.0)	1	2.0	4	
			Placebo	37	34 (91.9)	2.9 (1.0)	1	3.0	5	
	Change from baseline in 5-D degree score	Week 4	CR845	15	13 (86.7)	-0.4 (0.9)	-2	0.0	1	0.40 [-0.24, 1.04]
			Placebo	37	37 (100.0)	-0.8 (1.0)	-3	-1.0	1	
		Week 8	CR845	15	13 (86.7)	-0.5 (0.7)	-1	-1.0	1	0.45 [-0.19, 1.10]
			Placebo	37	35 (94.6)	-0.8 (0.9)	-2	-1.0	1	
		Week 10	CR845	15	12 (80.0)	-0.8 (1.0)	-2	-1.0	1	-0.21 [-0.88, 0.45]
			Placebo	37	32 (86.5)	-0.6 (0.8)	-2	-1.0	1	
		Week 12	CR845	15	13 (86.7)	-0.6 (0.8)	-2	-1.0	1	0.20 [-0.44, 0.84]
			Placebo	37	34 (91.9)	-0.8 (0.9)	-2	-1.0	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DLC_ISHA: Change from baseline in 5-D duration score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
< 65 years	5-D duration score	Baseline	CR845	147	143 (97.3)	2.8 (1.4)	1	2.0	5	
			Placebo	153	153 (100.0)	2.5 (1.3)	1	2.0	5	
		Week 4	CR845	147	135 (91.8)	2.0 (1.2)	1	2.0	5	
			Placebo	153	144 (94.1)	2.2 (1.3)	1	2.0	5	
		Week 8	CR845	147	132 (89.8)	1.9 (1.1)	1	1.0	5	
			Placebo	153	143 (93.5)	1.9 (1.1)	1	2.0	5	
		Week 10	CR845	147	132 (89.8)	1.9 (1.2)	1	2.0	5	
			Placebo	153	141 (92.2)	1.8 (1.1)	1	1.0	5	
		Week 12	CR845	147	131 (89.1)	1.8 (1.1)	1	1.0	5	
			Placebo	153	142 (92.8)	1.9 (1.2)	1	2.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	147	132 (89.8)	-0.7 (1.4)	-4	-1.0	2	-0.33 [-0.57, -0.09]
			Placebo	153	144 (94.1)	-0.3 (1.6)	-4	0.0	4	
		Week 8	CR845	147	129 (87.8)	-0.9 (1.5)	-4	-1.0	2	-0.18 [-0.42, 0.06]
			Placebo	153	143 (93.5)	-0.6 (1.4)	-4	0.0	4	
		Week 10	CR845	147	129 (87.8)	-0.9 (1.5)	-4	-1.0	2	-0.17 [-0.41, 0.07]
			Placebo	153	141 (92.2)	-0.7 (1.5)	-4	-1.0	4	
		Week 12	CR845	147	128 (87.1)	-1.0 (1.6)	-4	-1.0	3	-0.29 [-0.53, -0.05]
			Placebo	153	142 (92.8)	-0.5 (1.6)	-4	0.0	4	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DLC_ISHA: Change from baseline in 5-D duration score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 65 years	5-D duration score	Baseline	CR845	90	90 (100.0)	2.8 (1.5)	1	2.0	5	
			Placebo	83	83 (100.0)	2.5 (1.4)	1	2.0	5	
		Week 4	CR845	90	79 (87.8)	1.9 (1.2)	1	1.0	5	
			Placebo	83	81 (97.6)	2.0 (1.3)	1	2.0	5	
		Week 8	CR845	90	78 (86.7)	1.8 (1.2)	1	1.0	5	
			Placebo	83	79 (95.2)	2.0 (1.1)	1	2.0	5	
		Week 10	CR845	90	74 (82.2)	1.9 (1.2)	1	1.0	5	
			Placebo	83	76 (91.6)	2.0 (1.2)	1	2.0	5	
		Week 12	CR845	90	74 (82.2)	1.8 (1.2)	1	1.0	5	
			Placebo	83	77 (92.8)	2.0 (1.3)	1	2.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	90	79 (87.8)	-0.8 (1.4)	-4	-1.0	2	-0.25 [-0.56, 0.06]
			Placebo	83	81 (97.6)	-0.4 (1.4)	-4	0.0	4	
		Week 8	CR845	90	78 (86.7)	-1.0 (1.4)	-4	-1.0	2	-0.31 [-0.62, 0.01]
			Placebo	83	79 (95.2)	-0.5 (1.4)	-4	0.0	3	
		Week 10	CR845	90	74 (82.2)	-0.9 (1.5)	-4	-1.0	4	-0.28 [-0.60, 0.05]
			Placebo	83	76 (91.6)	-0.5 (1.3)	-4	0.0	4	
		Week 12	CR845	90	74 (82.2)	-1.0 (1.5)	-4	-1.0	4	-0.30 [-0.62, 0.02]
			Placebo	83	77 (92.8)	-0.5 (1.4)	-4	0.0	4	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DLC_ISHB: Change from baseline in 5-D duration score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Male	5-D duration score	Baseline	CR845	137	135 (98.5)	2.7 (1.4)	1	2.0	5	
			Placebo	139	139 (100.0)	2.5 (1.3)	1	2.0	5	
		Week 4	CR845	137	125 (91.2)	2.2 (1.3)	1	2.0	5	
			Placebo	139	131 (94.2)	2.1 (1.3)	1	2.0	5	
		Week 8	CR845	137	123 (89.8)	2.0 (1.2)	1	2.0	5	
			Placebo	139	132 (95.0)	1.8 (1.0)	1	2.0	5	
		Week 10	CR845	137	118 (86.1)	2.1 (1.3)	1	2.0	5	
			Placebo	139	127 (91.4)	1.8 (1.1)	1	1.0	5	
		Week 12	CR845	137	118 (86.1)	1.9 (1.2)	1	2.0	5	
			Placebo	139	127 (91.4)	1.9 (1.2)	1	2.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	137	124 (90.5)	-0.5 (1.2)	-4	0.0	2	-0.08 [-0.32, 0.17]
			Placebo	139	131 (94.2)	-0.4 (1.6)	-4	0.0	4	
		Week 8	CR845	137	122 (89.1)	-0.7 (1.4)	-4	-1.0	2	-0.03 [-0.28, 0.21]
			Placebo	139	132 (95.0)	-0.7 (1.3)	-4	-0.5	3	
		Week 10	CR845	137	117 (85.4)	-0.6 (1.5)	-4	0.0	4	0.04 [-0.21, 0.29]
			Placebo	139	127 (91.4)	-0.7 (1.3)	-4	-1.0	4	
		Week 12	CR845	137	117 (85.4)	-0.8 (1.5)	-4	-1.0	4	-0.17 [-0.42, 0.08]
			Placebo	139	127 (91.4)	-0.6 (1.4)	-4	0.0	4	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DLC_ISHB: Change from baseline in 5-D duration score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Female	5-D duration score	Baseline	CR845	100	98 (98.0)	2.8 (1.4)	1	2.0	5	
			Placebo	97	97 (100.0)	2.5 (1.4)	1	2.0	5	
		Week 4	CR845	100	89 (89.0)	1.7 (1.0)	1	1.0	5	
			Placebo	97	94 (96.9)	2.2 (1.3)	1	2.0	5	
		Week 8	CR845	100	87 (87.0)	1.6 (1.1)	1	1.0	5	
			Placebo	97	90 (92.8)	2.0 (1.3)	1	2.0	5	
		Week 10	CR845	100	88 (88.0)	1.6 (1.0)	1	1.0	5	
			Placebo	97	90 (92.8)	2.0 (1.3)	1	2.0	5	
		Week 12	CR845	100	87 (87.0)	1.7 (1.0)	1	1.0	5	
			Placebo	97	92 (94.8)	2.0 (1.4)	1	1.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	100	87 (87.0)	-1.2 (1.5)	-4	-1.0	2	-0.61 [-0.91, -0.31]
			Placebo	97	94 (96.9)	-0.3 (1.5)	-4	0.0	4	
		Week 8	CR845	100	85 (85.0)	-1.2 (1.5)	-4	-1.0	1	-0.47 [-0.77, -0.17]
			Placebo	97	90 (92.8)	-0.5 (1.6)	-4	0.0	4	
		Week 10	CR845	100	86 (86.0)	-1.3 (1.4)	-4	-1.0	2	-0.52 [-0.82, -0.22]
			Placebo	97	90 (92.8)	-0.5 (1.6)	-4	0.0	4	
		Week 12	CR845	100	85 (85.0)	-1.2 (1.6)	-4	-1.0	3	-0.44 [-0.74, -0.14]
			Placebo	97	92 (94.8)	-0.5 (1.7)	-4	0.0	4	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DLC_ISHC: Change from baseline in 5-D duration score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Black/African American	5-D duration score	Baseline	CR845	53	51 (96.2)	2.9 (1.5)	1	2.0	5	
			Placebo	38	38 (100.0)	2.4 (1.4)	1	2.0	5	
		Week 4	CR845	53	47 (88.7)	2.3 (1.2)	1	2.0	5	
			Placebo	38	35 (92.1)	2.1 (1.3)	1	2.0	5	
		Week 8	CR845	53	47 (88.7)	1.9 (1.2)	1	2.0	5	
			Placebo	38	37 (97.4)	2.1 (1.4)	1	2.0	5	
		Week 10	CR845	53	44 (83.0)	1.8 (1.1)	1	1.5	5	
			Placebo	38	36 (94.7)	2.2 (1.5)	1	2.0	5	
		Week 12	CR845	53	45 (84.9)	1.7 (1.1)	1	1.0	5	
			Placebo	38	37 (97.4)	2.0 (1.4)	1	1.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	53	45 (84.9)	-0.7 (1.3)	-4	0.0	2	-0.30 [-0.74, 0.14]
			Placebo	38	35 (92.1)	-0.3 (1.7)	-4	0.0	4	
		Week 8	CR845	53	45 (84.9)	-1.2 (1.6)	-4	-1.0	1	-0.50 [-0.94, -0.05]
			Placebo	38	37 (97.4)	-0.3 (1.9)	-4	0.0	4	
		Week 10	CR845	53	42 (79.2)	-1.2 (1.6)	-4	-1.0	1	-0.59 [-1.04, -0.13]
			Placebo	38	36 (94.7)	-0.3 (1.8)	-4	0.0	4	
		Week 12	CR845	53	43 (81.1)	-1.3 (1.4)	-4	-1.0	1	-0.58 [-1.03, -0.13]
			Placebo	38	37 (97.4)	-0.4 (1.7)	-4	0.0	4	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DLC_ISHC: Change from baseline in 5-D duration score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
White	5-D duration score	Baseline	CR845	164	162 (98.8)	2.8 (1.4)	1	3.0	5	
			Placebo	169	169 (100.0)	2.5 (1.3)	1	2.0	5	
		Week 4	CR845	164	150 (91.5)	1.9 (1.2)	1	1.0	5	
			Placebo	169	162 (95.9)	2.2 (1.3)	1	2.0	5	
		Week 8	CR845	164	146 (89.0)	1.9 (1.2)	1	1.0	5	
			Placebo	169	159 (94.1)	1.8 (1.0)	1	2.0	5	
		Week 10	CR845	164	146 (89.0)	1.9 (1.2)	1	1.5	5	
			Placebo	169	156 (92.3)	1.8 (1.0)	1	1.5	5	
		Week 12	CR845	164	144 (87.8)	1.8 (1.1)	1	1.0	5	
			Placebo	169	159 (94.1)	1.9 (1.2)	1	2.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	164	149 (90.9)	-0.8 (1.4)	-4	-1.0	2	-0.34 [-0.56, -0.11]
			Placebo	169	162 (95.9)	-0.3 (1.5)	-4	0.0	4	
		Week 8	CR845	164	145 (88.4)	-0.8 (1.4)	-4	-1.0	2	-0.15 [-0.37, 0.08]
			Placebo	169	159 (94.1)	-0.6 (1.3)	-4	0.0	3	
		Week 10	CR845	164	145 (88.4)	-0.8 (1.5)	-4	-1.0	4	-0.12 [-0.35, 0.10]
			Placebo	169	156 (92.3)	-0.6 (1.3)	-4	0.0	4	
		Week 12	CR845	164	143 (87.2)	-0.9 (1.5)	-4	-1.0	3	-0.29 [-0.51, -0.06]
			Placebo	169	159 (94.1)	-0.5 (1.5)	-4	0.0	4	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DLC_ISHC: Change from baseline in 5-D duration score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Other	5-D duration score	Baseline	CR845	20	20 (100.0)	2.3 (1.3)	1	2.0	5	
			Placebo	29	29 (100.0)	2.8 (1.5)	1	2.0	5	
		Week 4	CR845	20	17 (85.0)	1.6 (0.9)	1	1.0	4	
			Placebo	29	28 (96.6)	2.1 (1.1)	1	2.0	5	
		Week 8	CR845	20	17 (85.0)	1.3 (0.8)	1	1.0	4	
			Placebo	29	26 (89.7)	2.0 (1.2)	1	2.0	5	
		Week 10	CR845	20	16 (80.0)	1.5 (0.9)	1	1.0	4	
			Placebo	29	25 (86.2)	2.0 (1.3)	1	1.0	5	
		Week 12	CR845	20	16 (80.0)	1.9 (1.2)	1	1.5	5	
			Placebo	29	23 (79.3)	1.9 (1.3)	1	1.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	20	17 (85.0)	-0.8 (1.3)	-4	-1.0	1	-0.09 [-0.70, 0.51]
			Placebo	29	28 (96.6)	-0.6 (1.3)	-4	0.0	1	
		Week 8	CR845	20	17 (85.0)	-1.1 (1.4)	-4	-1.0	0	-0.20 [-0.82, 0.41]
			Placebo	29	26 (89.7)	-0.8 (1.5)	-4	-1.0	2	
		Week 10	CR845	20	16 (80.0)	-0.9 (1.7)	-4	-0.5	2	0.00 [-0.62, 0.63]
			Placebo	29	25 (86.2)	-0.9 (1.3)	-4	-1.0	2	
		Week 12	CR845	20	16 (80.0)	-0.5 (2.2)	-4	0.0	4	0.23 [-0.41, 0.87]
			Placebo	29	23 (79.3)	-0.9 (1.5)	-4	-1.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DLC_ISHD: Change from baseline in 5-D duration score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 4 to < 7	5-D duration score	Baseline	CR845	102	100 (98.0)	2.4 (1.3)	1	2.0	5	
			Placebo	113	113 (100.0)	2.0 (1.2)	1	2.0	5	
		Week 4	CR845	102	96 (94.1)	1.8 (1.2)	1	1.0	5	
			Placebo	113	109 (96.5)	1.9 (1.1)	1	2.0	5	
		Week 8	CR845	102	95 (93.1)	1.5 (1.0)	1	1.0	5	
			Placebo	113	105 (92.9)	1.7 (0.9)	1	2.0	5	
		Week 10	CR845	102	92 (90.2)	1.6 (1.0)	1	1.0	5	
			Placebo	113	102 (90.3)	1.7 (1.0)	1	1.0	5	
		Week 12	CR845	102	91 (89.2)	1.6 (1.0)	1	1.0	5	
			Placebo	113	103 (91.2)	1.7 (1.1)	1	1.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	102	94 (92.2)	-0.6 (1.3)	-4	0.0	2	-0.30 [-0.57, -0.02]
			Placebo	113	109 (96.5)	-0.1 (1.4)	-4	0.0	3	
		Week 8	CR845	102	93 (91.2)	-0.8 (1.4)	-4	-1.0	2	-0.40 [-0.68, -0.12]
			Placebo	113	105 (92.9)	-0.3 (1.2)	-4	0.0	3	
		Week 10	CR845	102	90 (88.2)	-0.8 (1.2)	-4	0.0	2	-0.33 [-0.61, -0.04]
			Placebo	113	102 (90.3)	-0.4 (1.3)	-4	0.0	4	
		Week 12	CR845	102	89 (87.3)	-0.8 (1.6)	-4	-1.0	4	-0.32 [-0.61, -0.04]
			Placebo	113	103 (91.2)	-0.3 (1.3)	-4	0.0	4	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DLC_ISHD: Change from baseline in 5-D duration score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 7	5-D duration score	Baseline	CR845	135	133 (98.5)	3.0 (1.4)	1	3.0	5	
			Placebo	123	123 (100.0)	2.9 (1.4)	1	3.0	5	
		Week 4	CR845	135	118 (87.4)	2.2 (1.2)	1	2.0	5	
			Placebo	123	116 (94.3)	2.4 (1.4)	1	2.0	5	
		Week 8	CR845	135	115 (85.2)	2.1 (1.2)	1	2.0	5	
			Placebo	123	117 (95.1)	2.1 (1.3)	1	2.0	5	
		Week 10	CR845	135	114 (84.4)	2.1 (1.3)	1	2.0	5	
			Placebo	123	115 (93.5)	2.1 (1.2)	1	2.0	5	
		Week 12	CR845	135	114 (84.4)	2.0 (1.1)	1	2.0	5	
			Placebo	123	116 (94.3)	2.1 (1.4)	1	2.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	135	117 (86.7)	-0.9 (1.4)	-4	-1.0	2	-0.29 [-0.55, -0.03]
			Placebo	123	116 (94.3)	-0.5 (1.6)	-4	0.0	4	
		Week 8	CR845	135	114 (84.4)	-1.0 (1.5)	-4	-1.0	2	-0.10 [-0.36, 0.16]
			Placebo	123	117 (95.1)	-0.9 (1.6)	-4	-1.0	4	
		Week 10	CR845	135	113 (83.7)	-1.0 (1.7)	-4	-1.0	4	-0.12 [-0.38, 0.14]
			Placebo	123	115 (93.5)	-0.8 (1.5)	-4	-1.0	4	
		Week 12	CR845	135	113 (83.7)	-1.1 (1.5)	-4	-1.0	2	-0.26 [-0.52, 0.00]
			Placebo	123	116 (94.3)	-0.7 (1.6)	-4	-1.0	4	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DLC_ISHE: Change from baseline in 5-D duration score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	5-D duration score	Baseline	CR845	195	191 (97.9)	2.8 (1.4)	1	2.0	5	
			Placebo	199	199 (100.0)	2.4 (1.3)	1	2.0	5	
		Week 4	CR845	195	176 (90.3)	2.0 (1.2)	1	2.0	5	
			Placebo	199	191 (96.0)	2.2 (1.3)	1	2.0	5	
		Week 8	CR845	195	174 (89.2)	1.9 (1.2)	1	1.0	5	
			Placebo	199	185 (93.0)	1.9 (1.1)	1	2.0	5	
		Week 10	CR845	195	171 (87.7)	1.9 (1.1)	1	1.0	5	
			Placebo	199	180 (90.5)	1.9 (1.2)	1	1.5	5	
		Week 12	CR845	195	170 (87.2)	1.8 (1.1)	1	1.0	5	
			Placebo	199	183 (92.0)	2.0 (1.3)	1	2.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	195	173 (88.7)	-0.8 (1.4)	-4	-1.0	2	-0.36 [-0.56, -0.15]
			Placebo	199	191 (96.0)	-0.3 (1.6)	-4	0.0	4	
		Week 8	CR845	195	171 (87.7)	-0.9 (1.5)	-4	-1.0	2	-0.22 [-0.43, -0.01]
			Placebo	199	185 (93.0)	-0.6 (1.4)	-4	0.0	3	
		Week 10	CR845	195	168 (86.2)	-0.9 (1.4)	-4	-1.0	2	-0.25 [-0.46, -0.04]
			Placebo	199	180 (90.5)	-0.6 (1.5)	-4	0.0	4	
		Week 12	CR845	195	167 (85.6)	-1.0 (1.5)	-4	-1.0	4	-0.33 [-0.54, -0.11]
			Placebo	199	183 (92.0)	-0.5 (1.6)	-4	0.0	4	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DLC_ISHE: Change from baseline in 5-D duration score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	5-D duration score	Baseline	CR845	42	42 (100.0)	2.7 (1.3)	1	3.0	5	
			Placebo	37	37 (100.0)	2.8 (1.3)	1	2.0	5	
		Week 4	CR845	42	38 (90.5)	2.1 (1.2)	1	2.0	5	
			Placebo	37	34 (91.9)	2.1 (1.1)	1	2.0	5	
		Week 8	CR845	42	36 (85.7)	1.7 (1.0)	1	1.0	5	
			Placebo	37	37 (100.0)	2.1 (1.3)	1	2.0	5	
		Week 10	CR845	42	35 (83.3)	2.0 (1.4)	1	1.0	5	
			Placebo	37	37 (100.0)	2.0 (1.2)	1	2.0	5	
		Week 12	CR845	42	35 (83.3)	1.8 (1.0)	1	2.0	5	
			Placebo	37	36 (97.3)	1.9 (1.1)	1	2.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	42	38 (90.5)	-0.6 (1.3)	-4	-0.5	2	0.04 [-0.43, 0.50]
			Placebo	37	34 (91.9)	-0.7 (1.2)	-4	-1.0	2	
		Week 8	CR845	42	36 (85.7)	-1.1 (1.4)	-4	-1.0	1	-0.27 [-0.73, 0.19]
			Placebo	37	37 (100.0)	-0.7 (1.5)	-3	-1.0	4	
		Week 10	CR845	42	35 (83.3)	-0.8 (1.8)	-4	-1.0	4	-0.01 [-0.47, 0.45]
			Placebo	37	37 (100.0)	-0.8 (1.3)	-3	-1.0	1	
		Week 12	CR845	42	35 (83.3)	-0.9 (1.5)	-4	-1.0	1	-0.10 [-0.56, 0.37]
			Placebo	37	36 (97.3)	-0.8 (1.3)	-4	-1.0	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DLC_ISHF: Change from baseline in 5-D duration score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	5-D duration score	Baseline	CR845	150	146 (97.3)	2.8 (1.4)	1	3.0	5	
			Placebo	151	151 (100.0)	2.5 (1.4)	1	2.0	5	
		Week 4	CR845	150	140 (93.3)	2.0 (1.2)	1	2.0	5	
			Placebo	151	146 (96.7)	2.2 (1.3)	1	2.0	5	
		Week 8	CR845	150	138 (92.0)	1.8 (1.2)	1	1.0	5	
			Placebo	151	142 (94.0)	1.9 (1.1)	1	2.0	5	
		Week 10	CR845	150	133 (88.7)	1.9 (1.2)	1	1.0	5	
			Placebo	151	140 (92.7)	1.9 (1.1)	1	2.0	5	
		Week 12	CR845	150	134 (89.3)	1.8 (1.1)	1	1.0	5	
			Placebo	151	141 (93.4)	2.0 (1.2)	1	2.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	150	137 (91.3)	-0.8 (1.4)	-4	-1.0	2	-0.33 [-0.57, -0.10]
			Placebo	151	146 (96.7)	-0.3 (1.6)	-4	0.0	4	
		Week 8	CR845	150	135 (90.0)	-1.0 (1.5)	-4	-1.0	2	-0.24 [-0.48, -0.00]
			Placebo	151	142 (94.0)	-0.6 (1.3)	-4	0.0	3	
		Week 10	CR845	150	130 (86.7)	-0.9 (1.5)	-4	-1.0	4	-0.20 [-0.44, 0.04]
			Placebo	151	140 (92.7)	-0.6 (1.4)	-4	0.0	4	
		Week 12	CR845	150	131 (87.3)	-1.0 (1.6)	-4	-1.0	4	-0.29 [-0.53, -0.05]
			Placebo	151	141 (93.4)	-0.5 (1.6)	-4	0.0	4	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DLC_ISHF: Change from baseline in 5-D duration score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	5-D duration score	Baseline	CR845	87	87 (100.0)	2.7 (1.4)	1	2.0	5	
			Placebo	85	85 (100.0)	2.5 (1.3)	1	2.0	5	
		Week 4	CR845	87	74 (85.1)	2.0 (1.2)	1	2.0	5	
			Placebo	85	79 (92.9)	2.1 (1.3)	1	2.0	5	
		Week 8	CR845	87	72 (82.8)	1.9 (1.1)	1	2.0	5	
			Placebo	85	80 (94.1)	2.0 (1.2)	1	2.0	5	
		Week 10	CR845	87	73 (83.9)	1.9 (1.1)	1	2.0	5	
			Placebo	85	77 (90.6)	2.0 (1.3)	1	1.0	5	
		Week 12	CR845	87	71 (81.6)	1.8 (1.1)	1	1.0	5	
			Placebo	85	78 (91.8)	1.9 (1.3)	1	1.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	87	74 (85.1)	-0.7 (1.3)	-4	-1.0	2	-0.24 [-0.55, 0.08]
			Placebo	85	79 (92.9)	-0.4 (1.4)	-4	0.0	4	
		Week 8	CR845	87	72 (82.8)	-0.8 (1.4)	-4	-1.0	2	-0.20 [-0.52, 0.12]
			Placebo	85	80 (94.1)	-0.5 (1.6)	-4	0.0	4	
		Week 10	CR845	87	73 (83.9)	-0.8 (1.5)	-4	-1.0	3	-0.22 [-0.54, 0.11]
			Placebo	85	77 (90.6)	-0.5 (1.4)	-4	0.0	4	
		Week 12	CR845	87	71 (81.6)	-0.9 (1.4)	-4	-1.0	3	-0.29 [-0.61, 0.04]
			Placebo	85	78 (91.8)	-0.5 (1.5)	-4	-1.0	4	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DLC_ISHG: Change from baseline in 5-D duration score by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
USA	5-D duration score	Baseline	CR845	146	142 (97.3)	2.9 (1.4)	1	3.0	5	
			Placebo	133	133 (100.0)	2.6 (1.4)	1	2.0	5	
		Week 4	CR845	146	133 (91.1)	2.2 (1.2)	1	2.0	5	
			Placebo	133	123 (92.5)	2.3 (1.3)	1	2.0	5	
		Week 8	CR845	146	131 (89.7)	2.0 (1.2)	1	2.0	5	
			Placebo	133	125 (94.0)	2.0 (1.2)	1	2.0	5	
		Week 10	CR845	146	129 (88.4)	2.0 (1.2)	1	2.0	5	
			Placebo	133	122 (91.7)	2.0 (1.2)	1	2.0	5	
		Week 12	CR845	146	129 (88.4)	1.9 (1.1)	1	2.0	5	
			Placebo	133	125 (94.0)	2.0 (1.2)	1	2.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	146	130 (89.0)	-0.6 (1.4)	-4	0.0	2	-0.26 [-0.50, -0.01]
			Placebo	133	123 (92.5)	-0.2 (1.5)	-4	0.0	4	
		Week 8	CR845	146	128 (87.7)	-0.9 (1.5)	-4	-1.0	2	-0.19 [-0.43, 0.06]
			Placebo	133	125 (94.0)	-0.6 (1.5)	-4	0.0	4	
		Week 10	CR845	146	126 (86.3)	-0.9 (1.6)	-4	-1.0	4	-0.17 [-0.42, 0.08]
			Placebo	133	122 (91.7)	-0.6 (1.5)	-4	-0.5	4	
		Week 12	CR845	146	126 (86.3)	-1.0 (1.5)	-4	-1.0	2	-0.27 [-0.52, -0.02]
			Placebo	133	125 (94.0)	-0.6 (1.5)	-4	0.0	4	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DLC_ISHG: Change from baseline in 5-D duration score by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Asia	5-D duration score	Baseline	CR845	8	8 (100.0)	2.3 (1.5)	1	2.0	5	
			Placebo	12	12 (100.0)	2.8 (1.4)	1	2.0	5	
		Week 4	CR845	8	8 (100.0)	1.0 (0.0)	1	1.0	1	
			Placebo	12	12 (100.0)	1.9 (1.0)	1	2.0	4	
		Week 8	CR845	8	7 (87.5)	1.1 (0.4)	1	1.0	2	
			Placebo	12	12 (100.0)	1.9 (1.1)	1	1.5	4	
		Week 10	CR845	8	7 (87.5)	1.1 (0.4)	1	1.0	2	
			Placebo	12	11 (91.7)	1.7 (1.0)	1	1.0	4	
		Week 12	CR845	8	7 (87.5)	1.1 (0.4)	1	1.0	2	
			Placebo	12	11 (91.7)	1.9 (1.4)	1	1.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	8	8 (100.0)	-1.3 (1.5)	-4	-1.0	0	-0.25 [-1.15, 0.65]
			Placebo	12	12 (100.0)	-0.8 (1.7)	-4	-0.5	1	
		Week 8	CR845	8	7 (87.5)	-1.1 (1.7)	-4	0.0	0	-0.17 [-1.10, 0.76]
			Placebo	12	12 (100.0)	-0.8 (1.9)	-4	-1.0	2	
		Week 10	CR845	8	7 (87.5)	-1.1 (1.7)	-4	0.0	0	0.02 [-0.92, 0.97]
			Placebo	12	11 (91.7)	-1.2 (1.7)	-4	-1.0	2	
		Week 12	CR845	8	7 (87.5)	-1.1 (1.7)	-4	0.0	0	-0.08 [-1.02, 0.87]
			Placebo	12	11 (91.7)	-1.0 (2.0)	-4	-1.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DLC_ISHG: Change from baseline in 5-D duration score by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Eastern Europe	5-D duration score	Baseline	CR845	54	54 (100.0)	2.6 (1.4)	1	2.0	5	
			Placebo	60	60 (100.0)	2.2 (1.1)	1	2.0	5	
		Week 4	CR845	54	51 (94.4)	1.6 (1.1)	1	1.0	5	
			Placebo	60	59 (98.3)	1.8 (1.2)	1	1.0	5	
		Week 8	CR845	54	49 (90.7)	1.5 (1.0)	1	1.0	5	
			Placebo	60	59 (98.3)	1.6 (0.9)	1	1.0	5	
		Week 10	CR845	54	48 (88.9)	1.5 (0.9)	1	1.0	5	
			Placebo	60	59 (98.3)	1.7 (1.1)	1	1.0	5	
		Week 12	CR845	54	47 (87.0)	1.6 (1.1)	1	1.0	5	
			Placebo	60	58 (96.7)	1.9 (1.2)	1	1.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	54	51 (94.4)	-1.0 (1.4)	-4	-1.0	2	-0.41 [-0.79, -0.03]
			Placebo	60	59 (98.3)	-0.4 (1.5)	-4	0.0	4	
		Week 8	CR845	54	49 (90.7)	-1.0 (1.5)	-4	-1.0	2	-0.38 [-0.76, 0.00]
			Placebo	60	59 (98.3)	-0.5 (1.2)	-4	0.0	2	
		Week 10	CR845	54	48 (88.9)	-1.0 (1.4)	-4	-1.0	2	-0.45 [-0.84, -0.07]
			Placebo	60	59 (98.3)	-0.4 (1.2)	-3	0.0	4	
		Week 12	CR845	54	47 (87.0)	-1.0 (1.6)	-4	-1.0	3	-0.46 [-0.85, -0.07]
			Placebo	60	58 (96.7)	-0.3 (1.2)	-3	0.0	4	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DLC_ISHG: Change from baseline in 5-D duration score by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Western Europe/European origin	5-D duration score	Baseline	CR845	29	29 (100.0)	2.7 (1.5)	1	2.0	5	
			Placebo	31	31 (100.0)	2.6 (1.5)	1	2.0	5	
		Week 4	CR845	29	22 (75.9)	1.8 (1.3)	1	1.0	5	
			Placebo	31	31 (100.0)	2.3 (1.6)	1	2.0	5	
		Week 8	CR845	29	23 (79.3)	1.7 (1.4)	1	1.0	5	
			Placebo	31	26 (83.9)	2.0 (1.3)	1	2.0	5	
		Week 10	CR845	29	22 (75.9)	2.0 (1.5)	1	1.0	5	
			Placebo	31	25 (80.6)	2.0 (1.4)	1	1.0	5	
		Week 12	CR845	29	22 (75.9)	2.1 (1.4)	1	2.0	5	
			Placebo	31	25 (80.6)	2.2 (1.5)	1	2.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	29	22 (75.9)	-1.0 (1.3)	-4	-1.0	1	-0.45 [-1.01, 0.10]
			Placebo	31	31 (100.0)	-0.3 (1.5)	-3	0.0	4	
		Week 8	CR845	29	23 (79.3)	-0.9 (1.1)	-4	-1.0	0	-0.20 [-0.76, 0.36]
			Placebo	31	26 (83.9)	-0.7 (1.4)	-3	0.0	3	
		Week 10	CR845	29	22 (75.9)	-0.7 (1.4)	-4	-1.0	3	-0.03 [-0.60, 0.55]
			Placebo	31	25 (80.6)	-0.6 (1.7)	-4	0.0	4	
		Week 12	CR845	29	22 (75.9)	-0.5 (1.8)	-4	0.0	4	-0.15 [-0.72, 0.42]
			Placebo	31	25 (80.6)	-0.3 (1.8)	-4	0.0	4	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DLC_ISHH: Change from baseline in 5-D duration score by dialysis method
ITT

H: Dialysis method	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Hemodialysis (HD)	5-D duration score	Baseline	CR845	222	218 (98.2)	2.8 (1.4)	1	2.0	5	
			Placebo	199	199 (100.0)	2.6 (1.3)	1	2.0	5	
		Week 4	CR845	222	201 (90.5)	2.0 (1.2)	1	2.0	5	
			Placebo	199	188 (94.5)	2.2 (1.3)	1	2.0	5	
		Week 8	CR845	222	197 (88.7)	1.8 (1.1)	1	1.0	5	
			Placebo	199	187 (94.0)	1.9 (1.1)	1	2.0	5	
		Week 10	CR845	222	194 (87.4)	1.9 (1.2)	1	2.0	5	
			Placebo	199	185 (93.0)	1.9 (1.2)	1	2.0	5	
		Week 12	CR845	222	192 (86.5)	1.8 (1.1)	1	1.0	5	
			Placebo	199	185 (93.0)	1.9 (1.2)	1	2.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	222	198 (89.2)	-0.8 (1.4)	-4	-1.0	2	-0.28 [-0.48, -0.08]
			Placebo	199	188 (94.5)	-0.4 (1.5)	-4	0.0	4	
		Week 8	CR845	222	194 (87.4)	-0.9 (1.4)	-4	-1.0	2	-0.21 [-0.41, -0.01]
			Placebo	199	187 (94.0)	-0.6 (1.4)	-4	0.0	4	
		Week 10	CR845	222	191 (86.0)	-0.9 (1.5)	-4	-1.0	4	-0.17 [-0.38, 0.03]
			Placebo	199	185 (93.0)	-0.6 (1.4)	-4	0.0	4	
		Week 12	CR845	222	189 (85.1)	-1.0 (1.5)	-4	-1.0	4	-0.25 [-0.45, -0.04]
			Placebo	199	185 (93.0)	-0.6 (1.5)	-4	0.0	4	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DLC_ISHH: Change from baseline in 5-D duration score by dialysis method
ITT

H: Dialysis method	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Hemodiafiltration (HDF)	5-D duration score	Baseline	CR845	15	15 (100.0)	2.5 (1.5)	1	2.0	5	
			Placebo	37	37 (100.0)	2.1 (1.4)	1	2.0	5	
		Week 4	CR845	15	13 (86.7)	1.8 (1.3)	1	1.0	5	
			Placebo	37	37 (100.0)	2.0 (1.5)	1	1.0	5	
		Week 8	CR845	15	13 (86.7)	1.8 (1.4)	1	1.0	5	
			Placebo	37	35 (94.6)	1.7 (1.0)	1	1.0	5	
		Week 10	CR845	15	12 (80.0)	1.6 (1.4)	1	1.0	5	
			Placebo	37	32 (86.5)	1.8 (1.2)	1	1.0	5	
		Week 12	CR845	15	13 (86.7)	1.8 (1.5)	1	1.0	5	
			Placebo	37	34 (91.9)	2.1 (1.5)	1	1.5	5	
	Change from baseline in 5-D duration score	Week 4	CR845	15	13 (86.7)	-0.7 (1.4)	-4	-1.0	2	-0.35 [-0.98, 0.29]
			Placebo	37	37 (100.0)	-0.1 (1.8)	-4	0.0	4	
		Week 8	CR845	15	13 (86.7)	-0.8 (1.7)	-4	-1.0	2	-0.24 [-0.88, 0.39]
			Placebo	37	35 (94.6)	-0.4 (1.4)	-4	0.0	3	
		Week 10	CR845	15	12 (80.0)	-1.0 (1.7)	-4	-1.0	2	-0.40 [-1.07, 0.27]
			Placebo	37	32 (86.5)	-0.3 (1.6)	-3	0.0	4	
		Week 12	CR845	15	13 (86.7)	-0.8 (1.5)	-4	0.0	2	-0.44 [-1.09, 0.21]
			Placebo	37	34 (91.9)	-0.0 (1.7)	-3	0.0	4	

ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DWC_ISHA: Change from baseline in 5-D direction score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
< 65 years	5-D direction score	Baseline	CR845	147	144 (98.0)	3.9 (0.6)	2	4.0	5	
			Placebo	153	153 (100.0)	3.8 (0.7)	2	4.0	5	
		Week 4	CR845	147	135 (91.8)	2.7 (0.8)	1	3.0	5	
			Placebo	153	144 (94.1)	3.1 (0.9)	2	3.0	5	
		Week 8	CR845	147	131 (89.1)	2.6 (0.8)	1	2.0	5	
			Placebo	153	143 (93.5)	2.9 (0.9)	1	3.0	5	
		Week 10	CR845	147	132 (89.8)	2.6 (0.8)	1	2.0	5	
			Placebo	153	141 (92.2)	2.9 (0.9)	1	3.0	5	
		Week 12	CR845	147	131 (89.1)	2.6 (0.9)	1	2.0	5	
			Placebo	153	142 (92.8)	2.9 (1.0)	1	3.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	147	133 (90.5)	-1.3 (1.0)	-4	-1.0	2	-0.55 [-0.79, -0.31]
			Placebo	153	144 (94.1)	-0.7 (1.0)	-3	-1.0	2	
		Week 8	CR845	147	129 (87.8)	-1.4 (0.8)	-3	-1.0	1	-0.49 [-0.74, -0.25]
			Placebo	153	143 (93.5)	-0.9 (1.1)	-3	-1.0	2	
		Week 10	CR845	147	130 (88.4)	-1.3 (0.9)	-3	-1.0	1	-0.41 [-0.65, -0.17]
			Placebo	153	141 (92.2)	-0.9 (1.1)	-3	-1.0	3	
		Week 12	CR845	147	129 (87.8)	-1.3 (1.0)	-3	-2.0	2	-0.40 [-0.65, -0.16]
			Placebo	153	142 (92.8)	-0.9 (1.1)	-4	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DWC_ISHA: Change from baseline in 5-D direction score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 65 years	5-D direction score	Baseline	CR845	90	90 (100.0)	3.8 (0.7)	1	4.0	5	
			Placebo	83	83 (100.0)	3.8 (0.8)	2	4.0	5	
		Week 4	CR845	90	80 (88.9)	2.7 (0.9)	1	3.0	5	
			Placebo	83	81 (97.6)	3.1 (0.9)	1	3.0	5	
		Week 8	CR845	90	78 (86.7)	2.8 (0.9)	1	3.0	5	
			Placebo	83	79 (95.2)	2.9 (0.8)	1	3.0	5	
		Week 10	CR845	90	74 (82.2)	2.6 (0.9)	1	2.0	5	
			Placebo	83	76 (91.6)	3.1 (0.9)	1	3.0	5	
		Week 12	CR845	90	73 (81.1)	2.7 (1.0)	1	2.0	5	
			Placebo	83	77 (92.8)	2.9 (1.0)	1	3.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	90	80 (88.9)	-1.1 (1.1)	-3	-1.0	2	-0.29 [-0.60, 0.02]
			Placebo	83	81 (97.6)	-0.8 (1.0)	-3	-1.0	2	
		Week 8	CR845	90	78 (86.7)	-1.0 (1.1)	-4	-1.0	2	-0.05 [-0.36, 0.27]
			Placebo	83	79 (95.2)	-0.9 (1.0)	-3	-1.0	2	
		Week 10	CR845	90	74 (82.2)	-1.1 (1.0)	-4	-1.0	1	-0.40 [-0.72, -0.07]
			Placebo	83	76 (91.6)	-0.7 (1.2)	-3	-1.0	3	
		Week 12	CR845	90	73 (81.1)	-1.1 (1.1)	-4	-1.0	1	-0.09 [-0.41, 0.23]
			Placebo	83	77 (92.8)	-1.0 (1.2)	-3	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DWC_ISHB: Change from baseline in 5-D direction score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Male	5-D direction score	Baseline	CR845	137	135 (98.5)	3.9 (0.6)	1	4.0	5	
			Placebo	139	139 (100.0)	3.8 (0.7)	2	4.0	5	
		Week 4	CR845	137	125 (91.2)	2.8 (0.8)	1	3.0	5	
			Placebo	139	131 (94.2)	3.0 (0.8)	1	3.0	4	
		Week 8	CR845	137	122 (89.1)	2.9 (0.8)	1	3.0	5	
			Placebo	139	132 (95.0)	2.9 (0.9)	1	3.0	5	
		Week 10	CR845	137	118 (86.1)	2.8 (0.9)	1	3.0	5	
			Placebo	139	127 (91.4)	2.9 (0.8)	1	3.0	5	
		Week 12	CR845	137	118 (86.1)	2.8 (1.0)	1	2.0	5	
			Placebo	139	127 (91.4)	2.9 (1.0)	1	3.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	137	124 (90.5)	-1.1 (1.0)	-3	-1.0	2	-0.31 [-0.56, -0.06]
			Placebo	139	131 (94.2)	-0.8 (1.0)	-3	-1.0	2	
		Week 8	CR845	137	121 (88.3)	-1.0 (0.9)	-3	-1.0	2	-0.11 [-0.36, 0.13]
			Placebo	139	132 (95.0)	-0.9 (1.1)	-3	-1.0	2	
		Week 10	CR845	137	117 (85.4)	-1.1 (0.9)	-3	-1.0	1	-0.22 [-0.47, 0.03]
			Placebo	139	127 (91.4)	-0.9 (1.0)	-3	-1.0	2	
		Week 12	CR845	137	117 (85.4)	-1.1 (1.0)	-3	-1.0	2	-0.17 [-0.43, 0.08]
			Placebo	139	127 (91.4)	-0.9 (1.1)	-3	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DWC_ISHB: Change from baseline in 5-D direction score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Female	5-D direction score	Baseline	CR845	100	99 (99.0)	3.8 (0.7)	2	4.0	5	
			Placebo	97	97 (100.0)	3.8 (0.7)	2	4.0	5	
		Week 4	CR845	100	90 (90.0)	2.5 (0.8)	1	2.0	5	
			Placebo	97	94 (96.9)	3.2 (0.9)	2	3.0	5	
		Week 8	CR845	100	87 (87.0)	2.3 (0.7)	1	2.0	5	
			Placebo	97	90 (92.8)	2.9 (0.9)	1	3.0	5	
		Week 10	CR845	100	88 (88.0)	2.4 (0.8)	1	2.0	4	
			Placebo	97	90 (92.8)	3.1 (1.0)	1	3.0	5	
		Week 12	CR845	100	86 (86.0)	2.4 (0.9)	1	2.0	5	
			Placebo	97	92 (94.8)	2.9 (1.0)	1	3.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	100	89 (89.0)	-1.3 (1.1)	-4	-1.0	1	-0.63 [-0.93, -0.33]
			Placebo	97	94 (96.9)	-0.6 (1.1)	-3	-1.0	2	
		Week 8	CR845	100	86 (86.0)	-1.5 (1.0)	-4	-2.0	1	-0.61 [-0.91, -0.31]
			Placebo	97	90 (92.8)	-0.9 (1.0)	-3	-1.0	2	
		Week 10	CR845	100	87 (87.0)	-1.5 (1.0)	-4	-2.0	1	-0.61 [-0.91, -0.31]
			Placebo	97	90 (92.8)	-0.8 (1.3)	-3	-1.0	3	
		Week 12	CR845	100	85 (85.0)	-1.4 (1.1)	-4	-1.0	2	-0.42 [-0.72, -0.13]
			Placebo	97	92 (94.8)	-0.9 (1.2)	-4	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DWC_ISHC: Change from baseline in 5-D direction score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Black/African American	5-D direction score	Baseline	CR845	53	51 (96.2)	4.0 (0.6)	2	4.0	5	
			Placebo	38	38 (100.0)	3.7 (0.9)	2	4.0	5	
		Week 4	CR845	53	47 (88.7)	2.8 (0.8)	2	3.0	5	
			Placebo	38	35 (92.1)	3.1 (0.9)	2	3.0	5	
		Week 8	CR845	53	47 (88.7)	2.6 (0.8)	1	3.0	5	
			Placebo	38	37 (97.4)	2.8 (0.9)	1	3.0	5	
		Week 10	CR845	53	44 (83.0)	2.5 (0.8)	1	2.0	5	
			Placebo	38	36 (94.7)	2.9 (1.0)	1	3.0	5	
		Week 12	CR845	53	44 (83.0)	2.4 (0.7)	1	2.0	4	
			Placebo	38	37 (97.4)	2.8 (0.9)	1	3.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	53	45 (84.9)	-1.2 (1.0)	-3	-1.0	1	-0.53 [-0.98, -0.08]
			Placebo	38	35 (92.1)	-0.6 (1.2)	-3	-1.0	2	
		Week 8	CR845	53	45 (84.9)	-1.3 (1.1)	-4	-1.0	1	-0.34 [-0.78, 0.10]
			Placebo	38	37 (97.4)	-0.9 (1.2)	-3	-1.0	2	
		Week 10	CR845	53	42 (79.2)	-1.5 (1.0)	-4	-2.0	1	-0.48 [-0.93, -0.03]
			Placebo	38	36 (94.7)	-0.9 (1.3)	-3	-1.0	3	
		Week 12	CR845	53	42 (79.2)	-1.5 (1.0)	-4	-2.0	1	-0.54 [-0.99, -0.09]
			Placebo	38	37 (97.4)	-0.9 (1.2)	-3	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DWC_ISHC: Change from baseline in 5-D direction score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
White	5-D direction score	Baseline	CR845	164	163 (99.4)	3.9 (0.6)	2	4.0	5	
			Placebo	169	169 (100.0)	3.8 (0.7)	2	4.0	5	
		Week 4	CR845	164	151 (92.1)	2.7 (0.9)	1	3.0	5	
			Placebo	169	162 (95.9)	3.1 (0.9)	1	3.0	5	
		Week 8	CR845	164	145 (88.4)	2.7 (0.9)	1	3.0	5	
			Placebo	169	159 (94.1)	3.0 (0.9)	1	3.0	5	
		Week 10	CR845	164	146 (89.0)	2.6 (0.9)	1	2.0	5	
			Placebo	169	156 (92.3)	3.0 (0.9)	1	3.0	5	
		Week 12	CR845	164	144 (87.8)	2.7 (1.1)	1	2.0	5	
			Placebo	169	159 (94.1)	3.0 (1.0)	1	3.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	164	151 (92.1)	-1.2 (1.0)	-4	-1.0	2	-0.45 [-0.68, -0.23]
			Placebo	169	162 (95.9)	-0.7 (1.0)	-3	-1.0	2	
		Week 8	CR845	164	145 (88.4)	-1.2 (0.9)	-3	-1.0	1	-0.36 [-0.59, -0.14]
			Placebo	169	159 (94.1)	-0.8 (1.1)	-3	-1.0	2	
		Week 10	CR845	164	146 (89.0)	-1.2 (1.0)	-3	-1.0	1	-0.39 [-0.62, -0.17]
			Placebo	169	156 (92.3)	-0.8 (1.1)	-3	-1.0	2	
		Week 12	CR845	164	144 (87.8)	-1.2 (1.1)	-3	-1.0	2	-0.26 [-0.49, -0.04]
			Placebo	169	159 (94.1)	-0.9 (1.1)	-4	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DWC_ISHC: Change from baseline in 5-D direction score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Other	5-D direction score	Baseline	CR845	20	20 (100.0)	3.6 (0.9)	1	4.0	5	
			Placebo	29	29 (100.0)	3.9 (0.6)	3	4.0	5	
		Week 4	CR845	20	17 (85.0)	2.5 (0.7)	1	2.0	4	
			Placebo	29	28 (96.6)	3.0 (0.9)	2	3.0	5	
		Week 8	CR845	20	17 (85.0)	2.6 (0.6)	2	3.0	4	
			Placebo	29	26 (89.7)	2.7 (0.7)	2	3.0	4	
		Week 10	CR845	20	16 (80.0)	2.4 (0.5)	2	2.0	3	
			Placebo	29	25 (86.2)	2.8 (0.8)	2	3.0	5	
		Week 12	CR845	20	16 (80.0)	2.6 (0.7)	2	2.0	4	
			Placebo	29	23 (79.3)	2.7 (0.9)	1	3.0	4	
	Change from baseline in 5-D direction score	Week 4	CR845	20	17 (85.0)	-1.1 (1.2)	-3	-1.0	2	-0.29 [-0.90, 0.31]
			Placebo	29	28 (96.6)	-0.8 (0.9)	-3	-1.0	1	
		Week 8	CR845	20	17 (85.0)	-0.9 (1.1)	-3	-1.0	2	0.20 [-0.41, 0.81]
			Placebo	29	26 (89.7)	-1.1 (0.7)	-2	-1.0	0	
		Week 10	CR845	20	16 (80.0)	-1.2 (0.9)	-3	-1.0	1	-0.22 [-0.85, 0.41]
			Placebo	29	25 (86.2)	-1.0 (0.8)	-2	-1.0	0	
		Week 12	CR845	20	16 (80.0)	-0.9 (0.9)	-2	-1.0	1	0.20 [-0.44, 0.84]
			Placebo	29	23 (79.3)	-1.1 (1.0)	-3	-1.0	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DWC_ISHD: Change from baseline in 5-D direction score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 4 to < 7	5-D direction score	Baseline	CR845	102	101 (99.0)	3.7 (0.7)	1	4.0	5	
			Placebo	113	113 (100.0)	3.6 (0.7)	2	4.0	5	
		Week 4	CR845	102	96 (94.1)	2.5 (0.8)	1	2.0	5	
			Placebo	113	109 (96.5)	2.9 (0.9)	1	3.0	5	
		Week 8	CR845	102	95 (93.1)	2.5 (0.7)	1	2.0	4	
			Placebo	113	105 (92.9)	2.9 (0.9)	1	3.0	5	
		Week 10	CR845	102	92 (90.2)	2.4 (0.8)	1	2.0	5	
			Placebo	113	102 (90.3)	2.9 (0.9)	1	3.0	5	
		Week 12	CR845	102	91 (89.2)	2.5 (0.9)	1	2.0	5	
			Placebo	113	103 (91.2)	2.8 (1.0)	1	3.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	102	95 (93.1)	-1.1 (1.0)	-4	-1.0	2	-0.43 [-0.71, -0.15]
			Placebo	113	109 (96.5)	-0.7 (1.0)	-3	-1.0	2	
		Week 8	CR845	102	94 (92.2)	-1.1 (0.9)	-3	-1.0	2	-0.42 [-0.70, -0.14]
			Placebo	113	105 (92.9)	-0.7 (1.0)	-3	-1.0	2	
		Week 10	CR845	102	91 (89.2)	-1.2 (0.9)	-3	-1.0	1	-0.50 [-0.78, -0.21]
			Placebo	113	102 (90.3)	-0.7 (1.1)	-3	-1.0	2	
		Week 12	CR845	102	90 (88.2)	-1.1 (1.1)	-3	-1.0	2	-0.27 [-0.55, 0.02]
			Placebo	113	103 (91.2)	-0.8 (1.1)	-3	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DWC_ISHD: Change from baseline in 5-D direction score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 7	5-D direction score	Baseline	CR845	135	133 (98.5)	4.0 (0.5)	2	4.0	5	
			Placebo	123	123 (100.0)	4.0 (0.7)	2	4.0	5	
		Week 4	CR845	135	119 (88.1)	2.8 (0.9)	1	3.0	5	
			Placebo	123	116 (94.3)	3.2 (0.8)	2	3.0	5	
		Week 8	CR845	135	114 (84.4)	2.8 (0.9)	1	3.0	5	
			Placebo	123	117 (95.1)	2.9 (0.8)	1	3.0	5	
		Week 10	CR845	135	114 (84.4)	2.8 (0.9)	1	3.0	5	
			Placebo	123	115 (93.5)	3.1 (0.9)	1	3.0	5	
		Week 12	CR845	135	113 (83.7)	2.7 (1.0)	1	3.0	5	
			Placebo	123	116 (94.3)	3.0 (1.0)	1	3.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	135	118 (87.4)	-1.2 (1.0)	-3	-1.0	2	-0.46 [-0.72, -0.20]
			Placebo	123	116 (94.3)	-0.8 (1.0)	-3	-1.0	2	
		Week 8	CR845	135	113 (83.7)	-1.3 (1.0)	-4	-1.0	1	-0.23 [-0.49, 0.03]
			Placebo	123	117 (95.1)	-1.0 (1.1)	-3	-1.0	2	
		Week 10	CR845	135	113 (83.7)	-1.3 (1.0)	-4	-1.0	1	-0.32 [-0.58, -0.06]
			Placebo	123	115 (93.5)	-0.9 (1.1)	-3	-1.0	3	
		Week 12	CR845	135	112 (83.0)	-1.3 (1.1)	-4	-1.0	2	-0.29 [-0.55, -0.03]
			Placebo	123	116 (94.3)	-1.0 (1.1)	-4	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DWC_ISHE: Change from baseline in 5-D direction score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	5-D direction score	Baseline	CR845	195	192 (98.5)	3.9 (0.6)	1	4.0	5	
			Placebo	199	199 (100.0)	3.8 (0.7)	2	4.0	5	
		Week 4	CR845	195	177 (90.8)	2.7 (0.8)	1	3.0	5	
			Placebo	199	191 (96.0)	3.1 (0.9)	1	3.0	5	
		Week 8	CR845	195	173 (88.7)	2.7 (0.8)	1	3.0	5	
			Placebo	199	185 (93.0)	2.9 (0.9)	1	3.0	5	
		Week 10	CR845	195	171 (87.7)	2.6 (0.8)	1	2.0	5	
			Placebo	199	180 (90.5)	3.0 (1.0)	1	3.0	5	
		Week 12	CR845	195	170 (87.2)	2.6 (1.0)	1	2.0	5	
			Placebo	199	183 (92.0)	2.9 (1.0)	1	3.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	195	175 (89.7)	-1.2 (1.0)	-4	-1.0	2	-0.44 [-0.65, -0.24]
			Placebo	199	191 (96.0)	-0.7 (1.0)	-3	-1.0	2	
		Week 8	CR845	195	171 (87.7)	-1.2 (0.9)	-3	-1.0	2	-0.30 [-0.51, -0.09]
			Placebo	199	185 (93.0)	-0.9 (1.1)	-3	-1.0	2	
		Week 10	CR845	195	169 (86.7)	-1.3 (0.9)	-3	-1.0	1	-0.45 [-0.67, -0.24]
			Placebo	199	180 (90.5)	-0.8 (1.1)	-3	-1.0	3	
		Week 12	CR845	195	168 (86.2)	-1.2 (1.0)	-3	-1.0	2	-0.32 [-0.54, -0.11]
			Placebo	199	183 (92.0)	-0.9 (1.1)	-4	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DWC_ISHE: Change from baseline in 5-D direction score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	5-D direction score	Baseline	CR845	42	42 (100.0)	3.9 (0.6)	2	4.0	5	
			Placebo	37	37 (100.0)	3.9 (0.7)	2	4.0	5	
		Week 4	CR845	42	38 (90.5)	2.7 (0.8)	1	3.0	4	
			Placebo	37	34 (91.9)	3.2 (0.8)	2	3.0	5	
		Week 8	CR845	42	36 (85.7)	2.4 (0.9)	1	2.0	5	
			Placebo	37	37 (100.0)	2.9 (0.8)	2	3.0	4	
		Week 10	CR845	42	35 (83.3)	2.7 (0.9)	1	3.0	4	
			Placebo	37	37 (100.0)	2.9 (0.7)	2	3.0	4	
		Week 12	CR845	42	34 (81.0)	2.6 (1.0)	1	3.0	5	
			Placebo	37	36 (97.3)	2.8 (0.9)	1	3.0	4	
	Change from baseline in 5-D direction score	Week 4	CR845	42	38 (90.5)	-1.2 (1.0)	-3	-1.0	1	-0.48 [-0.95, -0.01]
			Placebo	37	34 (91.9)	-0.7 (0.8)	-2	-1.0	1	
		Week 8	CR845	42	36 (85.7)	-1.5 (1.1)	-4	-1.5	1	-0.37 [-0.84, 0.09]
			Placebo	37	37 (100.0)	-1.1 (1.0)	-3	-1.0	1	
		Week 10	CR845	42	35 (83.3)	-1.2 (1.1)	-4	-1.0	1	-0.14 [-0.61, 0.32]
			Placebo	37	37 (100.0)	-1.1 (1.0)	-3	-1.0	2	
		Week 12	CR845	42	34 (81.0)	-1.2 (1.2)	-4	-1.0	1	-0.09 [-0.56, 0.38]
			Placebo	37	36 (97.3)	-1.1 (1.0)	-3	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DWC_ISHF: Change from baseline in 5-D direction score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	5-D direction score	Baseline	CR845	150	147 (98.0)	3.9 (0.7)	1	4.0	5	
			Placebo	151	151 (100.0)	3.8 (0.8)	2	4.0	5	
		Week 4	CR845	150	141 (94.0)	2.7 (0.8)	1	3.0	5	
			Placebo	151	146 (96.7)	3.1 (0.8)	1	3.0	5	
		Week 8	CR845	150	137 (91.3)	2.7 (0.8)	1	3.0	5	
			Placebo	151	142 (94.0)	2.9 (0.9)	1	3.0	5	
		Week 10	CR845	150	133 (88.7)	2.7 (0.9)	1	3.0	5	
			Placebo	151	140 (92.7)	2.9 (0.9)	1	3.0	5	
		Week 12	CR845	150	134 (89.3)	2.7 (1.0)	1	2.0	5	
			Placebo	151	141 (93.4)	2.9 (1.0)	1	3.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	150	139 (92.7)	-1.2 (1.1)	-4	-1.0	2	-0.37 [-0.61, -0.14]
			Placebo	151	146 (96.7)	-0.8 (1.0)	-3	-1.0	2	
		Week 8	CR845	150	135 (90.0)	-1.2 (0.9)	-3	-1.0	2	-0.26 [-0.49, -0.02]
			Placebo	151	142 (94.0)	-0.9 (1.1)	-3	-1.0	2	
		Week 10	CR845	150	131 (87.3)	-1.1 (1.0)	-3	-1.0	1	-0.22 [-0.46, 0.02]
			Placebo	151	140 (92.7)	-0.9 (1.1)	-3	-1.0	2	
		Week 12	CR845	150	132 (88.0)	-1.1 (1.1)	-3	-1.0	2	-0.20 [-0.43, 0.04]
			Placebo	151	141 (93.4)	-0.9 (1.1)	-3	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DWC_ISHF: Change from baseline in 5-D direction score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	5-D direction score	Baseline	CR845	87	87 (100.0)	3.9 (0.6)	2	4.0	5	
			Placebo	85	85 (100.0)	3.8 (0.7)	2	4.0	5	
		Week 4	CR845	87	74 (85.1)	2.6 (0.8)	1	3.0	4	
			Placebo	85	79 (92.9)	3.1 (0.9)	2	3.0	5	
		Week 8	CR845	87	72 (82.8)	2.6 (0.9)	1	3.0	5	
			Placebo	85	80 (94.1)	2.9 (0.9)	2	3.0	5	
		Week 10	CR845	87	73 (83.9)	2.4 (0.8)	1	2.0	4	
			Placebo	85	77 (90.6)	3.1 (0.9)	2	3.0	5	
		Week 12	CR845	87	70 (80.5)	2.5 (0.9)	1	2.0	5	
			Placebo	85	78 (91.8)	2.9 (0.9)	1	3.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	87	74 (85.1)	-1.2 (1.0)	-3	-1.0	1	-0.60 [-0.92, -0.28]
			Placebo	85	79 (92.9)	-0.6 (1.0)	-3	-1.0	2	
		Week 8	CR845	87	72 (82.8)	-1.3 (1.0)	-4	-1.0	1	-0.42 [-0.74, -0.10]
			Placebo	85	80 (94.1)	-0.8 (1.1)	-3	-1.0	2	
		Week 10	CR845	87	73 (83.9)	-1.5 (1.0)	-4	-1.0	1	-0.72 [-1.05, -0.39]
			Placebo	85	77 (90.6)	-0.7 (1.2)	-3	-1.0	3	
		Week 12	CR845	87	70 (80.5)	-1.4 (1.0)	-4	-1.0	1	-0.46 [-0.78, -0.13]
			Placebo	85	78 (91.8)	-0.9 (1.1)	-4	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DWC_ISHG: Change from baseline in 5-D direction score by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
USA	5-D direction score	Baseline	CR845	146	143 (97.9)	3.9 (0.6)	2	4.0	5	
			Placebo	133	133 (100.0)	3.8 (0.8)	2	4.0	5	
		Week 4	CR845	146	133 (91.1)	2.7 (0.7)	1	3.0	5	
			Placebo	133	123 (92.5)	3.1 (0.8)	2	3.0	5	
		Week 8	CR845	146	131 (89.7)	2.6 (0.7)	1	3.0	5	
			Placebo	133	125 (94.0)	2.8 (0.9)	1	3.0	5	
		Week 10	CR845	146	129 (88.4)	2.6 (0.8)	1	2.0	5	
			Placebo	133	122 (91.7)	2.8 (0.8)	1	3.0	5	
		Week 12	CR845	146	128 (87.7)	2.6 (0.9)	1	2.0	5	
			Placebo	133	125 (94.0)	2.8 (1.0)	1	3.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	146	131 (89.7)	-1.1 (0.9)	-3	-1.0	1	-0.46 [-0.71, -0.22]
			Placebo	133	123 (92.5)	-0.7 (1.0)	-3	-1.0	2	
		Week 8	CR845	146	129 (88.4)	-1.2 (0.9)	-4	-1.0	1	-0.29 [-0.53, -0.04]
			Placebo	133	125 (94.0)	-1.0 (1.1)	-3	-1.0	2	
		Week 10	CR845	146	127 (87.0)	-1.3 (0.9)	-4	-1.0	1	-0.30 [-0.55, -0.05]
			Placebo	133	122 (91.7)	-1.0 (1.1)	-3	-1.0	3	
		Week 12	CR845	146	126 (86.3)	-1.3 (1.0)	-4	-1.0	2	-0.29 [-0.54, -0.04]
			Placebo	133	125 (94.0)	-1.0 (1.2)	-4	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DWC_ISHG: Change from baseline in 5-D direction score by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Asia	5-D direction score	Baseline	CR845	8	8 (100.0)	3.1 (1.0)	1	3.0	4	
			Placebo	12	12 (100.0)	3.8 (0.4)	3	4.0	4	
		Week 4	CR845	8	8 (100.0)	2.3 (0.7)	1	2.0	3	
			Placebo	12	12 (100.0)	3.0 (0.7)	2	3.0	4	
		Week 8	CR845	8	7 (87.5)	2.6 (0.5)	2	3.0	3	
			Placebo	12	12 (100.0)	2.6 (0.5)	2	3.0	3	
		Week 10	CR845	8	7 (87.5)	2.1 (0.4)	2	2.0	3	
			Placebo	12	11 (91.7)	2.7 (0.6)	2	3.0	4	
		Week 12	CR845	8	7 (87.5)	2.1 (0.4)	2	2.0	3	
			Placebo	12	11 (91.7)	2.6 (1.0)	1	2.0	4	
	Change from baseline in 5-D direction score	Week 4	CR845	8	8 (100.0)	-0.9 (1.4)	-2	-1.0	2	-0.04 [-0.93, 0.86]
			Placebo	12	12 (100.0)	-0.8 (0.8)	-2	-1.0	1	
		Week 8	CR845	8	7 (87.5)	-0.4 (1.1)	-1	-1.0	2	0.91 [-0.07, 1.89]
			Placebo	12	12 (100.0)	-1.3 (0.8)	-2	-1.0	0	
		Week 10	CR845	8	7 (87.5)	-0.9 (0.9)	-2	-1.0	1	0.27 [-0.68, 1.22]
			Placebo	12	11 (91.7)	-1.1 (0.8)	-2	-1.0	0	
		Week 12	CR845	8	7 (87.5)	-0.9 (0.9)	-2	-1.0	1	0.30 [-0.65, 1.26]
			Placebo	12	11 (91.7)	-1.2 (1.2)	-3	-1.0	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DWC_ISHG: Change from baseline in 5-D direction score by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Eastern Europe	5-D direction score	Baseline	CR845	54	54 (100.0)	3.9 (0.7)	2	4.0	5	
			Placebo	60	60 (100.0)	3.9 (0.6)	2	4.0	5	
		Week 4	CR845	54	52 (96.3)	2.7 (0.9)	1	3.0	4	
			Placebo	60	59 (98.3)	3.1 (0.9)	1	3.0	5	
		Week 8	CR845	54	48 (88.9)	2.7 (1.0)	1	3.0	5	
			Placebo	60	59 (98.3)	3.1 (0.9)	1	3.0	5	
		Week 10	CR845	54	48 (88.9)	2.7 (1.0)	1	2.5	5	
			Placebo	60	59 (98.3)	3.2 (0.9)	1	3.0	5	
		Week 12	CR845	54	47 (87.0)	2.7 (1.2)	1	2.0	5	
			Placebo	60	58 (96.7)	3.0 (0.9)	1	3.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	54	52 (96.3)	-1.2 (1.0)	-3	-1.0	2	-0.43 [-0.81, -0.05]
			Placebo	60	59 (98.3)	-0.8 (1.0)	-3	-1.0	2	
		Week 8	CR845	54	48 (88.9)	-1.2 (0.9)	-3	-1.0	1	-0.45 [-0.84, -0.06]
			Placebo	60	59 (98.3)	-0.8 (1.0)	-3	-1.0	1	
		Week 10	CR845	54	48 (88.9)	-1.2 (1.0)	-3	-1.0	1	-0.47 [-0.85, -0.08]
			Placebo	60	59 (98.3)	-0.7 (1.1)	-3	-1.0	2	
		Week 12	CR845	54	47 (87.0)	-1.1 (1.2)	-3	-1.0	2	-0.25 [-0.64, 0.13]
			Placebo	60	58 (96.7)	-0.9 (1.0)	-3	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DWC_ISHG: Change from baseline in 5-D direction score by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Western Europe/European origin	5-D direction score	Baseline	CR845	29	29 (100.0)	4.0 (0.5)	3	4.0	5	
			Placebo	31	31 (100.0)	3.9 (0.7)	2	4.0	5	
		Week 4	CR845	29	22 (75.9)	2.6 (1.2)	1	2.0	5	
			Placebo	31	31 (100.0)	3.2 (0.9)	2	3.0	5	
		Week 8	CR845	29	23 (79.3)	2.8 (1.1)	1	2.0	5	
			Placebo	31	26 (83.9)	3.2 (1.0)	2	3.0	5	
		Week 10	CR845	29	22 (75.9)	2.7 (1.0)	1	2.5	5	
			Placebo	31	25 (80.6)	3.4 (1.0)	2	3.0	5	
		Week 12	CR845	29	22 (75.9)	2.9 (1.0)	1	3.0	5	
			Placebo	31	25 (80.6)	3.2 (1.1)	1	4.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	29	22 (75.9)	-1.5 (1.5)	-4	-2.0	1	-0.61 [-1.17, -0.05]
			Placebo	31	31 (100.0)	-0.7 (1.1)	-3	-1.0	2	
		Week 8	CR845	29	23 (79.3)	-1.3 (1.4)	-3	-2.0	1	-0.48 [-1.05, 0.09]
			Placebo	31	26 (83.9)	-0.7 (1.2)	-2	-1.0	2	
		Week 10	CR845	29	22 (75.9)	-1.4 (1.3)	-3	-1.5	1	-0.81 [-1.41, -0.22]
			Placebo	31	25 (80.6)	-0.4 (1.2)	-2	0.0	3	
		Week 12	CR845	29	22 (75.9)	-1.2 (1.3)	-3	-1.0	1	-0.48 [-1.06, 0.10]
			Placebo	31	25 (80.6)	-0.6 (1.1)	-3	0.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DWC_ISHH: Change from baseline in 5-D direction score by dialysis method
ITT

H: Dialysis method	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Hemodialysis (HD)	5-D direction score	Baseline	CR845	222	219 (98.6)	3.8 (0.6)	1	4.0	5	
			Placebo	199	199 (100.0)	3.8 (0.7)	2	4.0	5	
		Week 4	CR845	222	202 (91.0)	2.7 (0.8)	1	3.0	5	
			Placebo	199	188 (94.5)	3.1 (0.8)	2	3.0	5	
		Week 8	CR845	222	196 (88.3)	2.6 (0.8)	1	3.0	5	
			Placebo	199	187 (94.0)	2.9 (0.9)	1	3.0	5	
		Week 10	CR845	222	194 (87.4)	2.6 (0.8)	1	2.0	5	
			Placebo	199	185 (93.0)	2.9 (0.9)	1	3.0	5	
		Week 12	CR845	222	191 (86.0)	2.6 (0.9)	1	2.0	5	
			Placebo	199	185 (93.0)	2.9 (1.0)	1	3.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	222	200 (90.1)	-1.2 (1.0)	-4	-1.0	2	-0.45 [-0.66, -0.25]
			Placebo	199	188 (94.5)	-0.7 (1.0)	-3	-1.0	2	
		Week 8	CR845	222	194 (87.4)	-1.2 (1.0)	-4	-1.0	2	-0.34 [-0.54, -0.14]
			Placebo	199	187 (94.0)	-0.9 (1.0)	-3	-1.0	2	
		Week 10	CR845	222	192 (86.5)	-1.2 (1.0)	-4	-1.0	1	-0.35 [-0.55, -0.15]
			Placebo	199	185 (93.0)	-0.9 (1.1)	-3	-1.0	3	
		Week 12	CR845	222	189 (85.1)	-1.2 (1.1)	-4	-1.0	2	-0.27 [-0.48, -0.07]
			Placebo	199	185 (93.0)	-0.9 (1.1)	-4	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DWC_ISHH: Change from baseline in 5-D direction score by dialysis method
ITT

H: Dialysis method	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Hemodiafiltration (HDF)	5-D direction score	Baseline	CR845	15	15 (100.0)	4.3 (0.5)	4	4.0	5	
			Placebo	37	37 (100.0)	3.9 (0.6)	2	4.0	5	
		Week 4	CR845	15	13 (86.7)	2.8 (1.0)	1	3.0	4	
			Placebo	37	37 (100.0)	3.1 (0.9)	1	3.0	5	
		Week 8	CR845	15	13 (86.7)	3.2 (0.9)	2	3.0	5	
			Placebo	37	35 (94.6)	2.9 (1.0)	1	3.0	5	
		Week 10	CR845	15	12 (80.0)	2.8 (1.0)	1	3.0	4	
			Placebo	37	32 (86.5)	3.3 (1.1)	1	3.0	5	
		Week 12	CR845	15	13 (86.7)	3.3 (1.3)	1	4.0	5	
			Placebo	37	34 (91.9)	3.2 (1.0)	1	3.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	15	13 (86.7)	-1.5 (1.0)	-3	-1.0	0	-0.59 [-1.23, 0.06]
			Placebo	37	37 (100.0)	-0.8 (1.1)	-3	-1.0	2	
		Week 8	CR845	15	13 (86.7)	-1.1 (0.8)	-2	-1.0	0	-0.10 [-0.73, 0.54]
			Placebo	37	35 (94.6)	-1.0 (1.2)	-3	-1.0	2	
		Week 10	CR845	15	12 (80.0)	-1.5 (1.0)	-3	-1.5	0	-0.78 [-1.46, -0.10]
			Placebo	37	32 (86.5)	-0.6 (1.2)	-2	-1.0	3	
		Week 12	CR845	15	13 (86.7)	-1.0 (1.2)	-3	-1.0	1	-0.22 [-0.86, 0.42]
			Placebo	37	34 (91.9)	-0.8 (1.0)	-2	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DNC_ISHA: Change from baseline in 5-D disability score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
< 65 years	5-D disability score	Baseline	CR845	147	144 (98.0)	3.6 (1.1)	1	4.0	5	
			Placebo	153	153 (100.0)	3.6 (1.2)	1	4.0	5	
		Week 4	CR845	147	135 (91.8)	2.9 (1.2)	1	3.0	5	
			Placebo	153	144 (94.1)	3.0 (1.2)	1	3.0	5	
		Week 8	CR845	147	132 (89.8)	2.6 (1.2)	1	2.5	5	
			Placebo	153	143 (93.5)	2.7 (1.2)	1	3.0	5	
		Week 10	CR845	147	132 (89.8)	2.5 (1.2)	1	2.0	5	
			Placebo	153	141 (92.2)	2.6 (1.2)	1	2.0	5	
		Week 12	CR845	147	131 (89.1)	2.5 (1.2)	1	2.0	5	
			Placebo	153	142 (92.8)	2.6 (1.2)	1	2.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	147	133 (90.5)	-0.7 (1.2)	-4	-1.0	2	-0.08 [-0.31, 0.16]
			Placebo	153	144 (94.1)	-0.6 (1.4)	-4	-1.0	3	
		Week 8	CR845	147	130 (88.4)	-1.0 (1.3)	-4	-1.0	2	-0.04 [-0.28, 0.20]
			Placebo	153	143 (93.5)	-0.9 (1.4)	-4	-1.0	4	
		Week 10	CR845	147	130 (88.4)	-1.1 (1.3)	-4	-1.0	2	-0.09 [-0.33, 0.15]
			Placebo	153	141 (92.2)	-1.0 (1.3)	-4	-1.0	3	
		Week 12	CR845	147	129 (87.8)	-1.2 (1.3)	-4	-1.0	2	-0.16 [-0.40, 0.08]
			Placebo	153	142 (92.8)	-1.0 (1.3)	-4	-1.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DNC_ISHA: Change from baseline in 5-D disability score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 65 years	5-D disability score	Baseline	CR845	90	89 (98.9)	3.4 (1.2)	1	3.0	5	
			Placebo	83	83 (100.0)	3.3 (1.2)	1	3.0	5	
		Week 4	CR845	90	80 (88.9)	2.8 (1.2)	1	3.0	5	
			Placebo	83	81 (97.6)	2.9 (1.1)	1	3.0	5	
		Week 8	CR845	90	78 (86.7)	2.4 (1.3)	1	2.0	5	
			Placebo	83	79 (95.2)	2.9 (1.2)	1	3.0	5	
		Week 10	CR845	90	74 (82.2)	2.3 (1.3)	1	2.0	5	
			Placebo	83	76 (91.6)	2.8 (1.2)	1	3.0	5	
		Week 12	CR845	90	74 (82.2)	2.4 (1.3)	1	2.0	5	
			Placebo	83	77 (92.8)	2.5 (1.1)	1	2.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	90	80 (88.9)	-0.6 (1.2)	-3	0.0	3	-0.11 [-0.42, 0.20]
			Placebo	83	81 (97.6)	-0.5 (1.1)	-3	0.0	3	
		Week 8	CR845	90	78 (86.7)	-0.9 (1.2)	-3	-1.0	3	-0.32 [-0.63, -0.00]
			Placebo	83	79 (95.2)	-0.5 (1.3)	-3	-1.0	3	
		Week 10	CR845	90	74 (82.2)	-1.0 (1.4)	-4	-1.0	3	-0.36 [-0.68, -0.04]
			Placebo	83	76 (91.6)	-0.5 (1.2)	-3	0.0	3	
		Week 12	CR845	90	74 (82.2)	-0.9 (1.5)	-4	-1.0	4	0.00 [-0.32, 0.32]
			Placebo	83	77 (92.8)	-0.9 (1.2)	-4	-1.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DNC_ISHB: Change from baseline in 5-D disability score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Male	5-D disability score	Baseline	CR845	137	135 (98.5)	3.6 (1.1)	1	4.0	5	
			Placebo	139	139 (100.0)	3.4 (1.2)	1	3.0	5	
		Week 4	CR845	137	125 (91.2)	3.0 (1.1)	1	3.0	5	
			Placebo	139	131 (94.2)	2.8 (1.1)	1	3.0	5	
		Week 8	CR845	137	123 (89.8)	2.8 (1.2)	1	3.0	5	
			Placebo	139	132 (95.0)	2.6 (1.2)	1	3.0	5	
		Week 10	CR845	137	118 (86.1)	2.6 (1.2)	1	2.0	5	
			Placebo	139	127 (91.4)	2.6 (1.2)	1	2.0	5	
		Week 12	CR845	137	118 (86.1)	2.6 (1.3)	1	2.0	5	
			Placebo	139	127 (91.4)	2.5 (1.1)	1	2.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	137	124 (90.5)	-0.6 (1.1)	-4	-1.0	2	-0.03 [-0.27, 0.22]
			Placebo	139	131 (94.2)	-0.6 (1.3)	-4	-1.0	3	
		Week 8	CR845	137	122 (89.1)	-0.8 (1.2)	-4	-1.0	3	-0.04 [-0.28, 0.21]
			Placebo	139	132 (95.0)	-0.8 (1.3)	-4	-1.0	3	
		Week 10	CR845	137	117 (85.4)	-1.0 (1.3)	-4	-1.0	2	-0.14 [-0.39, 0.12]
			Placebo	139	127 (91.4)	-0.8 (1.3)	-3	-1.0	3	
		Week 12	CR845	137	117 (85.4)	-1.0 (1.4)	-4	-1.0	4	-0.09 [-0.34, 0.16]
			Placebo	139	127 (91.4)	-0.9 (1.3)	-4	-1.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DNC_ISHB: Change from baseline in 5-D disability score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Female	5-D disability score	Baseline	CR845	100	98 (98.0)	3.4 (1.2)	1	3.0	5	
			Placebo	97	97 (100.0)	3.6 (1.1)	1	4.0	5	
		Week 4	CR845	100	90 (90.0)	2.6 (1.2)	1	2.0	5	
			Placebo	97	94 (96.9)	3.1 (1.3)	1	3.0	5	
		Week 8	CR845	100	87 (87.0)	2.3 (1.2)	1	2.0	5	
			Placebo	97	90 (92.8)	2.9 (1.2)	1	3.0	5	
		Week 10	CR845	100	88 (88.0)	2.2 (1.2)	1	2.0	5	
			Placebo	97	90 (92.8)	2.8 (1.3)	1	3.0	5	
		Week 12	CR845	100	87 (87.0)	2.2 (1.2)	1	2.0	5	
			Placebo	97	92 (94.8)	2.6 (1.3)	1	2.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	100	89 (89.0)	-0.7 (1.4)	-4	-1.0	3	-0.17 [-0.46, 0.12]
			Placebo	97	94 (96.9)	-0.5 (1.3)	-4	0.0	3	
		Week 8	CR845	100	86 (86.0)	-1.1 (1.3)	-4	-1.0	3	-0.26 [-0.56, 0.03]
			Placebo	97	90 (92.8)	-0.7 (1.4)	-4	-1.0	4	
		Week 10	CR845	100	87 (87.0)	-1.2 (1.3)	-4	-1.0	3	-0.24 [-0.54, 0.05]
			Placebo	97	90 (92.8)	-0.8 (1.4)	-4	-1.0	3	
		Week 12	CR845	100	86 (86.0)	-1.1 (1.4)	-4	-1.0	3	-0.11 [-0.40, 0.18]
			Placebo	97	92 (94.8)	-1.0 (1.3)	-4	-1.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DNC_ISHC: Change from baseline in 5-D disability score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Black/African American	5-D disability score	Baseline	CR845	53	50 (94.3)	3.4 (1.2)	1	3.0	5	
			Placebo	38	38 (100.0)	3.8 (1.1)	2	4.0	5	
		Week 4	CR845	53	47 (88.7)	3.0 (1.2)	1	3.0	5	
			Placebo	38	35 (92.1)	2.8 (1.2)	1	3.0	5	
		Week 8	CR845	53	47 (88.7)	2.7 (1.3)	1	2.0	5	
			Placebo	38	37 (97.4)	2.8 (1.3)	1	3.0	5	
		Week 10	CR845	53	44 (83.0)	2.5 (1.4)	1	2.0	5	
			Placebo	38	36 (94.7)	2.8 (1.4)	1	3.0	5	
		Week 12	CR845	53	45 (84.9)	2.6 (1.3)	1	2.0	5	
			Placebo	38	37 (97.4)	2.6 (1.4)	1	3.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	53	45 (84.9)	-0.4 (1.1)	-3	0.0	2	0.43 [-0.02, 0.87]
			Placebo	38	35 (92.1)	-0.9 (1.4)	-3	-1.0	3	
		Week 8	CR845	53	45 (84.9)	-0.7 (1.2)	-3	-1.0	3	0.22 [-0.22, 0.65]
			Placebo	38	37 (97.4)	-1.0 (1.5)	-4	-1.0	3	
		Week 10	CR845	53	42 (79.2)	-0.9 (1.2)	-4	-1.0	1	0.19 [-0.26, 0.63]
			Placebo	38	36 (94.7)	-1.1 (1.6)	-4	-1.0	3	
		Week 12	CR845	53	43 (81.1)	-0.9 (1.5)	-4	-1.0	2	0.25 [-0.19, 0.69]
			Placebo	38	37 (97.4)	-1.2 (1.5)	-4	-1.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DNC_ISHC: Change from baseline in 5-D disability score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
White	5-D disability score	Baseline	CR845	164	163 (99.4)	3.5 (1.1)	1	4.0	5	
			Placebo	169	169 (100.0)	3.4 (1.2)	1	4.0	5	
		Week 4	CR845	164	151 (92.1)	2.8 (1.2)	1	3.0	5	
			Placebo	169	162 (95.9)	3.0 (1.2)	1	3.0	5	
		Week 8	CR845	164	146 (89.0)	2.5 (1.2)	1	2.0	5	
			Placebo	169	159 (94.1)	2.7 (1.2)	1	3.0	5	
		Week 10	CR845	164	146 (89.0)	2.4 (1.2)	1	2.0	5	
			Placebo	169	156 (92.3)	2.7 (1.2)	1	2.0	5	
		Week 12	CR845	164	144 (87.8)	2.4 (1.2)	1	2.0	5	
			Placebo	169	159 (94.1)	2.5 (1.2)	1	2.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	164	151 (92.1)	-0.7 (1.2)	-4	-1.0	3	-0.19 [-0.41, 0.03]
			Placebo	169	162 (95.9)	-0.5 (1.3)	-4	0.0	3	
		Week 8	CR845	164	146 (89.0)	-1.0 (1.3)	-4	-1.0	3	-0.20 [-0.42, 0.03]
			Placebo	169	159 (94.1)	-0.7 (1.3)	-4	-1.0	3	
		Week 10	CR845	164	146 (89.0)	-1.1 (1.4)	-4	-1.0	3	-0.25 [-0.48, -0.02]
			Placebo	169	156 (92.3)	-0.7 (1.3)	-3	-1.0	3	
		Week 12	CR845	164	144 (87.8)	-1.1 (1.4)	-4	-1.0	3	-0.17 [-0.40, 0.05]
			Placebo	169	159 (94.1)	-0.9 (1.2)	-4	-1.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DNC_ISHC: Change from baseline in 5-D disability score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Other	5-D disability score	Baseline	CR845	20	20 (100.0)	3.9 (1.1)	1	4.0	5	
			Placebo	29	29 (100.0)	3.3 (1.3)	1	4.0	5	
		Week 4	CR845	20	17 (85.0)	2.9 (1.2)	1	3.0	5	
			Placebo	29	28 (96.6)	2.8 (1.1)	1	3.0	5	
		Week 8	CR845	20	17 (85.0)	2.7 (1.1)	1	3.0	5	
			Placebo	29	26 (89.7)	2.8 (1.0)	1	3.0	5	
		Week 10	CR845	20	16 (80.0)	2.4 (1.4)	1	2.0	5	
			Placebo	29	25 (86.2)	2.5 (1.2)	1	2.0	5	
		Week 12	CR845	20	16 (80.0)	2.5 (1.3)	1	2.0	5	
			Placebo	29	23 (79.3)	2.5 (1.2)	1	2.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	20	17 (85.0)	-0.8 (1.0)	-3	-1.0	0	-0.28 [-0.89, 0.33]
			Placebo	29	28 (96.6)	-0.5 (1.1)	-3	-1.0	1	
		Week 8	CR845	20	17 (85.0)	-1.1 (1.0)	-3	-1.0	0	-0.38 [-0.99, 0.24]
			Placebo	29	26 (89.7)	-0.6 (1.4)	-3	-1.0	4	
		Week 10	CR845	20	16 (80.0)	-1.3 (1.3)	-4	-1.0	0	-0.44 [-1.07, 0.20]
			Placebo	29	25 (86.2)	-0.8 (1.3)	-3	-1.0	2	
		Week 12	CR845	20	16 (80.0)	-1.2 (1.6)	-3	-2.0	4	-0.27 [-0.91, 0.37]
			Placebo	29	23 (79.3)	-0.8 (1.4)	-4	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DNC_ISHD: Change from baseline in 5-D disability score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 4 to < 7	5-D disability score	Baseline	CR845	102	101 (99.0)	3.1 (1.0)	1	3.0	5	
			Placebo	113	113 (100.0)	3.1 (1.2)	1	3.0	5	
		Week 4	CR845	102	96 (94.1)	2.5 (1.1)	1	2.0	5	
			Placebo	113	109 (96.5)	2.6 (1.1)	1	3.0	5	
		Week 8	CR845	102	95 (93.1)	2.2 (1.1)	1	2.0	5	
			Placebo	113	105 (92.9)	2.6 (1.2)	1	2.0	5	
		Week 10	CR845	102	92 (90.2)	2.1 (1.0)	1	2.0	4	
			Placebo	113	102 (90.3)	2.5 (1.2)	1	2.0	5	
		Week 12	CR845	102	91 (89.2)	2.1 (1.1)	1	2.0	5	
			Placebo	113	103 (91.2)	2.3 (1.2)	1	2.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	102	95 (93.1)	-0.6 (1.1)	-4	0.0	2	-0.06 [-0.33, 0.22]
			Placebo	113	109 (96.5)	-0.5 (1.4)	-4	0.0	3	
		Week 8	CR845	102	94 (92.2)	-0.8 (1.3)	-4	-1.0	3	-0.19 [-0.47, 0.09]
			Placebo	113	105 (92.9)	-0.6 (1.4)	-3	0.0	4	
		Week 10	CR845	102	91 (89.2)	-1.0 (1.3)	-4	-1.0	2	-0.26 [-0.55, 0.02]
			Placebo	113	102 (90.3)	-0.6 (1.3)	-3	-1.0	3	
		Week 12	CR845	102	90 (88.2)	-1.0 (1.3)	-4	-1.0	4	-0.17 [-0.45, 0.11]
			Placebo	113	103 (91.2)	-0.8 (1.3)	-3	-1.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DNC_ISHD: Change from baseline in 5-D disability score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 7	5-D disability score	Baseline	CR845	135	132 (97.8)	3.8 (1.1)	1	4.0	5	
			Placebo	123	123 (100.0)	3.8 (1.1)	1	4.0	5	
		Week 4	CR845	135	119 (88.1)	3.1 (1.2)	1	3.0	5	
			Placebo	123	116 (94.3)	3.2 (1.1)	1	3.0	5	
		Week 8	CR845	135	115 (85.2)	2.8 (1.3)	1	3.0	5	
			Placebo	123	117 (95.1)	2.9 (1.2)	1	3.0	5	
		Week 10	CR845	135	114 (84.4)	2.7 (1.3)	1	3.0	5	
			Placebo	123	115 (93.5)	2.8 (1.2)	1	3.0	5	
		Week 12	CR845	135	114 (84.4)	2.7 (1.3)	1	3.0	5	
			Placebo	123	116 (94.3)	2.7 (1.2)	1	3.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	135	118 (87.4)	-0.7 (1.2)	-4	-1.0	3	-0.11 [-0.36, 0.15]
			Placebo	123	116 (94.3)	-0.6 (1.3)	-4	-0.5	3	
		Week 8	CR845	135	114 (84.4)	-1.0 (1.2)	-4	-1.0	3	-0.07 [-0.33, 0.18]
			Placebo	123	117 (95.1)	-0.9 (1.3)	-4	-1.0	3	
		Week 10	CR845	135	113 (83.7)	-1.1 (1.4)	-4	-1.0	3	-0.11 [-0.37, 0.15]
			Placebo	123	115 (93.5)	-1.0 (1.3)	-4	-1.0	3	
		Week 12	CR845	135	113 (83.7)	-1.2 (1.5)	-4	-1.0	3	-0.03 [-0.29, 0.22]
			Placebo	123	116 (94.3)	-1.1 (1.3)	-4	-1.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DNC_ISHE: Change from baseline in 5-D disability score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	5-D disability score	Baseline	CR845	195	191 (97.9)	3.5 (1.1)	1	4.0	5	
			Placebo	199	199 (100.0)	3.4 (1.2)	1	4.0	5	
		Week 4	CR845	195	177 (90.8)	2.8 (1.2)	1	3.0	5	
			Placebo	199	191 (96.0)	2.9 (1.2)	1	3.0	5	
		Week 8	CR845	195	174 (89.2)	2.6 (1.2)	1	2.0	5	
			Placebo	199	185 (93.0)	2.7 (1.2)	1	3.0	5	
		Week 10	CR845	195	171 (87.7)	2.4 (1.2)	1	2.0	5	
			Placebo	199	180 (90.5)	2.6 (1.2)	1	2.0	5	
		Week 12	CR845	195	170 (87.2)	2.4 (1.3)	1	2.0	5	
			Placebo	199	183 (92.0)	2.5 (1.2)	1	2.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	195	175 (89.7)	-0.7 (1.2)	-4	-1.0	3	-0.13 [-0.33, 0.08]
			Placebo	199	191 (96.0)	-0.5 (1.3)	-4	0.0	3	
		Week 8	CR845	195	172 (88.2)	-0.9 (1.2)	-4	-1.0	3	-0.13 [-0.34, 0.08]
			Placebo	199	185 (93.0)	-0.8 (1.4)	-4	-1.0	4	
		Week 10	CR845	195	169 (86.7)	-1.1 (1.3)	-4	-1.0	3	-0.23 [-0.44, -0.02]
			Placebo	199	180 (90.5)	-0.8 (1.3)	-4	-1.0	3	
		Week 12	CR845	195	168 (86.2)	-1.1 (1.4)	-4	-1.0	4	-0.15 [-0.36, 0.06]
			Placebo	199	183 (92.0)	-0.9 (1.3)	-4	-1.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DNC_ISHE: Change from baseline in 5-D disability score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	5-D disability score	Baseline	CR845	42	42 (100.0)	3.5 (1.1)	1	3.0	5	
			Placebo	37	37 (100.0)	3.9 (1.1)	1	4.0	5	
		Week 4	CR845	42	38 (90.5)	2.8 (1.2)	1	3.0	5	
			Placebo	37	34 (91.9)	3.0 (1.2)	1	3.0	5	
		Week 8	CR845	42	36 (85.7)	2.6 (1.4)	1	2.5	5	
			Placebo	37	37 (100.0)	3.1 (1.3)	1	3.0	5	
		Week 10	CR845	42	35 (83.3)	2.6 (1.5)	1	2.0	5	
			Placebo	37	37 (100.0)	2.8 (1.2)	1	3.0	5	
		Week 12	CR845	42	35 (83.3)	2.4 (1.3)	1	2.0	5	
			Placebo	37	36 (97.3)	2.5 (1.1)	1	3.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	42	38 (90.5)	-0.7 (1.2)	-3	-1.0	2	0.14 [-0.32, 0.60]
			Placebo	37	34 (91.9)	-0.9 (1.2)	-3	-1.0	1	
		Week 8	CR845	42	36 (85.7)	-1.0 (1.5)	-4	-1.0	3	-0.15 [-0.61, 0.31]
			Placebo	37	37 (100.0)	-0.8 (1.4)	-3	-1.0	3	
		Week 10	CR845	42	35 (83.3)	-1.0 (1.6)	-4	-1.0	1	0.04 [-0.42, 0.50]
			Placebo	37	37 (100.0)	-1.1 (1.2)	-3	-1.0	1	
		Week 12	CR845	42	35 (83.3)	-1.1 (1.6)	-4	-1.0	2	0.14 [-0.33, 0.61]
			Placebo	37	36 (97.3)	-1.3 (1.1)	-3	-1.5	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DNC_ISHF: Change from baseline in 5-D disability score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	5-D disability score	Baseline	CR845	150	147 (98.0)	3.4 (1.1)	1	3.0	5	
			Placebo	151	151 (100.0)	3.5 (1.2)	1	4.0	5	
		Week 4	CR845	150	141 (94.0)	2.8 (1.2)	1	3.0	5	
			Placebo	151	146 (96.7)	3.0 (1.2)	1	3.0	5	
		Week 8	CR845	150	138 (92.0)	2.5 (1.2)	1	2.0	5	
			Placebo	151	142 (94.0)	2.7 (1.2)	1	3.0	5	
		Week 10	CR845	150	133 (88.7)	2.4 (1.1)	1	2.0	5	
			Placebo	151	140 (92.7)	2.6 (1.2)	1	2.0	5	
		Week 12	CR845	150	134 (89.3)	2.4 (1.3)	1	2.0	5	
			Placebo	151	141 (93.4)	2.5 (1.2)	1	2.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	150	139 (92.7)	-0.7 (1.2)	-4	-1.0	3	-0.13 [-0.36, 0.11]
			Placebo	151	146 (96.7)	-0.5 (1.3)	-4	0.0	3	
		Week 8	CR845	150	136 (90.7)	-0.9 (1.2)	-4	-1.0	3	-0.07 [-0.31, 0.16]
			Placebo	151	142 (94.0)	-0.8 (1.3)	-4	-1.0	2	
		Week 10	CR845	150	131 (87.3)	-1.0 (1.3)	-4	-1.0	3	-0.10 [-0.33, 0.14]
			Placebo	151	140 (92.7)	-0.9 (1.4)	-4	-1.0	3	
		Week 12	CR845	150	132 (88.0)	-1.0 (1.4)	-4	-1.0	3	-0.02 [-0.26, 0.22]
			Placebo	151	141 (93.4)	-1.0 (1.3)	-4	-1.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DNC_ISHF: Change from baseline in 5-D disability score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	5-D disability score	Baseline	CR845	87	86 (98.9)	3.6 (1.1)	1	4.0	5	
			Placebo	85	85 (100.0)	3.5 (1.2)	1	4.0	5	
		Week 4	CR845	87	74 (85.1)	3.0 (1.2)	1	3.0	5	
			Placebo	85	79 (92.9)	2.9 (1.2)	1	3.0	5	
		Week 8	CR845	87	72 (82.8)	2.6 (1.4)	1	2.5	5	
			Placebo	85	80 (94.1)	2.9 (1.3)	1	3.0	5	
		Week 10	CR845	87	73 (83.9)	2.5 (1.4)	1	2.0	5	
			Placebo	85	77 (90.6)	2.8 (1.3)	1	3.0	5	
		Week 12	CR845	87	71 (81.6)	2.5 (1.3)	1	2.0	5	
			Placebo	85	78 (91.8)	2.7 (1.3)	1	2.5	5	
	Change from baseline in 5-D disability score	Week 4	CR845	87	74 (85.1)	-0.7 (1.2)	-4	-1.0	2	-0.02 [-0.34, 0.29]
			Placebo	85	79 (92.9)	-0.6 (1.3)	-3	-1.0	3	
		Week 8	CR845	87	72 (82.8)	-1.0 (1.4)	-4	-1.0	3	-0.23 [-0.55, 0.09]
			Placebo	85	80 (94.1)	-0.7 (1.4)	-3	-1.0	4	
		Week 10	CR845	87	73 (83.9)	-1.2 (1.4)	-4	-1.0	1	-0.34 [-0.66, -0.02]
			Placebo	85	77 (90.6)	-0.7 (1.3)	-3	-1.0	3	
		Week 12	CR845	87	71 (81.6)	-1.2 (1.5)	-4	-1.0	4	-0.24 [-0.57, 0.08]
			Placebo	85	78 (91.8)	-0.9 (1.2)	-3	-1.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DNC_ISHG: Change from baseline in 5-D disability score by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
USA	5-D disability score	Baseline	CR845	146	142 (97.3)	3.5 (1.1)	1	4.0	5	
			Placebo	133	133 (100.0)	3.4 (1.1)	1	4.0	5	
		Week 4	CR845	146	133 (91.1)	2.9 (1.1)	1	3.0	5	
			Placebo	133	123 (92.5)	3.0 (1.1)	1	3.0	5	
		Week 8	CR845	146	131 (89.7)	2.7 (1.3)	1	3.0	5	
			Placebo	133	125 (94.0)	2.6 (1.2)	1	3.0	5	
		Week 10	CR845	146	129 (88.4)	2.6 (1.2)	1	2.0	5	
			Placebo	133	122 (91.7)	2.5 (1.2)	1	2.0	5	
		Week 12	CR845	146	129 (88.4)	2.5 (1.2)	1	2.0	5	
			Placebo	133	125 (94.0)	2.5 (1.2)	1	2.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	146	131 (89.7)	-0.6 (1.1)	-4	-1.0	2	-0.15 [-0.39, 0.10]
			Placebo	133	123 (92.5)	-0.4 (1.4)	-4	0.0	3	
		Week 8	CR845	146	129 (88.4)	-0.8 (1.3)	-4	-1.0	3	-0.04 [-0.29, 0.21]
			Placebo	133	125 (94.0)	-0.8 (1.4)	-4	-1.0	3	
		Week 10	CR845	146	127 (87.0)	-0.9 (1.3)	-4	-1.0	2	-0.02 [-0.27, 0.23]
			Placebo	133	122 (91.7)	-0.9 (1.3)	-4	-1.0	3	
		Week 12	CR845	146	127 (87.0)	-1.1 (1.3)	-4	-1.0	2	-0.12 [-0.36, 0.13]
			Placebo	133	125 (94.0)	-0.9 (1.4)	-4	-1.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DNC_ISHG: Change from baseline in 5-D disability score by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Asia	5-D disability score	Baseline	CR845	8	8 (100.0)	3.1 (1.1)	1	3.5	4	
			Placebo	12	12 (100.0)	3.5 (1.3)	1	4.0	5	
		Week 4	CR845	8	8 (100.0)	2.4 (1.2)	1	2.0	4	
			Placebo	12	12 (100.0)	2.8 (1.0)	1	3.0	5	
		Week 8	CR845	8	7 (87.5)	1.9 (0.7)	1	2.0	3	
			Placebo	12	12 (100.0)	2.8 (1.1)	1	3.0	5	
		Week 10	CR845	8	7 (87.5)	1.7 (1.1)	1	1.0	4	
			Placebo	12	11 (91.7)	2.6 (1.2)	1	3.0	5	
		Week 12	CR845	8	7 (87.5)	2.3 (1.4)	1	2.0	5	
			Placebo	12	11 (91.7)	2.3 (1.2)	1	2.0	4	
	Change from baseline in 5-D disability score	Week 4	CR845	8	8 (100.0)	-0.8 (1.0)	-3	-0.5	0	-0.09 [-0.98, 0.81]
			Placebo	12	12 (100.0)	-0.7 (0.9)	-2	-1.0	1	
		Week 8	CR845	8	7 (87.5)	-1.1 (0.9)	-2	-1.0	0	-0.25 [-1.19, 0.68]
			Placebo	12	12 (100.0)	-0.8 (1.8)	-3	-1.0	4	
		Week 10	CR845	8	7 (87.5)	-1.3 (1.1)	-3	-1.0	0	-0.33 [-1.28, 0.63]
			Placebo	12	11 (91.7)	-0.8 (1.6)	-3	-1.0	2	
		Week 12	CR845	8	7 (87.5)	-0.7 (2.2)	-2	-2.0	4	0.26 [-0.69, 1.21]
			Placebo	12	11 (91.7)	-1.2 (1.5)	-4	-1.0	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DNC_ISHG: Change from baseline in 5-D disability score by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Eastern Europe	5-D disability score	Baseline	CR845	54	54 (100.0)	3.4 (1.1)	1	3.0	5	
			Placebo	60	60 (100.0)	3.4 (1.1)	1	4.0	5	
		Week 4	CR845	54	52 (96.3)	2.8 (1.2)	1	3.0	5	
			Placebo	60	59 (98.3)	2.7 (1.1)	1	3.0	5	
		Week 8	CR845	54	49 (90.7)	2.3 (1.3)	1	2.0	5	
			Placebo	60	59 (98.3)	2.7 (1.1)	1	3.0	5	
		Week 10	CR845	54	48 (88.9)	2.1 (1.2)	1	2.0	5	
			Placebo	60	59 (98.3)	2.7 (1.1)	1	3.0	5	
		Week 12	CR845	54	47 (87.0)	2.2 (1.2)	1	2.0	5	
			Placebo	60	58 (96.7)	2.5 (1.1)	1	2.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	54	52 (96.3)	-0.6 (1.3)	-3	-1.0	3	0.06 [-0.31, 0.43]
			Placebo	60	59 (98.3)	-0.7 (1.2)	-3	0.0	1	
		Week 8	CR845	54	49 (90.7)	-1.0 (1.2)	-3	-1.0	3	-0.23 [-0.61, 0.15]
			Placebo	60	59 (98.3)	-0.7 (1.3)	-4	-1.0	3	
		Week 10	CR845	54	48 (88.9)	-1.3 (1.4)	-4	-1.0	3	-0.42 [-0.80, -0.03]
			Placebo	60	59 (98.3)	-0.7 (1.1)	-3	-1.0	2	
		Week 12	CR845	54	47 (87.0)	-1.1 (1.4)	-4	-1.0	3	-0.21 [-0.60, 0.18]
			Placebo	60	58 (96.7)	-0.9 (1.0)	-3	-1.0	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DNC_ISHG: Change from baseline in 5-D disability score by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Western Europe/European origin	5-D disability score	Baseline	CR845	29	29 (100.0)	3.7 (1.1)	1	4.0	5	
			Placebo	31	31 (100.0)	3.9 (1.2)	1	4.0	5	
		Week 4	CR845	29	22 (75.9)	2.8 (1.6)	1	2.5	5	
			Placebo	31	31 (100.0)	3.3 (1.4)	1	3.0	5	
		Week 8	CR845	29	23 (79.3)	2.6 (1.2)	1	2.0	5	
			Placebo	31	26 (83.9)	3.3 (1.3)	1	3.5	5	
		Week 10	CR845	29	22 (75.9)	2.5 (1.3)	1	2.0	5	
			Placebo	31	25 (80.6)	3.3 (1.4)	1	3.0	5	
		Week 12	CR845	29	22 (75.9)	2.8 (1.5)	1	2.0	5	
			Placebo	31	25 (80.6)	3.0 (1.4)	1	3.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	29	22 (75.9)	-1.0 (1.5)	-4	-1.0	2	-0.23 [-0.78, 0.32]
			Placebo	31	31 (100.0)	-0.7 (1.4)	-3	-1.0	3	
		Week 8	CR845	29	23 (79.3)	-1.3 (1.3)	-4	-1.0	1	-0.40 [-0.96, 0.17]
			Placebo	31	26 (83.9)	-0.7 (1.4)	-3	-1.0	3	
		Week 10	CR845	29	22 (75.9)	-1.3 (1.6)	-4	-1.0	1	-0.45 [-1.03, 0.13]
			Placebo	31	25 (80.6)	-0.6 (1.6)	-3	0.0	3	
		Week 12	CR845	29	22 (75.9)	-1.0 (1.7)	-4	-1.0	3	0.03 [-0.54, 0.60]
			Placebo	31	25 (80.6)	-1.0 (1.4)	-3	-2.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DNC_ISHH: Change from baseline in 5-D disability score by dialysis method
ITT

H: Dialysis method	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Hemodialysis (HD)	5-D disability score	Baseline	CR845	222	218 (98.2)	3.5 (1.1)	1	4.0	5	
			Placebo	199	199 (100.0)	3.4 (1.2)	1	4.0	5	
		Week 4	CR845	222	202 (91.0)	2.9 (1.2)	1	3.0	5	
			Placebo	199	188 (94.5)	2.9 (1.1)	1	3.0	5	
		Week 8	CR845	222	197 (88.7)	2.6 (1.2)	1	2.0	5	
			Placebo	199	187 (94.0)	2.7 (1.2)	1	3.0	5	
		Week 10	CR845	222	194 (87.4)	2.5 (1.2)	1	2.0	5	
			Placebo	199	185 (93.0)	2.7 (1.2)	1	2.0	5	
		Week 12	CR845	222	192 (86.5)	2.4 (1.2)	1	2.0	5	
			Placebo	199	185 (93.0)	2.5 (1.2)	1	2.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	222	200 (90.1)	-0.6 (1.2)	-4	-1.0	3	-0.11 [-0.31, 0.09]
			Placebo	199	188 (94.5)	-0.5 (1.3)	-4	0.0	3	
		Week 8	CR845	222	195 (87.8)	-0.9 (1.3)	-4	-1.0	3	-0.14 [-0.34, 0.06]
			Placebo	199	187 (94.0)	-0.7 (1.4)	-4	-1.0	4	
		Week 10	CR845	222	192 (86.5)	-1.0 (1.3)	-4	-1.0	3	-0.18 [-0.38, 0.02]
			Placebo	199	185 (93.0)	-0.8 (1.3)	-4	-1.0	3	
		Week 12	CR845	222	190 (85.6)	-1.1 (1.4)	-4	-1.0	4	-0.09 [-0.29, 0.11]
			Placebo	199	185 (93.0)	-0.9 (1.3)	-4	-1.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DNC_ISHH: Change from baseline in 5-D disability score by dialysis method
ITT

H: Dialysis method	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Hemodiafiltration (HDF)	5-D disability score	Baseline	CR845	15	15 (100.0)	3.4 (1.4)	1	3.0	5	
			Placebo	37	37 (100.0)	3.7 (1.1)	1	4.0	5	
		Week 4	CR845	15	13 (86.7)	2.5 (1.3)	1	2.0	4	
			Placebo	37	37 (100.0)	2.8 (1.4)	1	3.0	5	
		Week 8	CR845	15	13 (86.7)	2.2 (1.2)	1	2.0	5	
			Placebo	37	35 (94.6)	2.7 (1.3)	1	2.0	5	
		Week 10	CR845	15	12 (80.0)	2.0 (1.1)	1	2.0	4	
			Placebo	37	32 (86.5)	2.7 (1.3)	1	2.0	5	
		Week 12	CR845	15	13 (86.7)	2.3 (1.5)	1	2.0	5	
			Placebo	37	34 (91.9)	2.7 (1.4)	1	2.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	15	13 (86.7)	-1.2 (1.1)	-3	-1.0	1	-0.21 [-0.85, 0.42]
			Placebo	37	37 (100.0)	-0.9 (1.4)	-3	-1.0	3	
		Week 8	CR845	15	13 (86.7)	-1.4 (1.0)	-3	-2.0	0	-0.33 [-0.98, 0.31]
			Placebo	37	35 (94.6)	-1.0 (1.3)	-4	-1.0	3	
		Week 10	CR845	15	12 (80.0)	-1.5 (1.3)	-4	-1.5	1	-0.42 [-1.09, 0.25]
			Placebo	37	32 (86.5)	-0.9 (1.4)	-3	-1.0	3	
		Week 12	CR845	15	13 (86.7)	-1.3 (1.2)	-4	-1.0	0	-0.26 [-0.90, 0.38]
			Placebo	37	34 (91.9)	-1.0 (1.3)	-3	-1.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DVC_ISHA: Change from baseline in 5-D distribution score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
< 65 years	5-D distribution score	Baseline	CR845	147	144 (98.0)	3.1 (1.2)	1	3.0	5	
			Placebo	153	153 (100.0)	2.9 (1.0)	1	3.0	5	
		Week 4	CR845	147	135 (91.8)	2.5 (1.2)	1	2.0	5	
			Placebo	153	144 (94.1)	2.7 (1.1)	1	3.0	5	
		Week 8	CR845	147	132 (89.8)	2.4 (1.2)	1	2.0	5	
			Placebo	153	143 (93.5)	2.5 (1.2)	1	2.0	5	
		Week 10	CR845	147	132 (89.8)	2.4 (1.2)	1	2.0	5	
			Placebo	153	141 (92.2)	2.7 (1.1)	1	3.0	5	
		Week 12	CR845	147	131 (89.1)	2.4 (1.3)	1	2.0	5	
			Placebo	153	142 (92.8)	2.6 (1.2)	1	2.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	147	133 (90.5)	-0.5 (1.0)	-4	0.0	2	-0.28 [-0.51, -0.04]
			Placebo	153	144 (94.1)	-0.3 (1.0)	-4	0.0	2	
		Week 8	CR845	147	130 (88.4)	-0.6 (1.2)	-4	0.0	2	-0.24 [-0.47, 0.00]
			Placebo	153	143 (93.5)	-0.4 (1.1)	-4	0.0	2	
		Week 10	CR845	147	130 (88.4)	-0.7 (1.3)	-4	0.0	2	-0.38 [-0.62, -0.14]
			Placebo	153	141 (92.2)	-0.2 (1.0)	-3	0.0	3	
		Week 12	CR845	147	129 (87.8)	-0.7 (1.2)	-4	0.0	2	-0.34 [-0.58, -0.10]
			Placebo	153	142 (92.8)	-0.3 (1.1)	-3	0.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DVC_ISHA: Change from baseline in 5-D distribution score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 65 years	5-D distribution score	Baseline	CR845	90	90 (100.0)	3.0 (1.2)	1	3.0	5	
			Placebo	83	83 (100.0)	2.9 (1.1)	1	3.0	5	
		Week 4	CR845	90	80 (88.9)	2.5 (1.2)	1	3.0	5	
			Placebo	83	81 (97.6)	2.7 (1.2)	1	3.0	5	
		Week 8	CR845	90	78 (86.7)	2.5 (1.3)	1	2.0	5	
			Placebo	83	79 (95.2)	2.6 (1.1)	1	3.0	5	
		Week 10	CR845	90	74 (82.2)	2.6 (1.3)	1	3.0	5	
			Placebo	83	76 (91.6)	2.5 (1.1)	1	2.0	5	
		Week 12	CR845	90	74 (82.2)	2.5 (1.2)	1	2.0	5	
			Placebo	83	77 (92.8)	2.7 (1.1)	1	3.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	90	80 (88.9)	-0.5 (1.0)	-4	0.0	2	-0.27 [-0.58, 0.04]
			Placebo	83	81 (97.6)	-0.2 (1.1)	-4	0.0	2	
		Week 8	CR845	90	78 (86.7)	-0.5 (1.2)	-4	0.0	3	-0.15 [-0.46, 0.16]
			Placebo	83	79 (95.2)	-0.3 (1.0)	-3	0.0	3	
		Week 10	CR845	90	74 (82.2)	-0.4 (1.3)	-4	0.0	3	-0.02 [-0.34, 0.30]
			Placebo	83	76 (91.6)	-0.4 (1.0)	-4	0.0	2	
		Week 12	CR845	90	74 (82.2)	-0.5 (1.3)	-4	0.0	4	-0.18 [-0.50, 0.14]
			Placebo	83	77 (92.8)	-0.3 (1.0)	-3	0.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DVC_ISHB: Change from baseline in 5-D distribution score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Male	5-D distribution score	Baseline	CR845	137	135 (98.5)	3.1 (1.2)	1	3.0	5	
			Placebo	139	139 (100.0)	2.8 (1.1)	1	3.0	5	
		Week 4	CR845	137	125 (91.2)	2.6 (1.2)	1	2.0	5	
			Placebo	139	131 (94.2)	2.5 (1.1)	1	2.0	5	
		Week 8	CR845	137	123 (89.8)	2.5 (1.2)	1	2.0	5	
			Placebo	139	132 (95.0)	2.4 (1.2)	1	2.0	5	
		Week 10	CR845	137	118 (86.1)	2.6 (1.2)	1	2.0	5	
			Placebo	139	127 (91.4)	2.5 (1.1)	1	2.0	5	
		Week 12	CR845	137	118 (86.1)	2.5 (1.2)	1	2.0	5	
			Placebo	139	127 (91.4)	2.6 (1.1)	1	2.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	137	124 (90.5)	-0.4 (1.0)	-3	0.0	2	-0.10 [-0.35, 0.15]
			Placebo	139	131 (94.2)	-0.3 (1.1)	-4	0.0	2	
		Week 8	CR845	137	122 (89.1)	-0.5 (1.0)	-4	0.0	2	-0.16 [-0.40, 0.09]
			Placebo	139	132 (95.0)	-0.4 (1.1)	-3	0.0	2	
		Week 10	CR845	137	117 (85.4)	-0.5 (1.1)	-4	0.0	2	-0.21 [-0.47, 0.04]
			Placebo	139	127 (91.4)	-0.3 (1.1)	-4	0.0	3	
		Week 12	CR845	137	117 (85.4)	-0.5 (1.1)	-4	0.0	2	-0.26 [-0.51, -0.01]
			Placebo	139	127 (91.4)	-0.3 (1.1)	-3	0.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DVC_ISHB: Change from baseline in 5-D distribution score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Female	5-D distribution score	Baseline	CR845	100	99 (99.0)	3.1 (1.2)	1	3.0	5	
			Placebo	97	97 (100.0)	3.1 (1.0)	1	3.0	5	
		Week 4	CR845	100	90 (90.0)	2.4 (1.1)	1	2.0	5	
			Placebo	97	94 (96.9)	2.9 (1.2)	1	3.0	5	
		Week 8	CR845	100	87 (87.0)	2.4 (1.3)	1	2.0	5	
			Placebo	97	90 (92.8)	2.8 (1.1)	1	3.0	5	
		Week 10	CR845	100	88 (88.0)	2.4 (1.2)	1	2.0	5	
			Placebo	97	90 (92.8)	2.8 (1.1)	1	3.0	5	
		Week 12	CR845	100	87 (87.0)	2.3 (1.3)	1	2.0	5	
			Placebo	97	92 (94.8)	2.7 (1.2)	1	3.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	100	89 (89.0)	-0.7 (1.1)	-4	-1.0	2	-0.53 [-0.83, -0.24]
			Placebo	97	94 (96.9)	-0.1 (0.9)	-3	0.0	2	
		Week 8	CR845	100	86 (86.0)	-0.6 (1.5)	-4	-1.0	3	-0.26 [-0.56, 0.04]
			Placebo	97	90 (92.8)	-0.3 (1.1)	-4	0.0	3	
		Week 10	CR845	100	87 (87.0)	-0.7 (1.5)	-4	0.0	3	-0.30 [-0.59, 0.00]
			Placebo	97	90 (92.8)	-0.3 (0.9)	-2	0.0	2	
		Week 12	CR845	100	86 (86.0)	-0.7 (1.4)	-4	-1.0	4	-0.31 [-0.61, -0.02]
			Placebo	97	92 (94.8)	-0.4 (1.0)	-3	0.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DVC_ISHC: Change from baseline in 5-D distribution score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Black/African American	5-D distribution score	Baseline	CR845	53	51 (96.2)	3.0 (1.1)	1	3.0	5	
			Placebo	38	38 (100.0)	3.1 (1.1)	1	3.0	5	
		Week 4	CR845	53	47 (88.7)	2.6 (1.1)	1	2.0	5	
			Placebo	38	35 (92.1)	2.8 (1.1)	1	3.0	5	
		Week 8	CR845	53	47 (88.7)	2.6 (1.3)	1	2.0	5	
			Placebo	38	37 (97.4)	2.8 (1.3)	1	3.0	5	
		Week 10	CR845	53	44 (83.0)	2.8 (1.3)	1	3.0	5	
			Placebo	38	36 (94.7)	2.9 (1.1)	1	3.0	5	
		Week 12	CR845	53	45 (84.9)	2.6 (1.2)	1	2.0	5	
			Placebo	38	37 (97.4)	3.0 (1.2)	1	3.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	53	45 (84.9)	-0.3 (1.2)	-4	0.0	2	0.01 [-0.43, 0.45]
			Placebo	38	35 (92.1)	-0.3 (0.8)	-2	0.0	1	
		Week 8	CR845	53	45 (84.9)	-0.3 (1.1)	-4	0.0	2	-0.01 [-0.44, 0.43]
			Placebo	38	37 (97.4)	-0.3 (1.2)	-4	0.0	2	
		Week 10	CR845	53	42 (79.2)	-0.2 (1.3)	-4	0.0	2	0.07 [-0.37, 0.52]
			Placebo	38	36 (94.7)	-0.3 (0.9)	-2	0.0	2	
		Week 12	CR845	53	43 (81.1)	-0.3 (1.2)	-4	0.0	2	-0.08 [-0.52, 0.36]
			Placebo	38	37 (97.4)	-0.2 (1.0)	-2	0.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DVC_ISHC: Change from baseline in 5-D distribution score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
White	5-D distribution score	Baseline	CR845	164	163 (99.4)	3.1 (1.2)	1	3.0	5	
			Placebo	169	169 (100.0)	2.9 (1.0)	1	3.0	5	
		Week 4	CR845	164	151 (92.1)	2.5 (1.2)	1	2.0	5	
			Placebo	169	162 (95.9)	2.7 (1.1)	1	3.0	5	
		Week 8	CR845	164	146 (89.0)	2.5 (1.3)	1	2.0	5	
			Placebo	169	159 (94.1)	2.5 (1.1)	1	2.0	5	
		Week 10	CR845	164	146 (89.0)	2.4 (1.2)	1	2.0	5	
			Placebo	169	156 (92.3)	2.5 (1.1)	1	2.0	5	
		Week 12	CR845	164	144 (87.8)	2.3 (1.3)	1	2.0	5	
			Placebo	169	159 (94.1)	2.6 (1.1)	1	2.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	164	151 (92.1)	-0.6 (1.0)	-4	-1.0	2	-0.42 [-0.64, -0.20]
			Placebo	169	162 (95.9)	-0.2 (1.0)	-4	0.0	2	
		Week 8	CR845	164	146 (89.0)	-0.7 (1.3)	-4	-1.0	3	-0.32 [-0.54, -0.09]
			Placebo	169	159 (94.1)	-0.3 (1.1)	-3	0.0	3	
		Week 10	CR845	164	146 (89.0)	-0.7 (1.2)	-4	-1.0	3	-0.38 [-0.61, -0.15]
			Placebo	169	156 (92.3)	-0.3 (1.0)	-3	0.0	3	
		Week 12	CR845	164	144 (87.8)	-0.8 (1.3)	-4	-1.0	4	-0.46 [-0.68, -0.23]
			Placebo	169	159 (94.1)	-0.3 (1.0)	-3	0.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DVC_ISHC: Change from baseline in 5-D distribution score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Other	5-D distribution score	Baseline	CR845	20	20 (100.0)	2.8 (1.1)	1	3.0	5	
			Placebo	29	29 (100.0)	3.0 (1.2)	1	3.0	5	
		Week 4	CR845	20	17 (85.0)	2.5 (1.2)	1	2.0	5	
			Placebo	29	28 (96.6)	2.5 (1.3)	1	2.0	5	
		Week 8	CR845	20	17 (85.0)	2.2 (1.0)	1	2.0	4	
			Placebo	29	26 (89.7)	2.3 (1.0)	1	2.0	4	
		Week 10	CR845	20	16 (80.0)	2.3 (1.0)	1	2.0	4	
			Placebo	29	25 (86.2)	2.6 (1.1)	1	2.0	5	
		Week 12	CR845	20	16 (80.0)	2.5 (1.2)	1	2.0	5	
			Placebo	29	23 (79.3)	2.3 (1.1)	1	2.0	4	
	Change from baseline in 5-D distribution score	Week 4	CR845	20	17 (85.0)	-0.2 (0.9)	-2	0.0	1	0.13 [-0.48, 0.73]
			Placebo	29	28 (96.6)	-0.4 (1.4)	-4	0.0	2	
		Week 8	CR845	20	17 (85.0)	-0.5 (0.8)	-2	0.0	1	0.17 [-0.44, 0.79]
			Placebo	29	26 (89.7)	-0.7 (1.2)	-3	-0.5	2	
		Week 10	CR845	20	16 (80.0)	-0.5 (1.3)	-4	0.0	1	-0.05 [-0.68, 0.58]
			Placebo	29	25 (86.2)	-0.4 (1.2)	-4	0.0	1	
		Week 12	CR845	20	16 (80.0)	-0.1 (1.1)	-2	0.0	2	0.51 [-0.14, 1.16]
			Placebo	29	23 (79.3)	-0.7 (1.3)	-3	0.0	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DVC_ISHD: Change from baseline in 5-D distribution score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 4 to < 7	5-D distribution score	Baseline	CR845	102	101 (99.0)	2.7 (1.1)	1	3.0	5	
			Placebo	113	113 (100.0)	2.6 (0.9)	1	3.0	5	
		Week 4	CR845	102	96 (94.1)	2.2 (1.0)	1	2.0	5	
			Placebo	113	109 (96.5)	2.5 (1.1)	1	2.0	5	
		Week 8	CR845	102	95 (93.1)	2.2 (1.1)	1	2.0	5	
			Placebo	113	105 (92.9)	2.4 (1.1)	1	2.0	5	
		Week 10	CR845	102	92 (90.2)	2.2 (1.1)	1	2.0	5	
			Placebo	113	102 (90.3)	2.4 (1.1)	1	2.0	5	
		Week 12	CR845	102	91 (89.2)	2.1 (1.1)	1	2.0	5	
			Placebo	113	103 (91.2)	2.3 (1.0)	1	2.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	102	95 (93.1)	-0.5 (1.0)	-3	0.0	2	-0.34 [-0.62, -0.06]
			Placebo	113	109 (96.5)	-0.1 (1.1)	-3	0.0	2	
		Week 8	CR845	102	94 (92.2)	-0.5 (1.1)	-4	0.0	2	-0.20 [-0.48, 0.07]
			Placebo	113	105 (92.9)	-0.2 (1.1)	-3	0.0	3	
		Week 10	CR845	102	91 (89.2)	-0.5 (1.1)	-4	0.0	2	-0.23 [-0.51, 0.05]
			Placebo	113	102 (90.3)	-0.2 (1.0)	-3	0.0	2	
		Week 12	CR845	102	90 (88.2)	-0.6 (1.3)	-4	-0.5	4	-0.27 [-0.55, 0.02]
			Placebo	113	103 (91.2)	-0.3 (0.9)	-3	0.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DVC_ISHD: Change from baseline in 5-D distribution score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 7	5-D distribution score	Baseline	CR845	135	133 (98.5)	3.4 (1.2)	1	3.0	5	
			Placebo	123	123 (100.0)	3.2 (1.1)	1	3.0	5	
		Week 4	CR845	135	119 (88.1)	2.8 (1.2)	1	3.0	5	
			Placebo	123	116 (94.3)	2.8 (1.2)	1	3.0	5	
		Week 8	CR845	135	115 (85.2)	2.7 (1.4)	1	3.0	5	
			Placebo	123	117 (95.1)	2.7 (1.2)	1	3.0	5	
		Week 10	CR845	135	114 (84.4)	2.7 (1.3)	1	3.0	5	
			Placebo	123	115 (93.5)	2.8 (1.1)	1	3.0	5	
		Week 12	CR845	135	114 (84.4)	2.7 (1.3)	1	3.0	5	
			Placebo	123	116 (94.3)	2.9 (1.2)	1	3.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	135	118 (87.4)	-0.6 (1.1)	-4	0.0	2	-0.21 [-0.46, 0.05]
			Placebo	123	116 (94.3)	-0.3 (1.0)	-4	0.0	2	
		Week 8	CR845	135	114 (84.4)	-0.7 (1.3)	-4	0.0	3	-0.20 [-0.46, 0.06]
			Placebo	123	117 (95.1)	-0.4 (1.1)	-4	0.0	2	
		Week 10	CR845	135	113 (83.7)	-0.7 (1.4)	-4	-1.0	3	-0.26 [-0.52, -0.00]
			Placebo	123	115 (93.5)	-0.4 (1.1)	-4	0.0	3	
		Week 12	CR845	135	113 (83.7)	-0.6 (1.3)	-4	0.0	2	-0.30 [-0.56, -0.04]
			Placebo	123	116 (94.3)	-0.3 (1.1)	-3	0.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DVC_ISHE: Change from baseline in 5-D distribution score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	5-D distribution score	Baseline	CR845	195	192 (98.5)	3.1 (1.2)	1	3.0	5	
			Placebo	199	199 (100.0)	2.9 (1.0)	1	3.0	5	
		Week 4	CR845	195	177 (90.8)	2.5 (1.2)	1	2.0	5	
			Placebo	199	191 (96.0)	2.7 (1.2)	1	3.0	5	
		Week 8	CR845	195	174 (89.2)	2.5 (1.3)	1	2.0	5	
			Placebo	199	185 (93.0)	2.5 (1.2)	1	2.0	5	
		Week 10	CR845	195	171 (87.7)	2.5 (1.2)	1	2.0	5	
			Placebo	199	180 (90.5)	2.6 (1.1)	1	2.0	5	
		Week 12	CR845	195	170 (87.2)	2.4 (1.3)	1	2.0	5	
			Placebo	199	183 (92.0)	2.6 (1.2)	1	2.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	195	175 (89.7)	-0.5 (1.0)	-4	0.0	2	-0.28 [-0.48, -0.07]
			Placebo	199	191 (96.0)	-0.2 (1.1)	-4	0.0	2	
		Week 8	CR845	195	172 (88.2)	-0.6 (1.2)	-4	0.0	3	-0.21 [-0.42, -0.00]
			Placebo	199	185 (93.0)	-0.3 (1.1)	-4	0.0	3	
		Week 10	CR845	195	169 (86.7)	-0.6 (1.2)	-4	0.0	3	-0.26 [-0.47, -0.05]
			Placebo	199	180 (90.5)	-0.3 (1.1)	-4	0.0	3	
		Week 12	CR845	195	168 (86.2)	-0.6 (1.3)	-4	0.0	4	-0.29 [-0.50, -0.08]
			Placebo	199	183 (92.0)	-0.3 (1.1)	-3	0.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DVC_ISHE: Change from baseline in 5-D distribution score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	5-D distribution score	Baseline	CR845	42	42 (100.0)	3.0 (1.2)	1	3.0	5	
			Placebo	37	37 (100.0)	3.1 (1.0)	1	3.0	5	
		Week 4	CR845	42	38 (90.5)	2.4 (1.2)	1	2.0	5	
			Placebo	37	34 (91.9)	2.7 (1.1)	1	3.0	5	
		Week 8	CR845	42	36 (85.7)	2.4 (1.1)	1	2.5	5	
			Placebo	37	37 (100.0)	2.7 (1.1)	1	3.0	5	
		Week 10	CR845	42	35 (83.3)	2.4 (1.2)	1	2.0	5	
			Placebo	37	37 (100.0)	2.7 (0.9)	1	3.0	5	
		Week 12	CR845	42	35 (83.3)	2.3 (1.1)	1	2.0	5	
			Placebo	37	36 (97.3)	2.7 (1.0)	1	3.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	42	38 (90.5)	-0.6 (1.3)	-4	0.0	2	-0.24 [-0.71, 0.22]
			Placebo	37	34 (91.9)	-0.3 (0.8)	-2	0.0	1	
		Week 8	CR845	42	36 (85.7)	-0.6 (1.4)	-4	0.0	1	-0.18 [-0.64, 0.28]
			Placebo	37	37 (100.0)	-0.4 (0.9)	-2	0.0	1	
		Week 10	CR845	42	35 (83.3)	-0.7 (1.7)	-4	0.0	2	-0.22 [-0.68, 0.25]
			Placebo	37	37 (100.0)	-0.4 (0.8)	-2	0.0	1	
		Week 12	CR845	42	35 (83.3)	-0.6 (1.3)	-4	0.0	2	-0.24 [-0.71, 0.22]
			Placebo	37	36 (97.3)	-0.4 (0.9)	-2	0.0	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DVC_ISHF: Change from baseline in 5-D distribution score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	5-D distribution score	Baseline	CR845	150	147 (98.0)	3.0 (1.2)	1	3.0	5	
			Placebo	151	151 (100.0)	2.8 (1.0)	1	3.0	5	
		Week 4	CR845	150	141 (94.0)	2.4 (1.1)	1	2.0	5	
			Placebo	151	146 (96.7)	2.6 (1.1)	1	3.0	5	
		Week 8	CR845	150	138 (92.0)	2.4 (1.3)	1	2.0	5	
			Placebo	151	142 (94.0)	2.5 (1.1)	1	2.0	5	
		Week 10	CR845	150	133 (88.7)	2.5 (1.3)	1	2.0	5	
			Placebo	151	140 (92.7)	2.6 (1.1)	1	2.5	5	
		Week 12	CR845	150	134 (89.3)	2.4 (1.2)	1	2.0	5	
			Placebo	151	141 (93.4)	2.6 (1.1)	1	2.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	150	139 (92.7)	-0.5 (1.0)	-3	0.0	2	-0.29 [-0.52, -0.06]
			Placebo	151	146 (96.7)	-0.2 (1.0)	-4	0.0	2	
		Week 8	CR845	150	136 (90.7)	-0.5 (1.1)	-4	0.0	3	-0.22 [-0.46, 0.02]
			Placebo	151	142 (94.0)	-0.3 (1.1)	-3	0.0	3	
		Week 10	CR845	150	131 (87.3)	-0.5 (1.1)	-4	0.0	3	-0.21 [-0.45, 0.03]
			Placebo	151	140 (92.7)	-0.3 (1.1)	-4	0.0	2	
		Week 12	CR845	150	132 (88.0)	-0.6 (1.2)	-4	0.0	4	-0.24 [-0.48, -0.00]
			Placebo	151	141 (93.4)	-0.3 (1.1)	-3	0.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DVC_ISHF: Change from baseline in 5-D distribution score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	5-D distribution score	Baseline	CR845	87	87 (100.0)	3.2 (1.2)	1	3.0	5	
			Placebo	85	85 (100.0)	3.0 (1.1)	1	3.0	5	
		Week 4	CR845	87	74 (85.1)	2.7 (1.2)	1	3.0	5	
			Placebo	85	79 (92.9)	2.7 (1.3)	1	2.0	5	
		Week 8	CR845	87	72 (82.8)	2.5 (1.3)	1	2.0	5	
			Placebo	85	80 (94.1)	2.6 (1.2)	1	3.0	5	
		Week 10	CR845	87	73 (83.9)	2.5 (1.2)	1	2.0	5	
			Placebo	85	77 (90.6)	2.7 (1.1)	1	2.0	5	
		Week 12	CR845	87	71 (81.6)	2.5 (1.3)	1	2.0	5	
			Placebo	85	78 (91.8)	2.7 (1.2)	1	3.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	87	74 (85.1)	-0.6 (1.2)	-4	0.0	2	-0.25 [-0.57, 0.07]
			Placebo	85	79 (92.9)	-0.3 (1.0)	-4	0.0	2	
		Week 8	CR845	87	72 (82.8)	-0.7 (1.4)	-4	0.0	2	-0.18 [-0.50, 0.13]
			Placebo	85	80 (94.1)	-0.5 (1.1)	-4	0.0	2	
		Week 10	CR845	87	73 (83.9)	-0.7 (1.5)	-4	-1.0	2	-0.32 [-0.64, 0.01]
			Placebo	85	77 (90.6)	-0.4 (0.9)	-3	0.0	3	
		Week 12	CR845	87	71 (81.6)	-0.7 (1.4)	-4	0.0	2	-0.36 [-0.69, -0.04]
			Placebo	85	78 (91.8)	-0.3 (1.0)	-3	0.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DVC_ISHG: Change from baseline in 5-D distribution score by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
USA	5-D distribution score	Baseline	CR845	146	143 (97.9)	3.1 (1.2)	1	3.0	5	
			Placebo	133	133 (100.0)	2.9 (1.1)	1	3.0	5	
		Week 4	CR845	146	133 (91.1)	2.6 (1.1)	1	2.0	5	
			Placebo	133	123 (92.5)	2.6 (1.1)	1	3.0	5	
		Week 8	CR845	146	131 (89.7)	2.6 (1.2)	1	2.0	5	
			Placebo	133	125 (94.0)	2.6 (1.2)	1	2.0	5	
		Week 10	CR845	146	129 (88.4)	2.6 (1.2)	1	3.0	5	
			Placebo	133	122 (91.7)	2.6 (1.1)	1	2.5	5	
		Week 12	CR845	146	129 (88.4)	2.5 (1.3)	1	2.0	5	
			Placebo	133	125 (94.0)	2.6 (1.2)	1	2.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	146	131 (89.7)	-0.5 (1.1)	-4	0.0	2	-0.20 [-0.45, 0.04]
			Placebo	133	123 (92.5)	-0.2 (1.0)	-4	0.0	2	
		Week 8	CR845	146	129 (88.4)	-0.5 (1.2)	-4	0.0	2	-0.17 [-0.42, 0.08]
			Placebo	133	125 (94.0)	-0.3 (1.1)	-4	0.0	3	
		Week 10	CR845	146	127 (87.0)	-0.5 (1.2)	-4	0.0	2	-0.23 [-0.48, 0.02]
			Placebo	133	122 (91.7)	-0.2 (1.0)	-3	0.0	3	
		Week 12	CR845	146	127 (87.0)	-0.6 (1.3)	-4	0.0	4	-0.28 [-0.52, -0.03]
			Placebo	133	125 (94.0)	-0.2 (1.1)	-3	0.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DVC_ISHG: Change from baseline in 5-D distribution score by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Asia	5-D distribution score	Baseline	CR845	8	8 (100.0)	2.1 (1.1)	1	2.0	4	
			Placebo	12	12 (100.0)	3.1 (1.1)	1	3.0	5	
		Week 4	CR845	8	8 (100.0)	1.9 (1.1)	1	1.5	4	
			Placebo	12	12 (100.0)	2.3 (1.2)	1	2.0	5	
		Week 8	CR845	8	7 (87.5)	1.9 (1.1)	1	2.0	4	
			Placebo	12	12 (100.0)	2.3 (0.9)	1	2.0	4	
		Week 10	CR845	8	7 (87.5)	1.9 (1.1)	1	2.0	4	
			Placebo	12	11 (91.7)	2.5 (1.0)	1	2.0	4	
		Week 12	CR845	8	7 (87.5)	2.1 (0.9)	1	2.0	4	
			Placebo	12	11 (91.7)	2.5 (1.1)	1	2.0	4	
	Change from baseline in 5-D distribution score	Week 4	CR845	8	8 (100.0)	-0.3 (0.7)	-2	0.0	0	0.33 [-0.57, 1.23]
			Placebo	12	12 (100.0)	-0.8 (1.9)	-4	0.0	2	
		Week 8	CR845	8	7 (87.5)	-0.1 (0.4)	-1	0.0	0	0.57 [-0.38, 1.52]
			Placebo	12	12 (100.0)	-0.8 (1.3)	-3	0.0	1	
		Week 10	CR845	8	7 (87.5)	-0.1 (0.9)	-2	0.0	1	0.39 [-0.57, 1.35]
			Placebo	12	11 (91.7)	-0.6 (1.4)	-4	0.0	1	
		Week 12	CR845	8	7 (87.5)	0.1 (0.7)	-1	0.0	1	0.64 [-0.33, 1.62]
			Placebo	12	11 (91.7)	-0.6 (1.4)	-3	0.0	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DVC_ISHG: Change from baseline in 5-D distribution score by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Eastern Europe	5-D distribution score	Baseline	CR845	54	54 (100.0)	3.0 (1.2)	1	3.0	5	
			Placebo	60	60 (100.0)	2.9 (1.0)	1	3.0	5	
		Week 4	CR845	54	52 (96.3)	2.4 (1.2)	1	2.0	5	
			Placebo	60	59 (98.3)	2.7 (1.1)	1	3.0	5	
		Week 8	CR845	54	49 (90.7)	2.3 (1.4)	1	2.0	5	
			Placebo	60	59 (98.3)	2.5 (1.1)	1	2.0	5	
		Week 10	CR845	54	48 (88.9)	2.3 (1.3)	1	2.0	5	
			Placebo	60	59 (98.3)	2.6 (1.1)	1	2.0	5	
		Week 12	CR845	54	47 (87.0)	2.2 (1.3)	1	2.0	5	
			Placebo	60	58 (96.7)	2.6 (1.1)	1	2.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	54	52 (96.3)	-0.7 (1.1)	-4	-1.0	2	-0.54 [-0.92, -0.16]
			Placebo	60	59 (98.3)	-0.2 (0.9)	-3	0.0	2	
		Week 8	CR845	54	49 (90.7)	-0.7 (1.3)	-4	-1.0	3	-0.33 [-0.71, 0.06]
			Placebo	60	59 (98.3)	-0.4 (1.0)	-3	0.0	2	
		Week 10	CR845	54	48 (88.9)	-0.8 (1.4)	-4	-1.0	3	-0.40 [-0.79, -0.02]
			Placebo	60	59 (98.3)	-0.3 (1.0)	-3	0.0	2	
		Week 12	CR845	54	47 (87.0)	-0.8 (1.2)	-4	-1.0	1	-0.51 [-0.90, -0.12]
			Placebo	60	58 (96.7)	-0.3 (0.9)	-3	0.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DVC_ISHG: Change from baseline in 5-D distribution score by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Western Europe/European origin	5-D distribution score	Baseline	CR845	29	29 (100.0)	3.2 (1.1)	1	3.0	5	
			Placebo	31	31 (100.0)	3.1 (1.0)	2	3.0	5	
		Week 4	CR845	29	22 (75.9)	2.6 (1.3)	1	3.0	5	
			Placebo	31	31 (100.0)	2.9 (1.1)	1	3.0	5	
		Week 8	CR845	29	23 (79.3)	2.5 (1.1)	1	3.0	5	
			Placebo	31	26 (83.9)	2.9 (1.1)	1	3.0	5	
		Week 10	CR845	29	22 (75.9)	2.5 (1.2)	1	2.5	5	
			Placebo	31	25 (80.6)	2.6 (1.0)	1	3.0	5	
		Week 12	CR845	29	22 (75.9)	2.5 (1.1)	1	2.5	4	
			Placebo	31	25 (80.6)	2.8 (1.2)	1	3.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	29	22 (75.9)	-0.7 (0.9)	-3	-1.0	1	-0.53 [-1.08, 0.03]
			Placebo	31	31 (100.0)	-0.2 (0.9)	-2	0.0	1	
		Week 8	CR845	29	23 (79.3)	-0.7 (1.1)	-3	-1.0	1	-0.45 [-1.02, 0.12]
			Placebo	31	26 (83.9)	-0.3 (1.0)	-2	0.0	1	
		Week 10	CR845	29	22 (75.9)	-0.9 (1.3)	-4	-1.0	1	-0.35 [-0.93, 0.22]
			Placebo	31	25 (80.6)	-0.5 (0.8)	-2	-1.0	1	
		Week 12	CR845	29	22 (75.9)	-0.7 (1.0)	-3	-1.0	1	-0.24 [-0.82, 0.33]
			Placebo	31	25 (80.6)	-0.5 (1.0)	-3	0.0	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DVC_ISHH: Change from baseline in 5-D distribution score by dialysis method
ITT

H: Dialysis method	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Hemodialysis (HD)	5-D distribution score	Baseline	CR845	222	219 (98.6)	3.1 (1.2)	1	3.0	5	
			Placebo	199	199 (100.0)	2.9 (1.1)	1	3.0	5	
		Week 4	CR845	222	202 (91.0)	2.5 (1.1)	1	2.0	5	
			Placebo	199	188 (94.5)	2.6 (1.2)	1	2.0	5	
		Week 8	CR845	222	197 (88.7)	2.5 (1.3)	1	2.0	5	
			Placebo	199	187 (94.0)	2.5 (1.2)	1	2.0	5	
		Week 10	CR845	222	194 (87.4)	2.5 (1.2)	1	2.0	5	
			Placebo	199	185 (93.0)	2.6 (1.1)	1	2.0	5	
		Week 12	CR845	222	192 (86.5)	2.4 (1.2)	1	2.0	5	
			Placebo	199	185 (93.0)	2.6 (1.2)	1	2.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	222	200 (90.1)	-0.6 (1.0)	-4	0.0	2	-0.26 [-0.46, -0.06]
			Placebo	199	188 (94.5)	-0.3 (1.1)	-4	0.0	2	
		Week 8	CR845	222	195 (87.8)	-0.6 (1.2)	-4	0.0	3	-0.19 [-0.39, 0.01]
			Placebo	199	187 (94.0)	-0.4 (1.1)	-4	0.0	3	
		Week 10	CR845	222	192 (86.5)	-0.6 (1.3)	-4	0.0	3	-0.23 [-0.43, -0.02]
			Placebo	199	185 (93.0)	-0.3 (1.0)	-4	0.0	3	
		Week 12	CR845	222	190 (85.6)	-0.7 (1.3)	-4	0.0	4	-0.28 [-0.49, -0.08]
			Placebo	199	185 (93.0)	-0.3 (1.1)	-3	0.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DVC_ISHH: Change from baseline in 5-D distribution score by dialysis method
ITT

H: Dialysis method	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Hemodiafiltration (HDF)	5-D distribution score	Baseline	CR845	15	15 (100.0)	2.9 (1.2)	1	3.0	5	
			Placebo	37	37 (100.0)	2.9 (1.0)	1	3.0	5	
		Week 4	CR845	15	13 (86.7)	3.0 (1.5)	1	3.0	5	
			Placebo	37	37 (100.0)	2.9 (1.0)	1	3.0	5	
		Week 8	CR845	15	13 (86.7)	2.6 (1.4)	1	2.0	5	
			Placebo	37	35 (94.6)	2.7 (1.1)	1	3.0	5	
		Week 10	CR845	15	12 (80.0)	2.7 (1.6)	1	2.5	5	
			Placebo	37	32 (86.5)	2.7 (1.1)	1	3.0	5	
		Week 12	CR845	15	13 (86.7)	2.8 (1.4)	1	3.0	5	
			Placebo	37	34 (91.9)	2.8 (1.0)	1	3.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	15	13 (86.7)	0.0 (0.9)	-1	0.0	2	0.00 [-0.63, 0.63]
			Placebo	37	37 (100.0)	0.0 (0.8)	-2	0.0	2	
		Week 8	CR845	15	13 (86.7)	-0.4 (0.8)	-1	-1.0	1	-0.20 [-0.83, 0.44]
			Placebo	37	35 (94.6)	-0.2 (1.0)	-3	0.0	2	
		Week 10	CR845	15	12 (80.0)	-0.4 (0.9)	-2	-0.5	1	-0.31 [-0.98, 0.36]
			Placebo	37	32 (86.5)	-0.1 (1.1)	-3	0.0	2	
		Week 12	CR845	15	13 (86.7)	-0.2 (1.0)	-2	0.0	1	-0.05 [-0.69, 0.59]
			Placebo	37	34 (91.9)	-0.2 (1.0)	-3	0.0	2	

ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived, created on: 17FEB2022

Table BT2DTC_ISCA: Change from baseline in 5-D total score - MMRM results by age
ITT

Change from baseline in 5-D total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
A: Age									0.971
< 65 years	Week 4	CR845	147	131 (89.1)	-4.0 (0.3)	(-4.6, -3.3)	-1.4 (0.4)	(-2.2, -0.7)	<0.001 *
		Placebo	153	144 (94.1)	-2.5 (0.3)	(-3.2, -1.8)			
>= 65 years	Week 4	CR845	90	79 (87.8)	-3.6 (0.4)	(-4.4, -2.8)	-1.1 (0.5)	(-2.2, -0.1)	0.035 *
		Placebo	83	81 (97.6)	-2.5 (0.4)	(-3.3, -1.6)			
< 65 years	Week 8	CR845	147	128 (87.1)	-4.6 (0.4)	(-5.3, -3.9)	-0.8 (0.4)	(-1.7, -0.0)	0.046 *
		Placebo	153	143 (93.5)	-3.8 (0.3)	(-4.5, -3.1)			
>= 65 years	Week 8	CR845	90	78 (86.7)	-4.0 (0.4)	(-4.9, -3.1)	-1.2 (0.6)	(-2.3, -0.1)	0.036 *
		Placebo	83	79 (95.2)	-2.8 (0.4)	(-3.7, -1.9)			
< 65 years	Week 10	CR845	147	129 (87.8)	-4.8 (0.4)	(-5.5, -4.0)	-1.0 (0.4)	(-1.9, -0.2)	0.018 *
		Placebo	153	141 (92.2)	-3.7 (0.4)	(-4.4, -3.0)			
>= 65 years	Week 10	CR845	90	74 (82.2)	-4.3 (0.4)	(-5.2, -3.4)	-1.6 (0.6)	(-2.7, -0.4)	0.008 *
		Placebo	83	76 (91.6)	-2.7 (0.4)	(-3.6, -1.8)			
< 65 years	Week 12	CR845	147	128 (87.1)	-5.1 (0.4)	(-5.8, -4.3)	-1.4 (0.5)	(-2.3, -0.5)	0.003 *
		Placebo	153	142 (92.8)	-3.7 (0.4)	(-4.4, -2.9)			
>= 65 years	Week 12	CR845	90	73 (81.1)	-4.1 (0.5)	(-5.1, -3.2)	-0.8 (0.6)	(-2.0, 0.4)	0.209
		Placebo	83	77 (92.8)	-3.4 (0.5)	(-4.3, -2.5)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DTC_ISCB: Change from baseline in 5-D total score - MMRM results by sex
ITT

Change from baseline in 5-D total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
B: Sex									<0.001 i
Male	Week 4	CR845	137	123 (89.8)	-2.8 (0.3)	(-3.5, -2.2)	-0.3 (0.4)	(-1.0, 0.5)	0.529
		Placebo	139	131 (94.2)	-2.6 (0.3)	(-3.2, -1.9)			
Female	Week 4	CR845	100	87 (87.0)	-5.1 (0.4)	(-5.9, -4.3)	-2.9 (0.5)	(-3.9, -1.9)	<0.001 *
		Placebo	97	94 (96.9)	-2.2 (0.4)	(-3.1, -1.4)			
Male	Week 8	CR845	137	121 (88.3)	-3.3 (0.3)	(-3.9, -2.6)	0.1 (0.4)	(-0.7, 0.8)	0.898
		Placebo	139	132 (95.0)	-3.3 (0.3)	(-4.0, -2.7)			
Female	Week 8	CR845	100	85 (85.0)	-5.8 (0.4)	(-6.7, -4.9)	-2.4 (0.6)	(-3.5, -1.3)	<0.001 *
		Placebo	97	90 (92.8)	-3.4 (0.4)	(-4.3, -2.6)			
Male	Week 10	CR845	137	117 (85.4)	-3.5 (0.3)	(-4.1, -2.8)	-0.1 (0.4)	(-0.9, 0.7)	0.798
		Placebo	139	127 (91.4)	-3.4 (0.3)	(-4.0, -2.7)			
Female	Week 10	CR845	100	86 (86.0)	-6.0 (0.5)	(-6.9, -5.1)	-2.8 (0.6)	(-3.9, -1.6)	<0.001 *
		Placebo	97	90 (92.8)	-3.2 (0.5)	(-4.1, -2.3)			
Male	Week 12	CR845	137	117 (85.4)	-3.7 (0.4)	(-4.5, -3.0)	-0.4 (0.4)	(-1.3, 0.5)	0.366
		Placebo	139	127 (91.4)	-3.3 (0.3)	(-4.0, -2.7)			
Female	Week 12	CR845	100	84 (84.0)	-6.0 (0.5)	(-6.9, -5.0)	-2.2 (0.6)	(-3.4, -1.0)	<0.001 *
		Placebo	97	92 (94.8)	-3.7 (0.5)	(-4.7, -2.8)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DTC_ISCC: Change from baseline in 5-D total score - MMRM results by race
ITT

Change from baseline in 5-D total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
C: Race									0.549
Black/African American	Week 4	CR845	53	45 (84.9)	-3.5 (0.5)	(-4.6, -2.4)	-0.5 (0.8)	(-2.0, 1.1)	0.560
		Placebo	38	35 (92.1)	-3.0 (0.6)	(-4.2, -1.8)			
White	Week 4	CR845	164	148 (90.2)	-4.0 (0.3)	(-4.7, -3.4)	-1.7 (0.4)	(-2.4, -1.0)	<0.001 *
		Placebo	169	162 (95.9)	-2.3 (0.3)	(-3.0, -1.7)			
Other	Week 4	CR845	20	17 (85.0)	-3.7 (0.9)	(-5.5, -1.8)	-1.0 (1.0)	(-3.0, 0.9)	0.284
		Placebo	29	28 (96.6)	-2.7 (0.8)	(-4.3, -1.0)			
Black/African American	Week 8	CR845	53	45 (84.9)	-4.4 (0.6)	(-5.6, -3.2)	-0.8 (0.8)	(-2.5, 0.9)	0.339
		Placebo	38	37 (97.4)	-3.6 (0.6)	(-4.9, -2.3)			
White	Week 8	CR845	164	144 (87.8)	-4.5 (0.3)	(-5.1, -3.8)	-1.1 (0.4)	(-1.9, -0.3)	0.006 *
		Placebo	169	159 (94.1)	-3.4 (0.3)	(-4.0, -2.7)			
Other	Week 8	CR845	20	17 (85.0)	-4.5 (0.9)	(-6.3, -2.7)	-1.0 (0.9)	(-2.9, 0.9)	0.285
		Placebo	29	26 (89.7)	-3.5 (0.8)	(-5.1, -1.9)			
Black/African American	Week 10	CR845	53	42 (79.2)	-4.7 (0.7)	(-6.0, -3.4)	-1.1 (0.9)	(-3.0, 0.7)	0.232
		Placebo	38	36 (94.7)	-3.6 (0.7)	(-5.0, -2.2)			
White	Week 10	CR845	164	145 (88.4)	-4.6 (0.3)	(-5.3, -4.0)	-1.4 (0.4)	(-2.2, -0.6)	<0.001 *
		Placebo	169	156 (92.3)	-3.3 (0.3)	(-3.9, -2.6)			
Other	Week 10	CR845	20	16 (80.0)	-4.6 (1.0)	(-6.6, -2.6)	-1.1 (1.1)	(-3.3, 1.1)	0.305
		Placebo	29	25 (86.2)	-3.5 (0.9)	(-5.2, -1.7)			
Black/African American	Week 12	CR845	53	42 (79.2)	-4.9 (0.6)	(-6.2, -3.7)	-1.0 (0.9)	(-2.8, 0.7)	0.245
		Placebo	38	37 (97.4)	-3.9 (0.7)	(-5.2, -2.6)			
White	Week 12	CR845	164	143 (87.2)	-4.9 (0.4)	(-5.6, -4.2)	-1.5 (0.4)	(-2.3, -0.6)	<0.001 *
		Placebo	169	159 (94.1)	-3.4 (0.3)	(-4.1, -2.7)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DTC_ISCC: Change from baseline in 5-D total score - MMRM results by race
ITT

Change from baseline in 5-D total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Other	Week 12	CR845	20	16 (80.0)	-3.8 (1.1)	(-6.1, -1.5)	0.2 (1.3)	(-2.4, 2.9)	0.852
		Placebo	29	23 (79.3)	-4.0 (1.0)	(-6.0, -2.1)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DTC_ISCD: Change from baseline in 5-D total score - MMRM results by baseline WI-NRS
ITT

Change from baseline in 5-D total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
D: Baseline worst itching NRS score (WI-NRS)									0.613
>= 4 to < 7	Week 4	CR845	102	93 (91.2)	-3.4 (0.4)	(-4.1, -2.7)	-1.3 (0.4)	(-2.2, -0.5)	0.002 *
		Placebo	113	109 (96.5)	-2.1 (0.4)	(-2.8, -1.4)			
>= 7	Week 4	CR845	135	117 (86.7)	-4.3 (0.4)	(-5.0, -3.6)	-1.4 (0.5)	(-2.3, -0.5)	0.003 *
		Placebo	123	116 (94.3)	-2.9 (0.4)	(-3.6, -2.1)			
>= 4 to < 7	Week 8	CR845	102	93 (91.2)	-4.0 (0.4)	(-4.7, -3.3)	-1.4 (0.4)	(-2.3, -0.6)	<0.001 *
		Placebo	113	105 (92.9)	-2.6 (0.4)	(-3.3, -1.9)			
>= 7	Week 8	CR845	135	113 (83.7)	-4.8 (0.4)	(-5.6, -4.0)	-0.6 (0.5)	(-1.6, 0.4)	0.246
		Placebo	123	117 (95.1)	-4.2 (0.4)	(-5.0, -3.4)			
>= 4 to < 7	Week 10	CR845	102	90 (88.2)	-4.2 (0.4)	(-5.0, -3.5)	-1.6 (0.4)	(-2.5, -0.7)	<0.001 *
		Placebo	113	102 (90.3)	-2.6 (0.4)	(-3.4, -1.9)			
>= 7	Week 10	CR845	135	113 (83.7)	-5.0 (0.4)	(-5.8, -4.2)	-1.0 (0.5)	(-2.0, 0.1)	0.067
		Placebo	123	115 (93.5)	-4.0 (0.4)	(-4.8, -3.2)			
>= 4 to < 7	Week 12	CR845	102	89 (87.3)	-4.3 (0.4)	(-5.1, -3.5)	-1.3 (0.5)	(-2.2, -0.3)	0.009 *
		Placebo	113	103 (91.2)	-3.1 (0.4)	(-3.8, -2.3)			
>= 7	Week 12	CR845	135	112 (83.0)	-5.2 (0.4)	(-6.0, -4.4)	-1.2 (0.5)	(-2.2, -0.1)	0.036 *
		Placebo	123	116 (94.3)	-4.0 (0.4)	(-4.9, -3.2)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DTC_ISCE: Change from baseline in 5-D total score - MMRM results by specific medical condition
ITT

Change from baseline in 5-D total score					Repeated measures analysis					
					Change from Baseline		Treatment Difference			
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value	
E: Presence of specific medical conditions									0.940	
No	Week 4	CR845	195	172 (88.2)	-3.7 (0.3)	(-4.2, -3.1)	-1.4 (0.4)	(-2.1, -0.7)	<0.001	*
		Placebo	199	191 (96.0)	-2.3 (0.2)	(-2.8, -1.8)				
Yes	Week 4	CR845	42	38 (90.5)	-4.2 (0.5)	(-5.3, -3.1)	-1.2 (0.8)	(-2.8, 0.3)	0.122	
		Placebo	37	34 (91.9)	-3.0 (0.6)	(-4.1, -1.9)				
No	Week 8	CR845	195	170 (87.2)	-4.2 (0.3)	(-4.7, -3.6)	-0.8 (0.4)	(-1.5, -0.1)	0.025	*
		Placebo	199	185 (93.0)	-3.3 (0.3)	(-3.8, -2.8)				
Yes	Week 8	CR845	42	36 (85.7)	-5.1 (0.6)	(-6.4, -3.9)	-1.7 (0.9)	(-3.4, 0.0)	0.057	
		Placebo	37	37 (100.0)	-3.4 (0.6)	(-4.7, -2.2)				
No	Week 10	CR845	195	168 (86.2)	-4.4 (0.3)	(-5.0, -3.9)	-1.3 (0.4)	(-2.0, -0.5)	<0.001	*
		Placebo	199	180 (90.5)	-3.1 (0.3)	(-3.7, -2.6)				
Yes	Week 10	CR845	42	35 (83.3)	-4.9 (0.7)	(-6.2, -3.5)	-1.0 (0.9)	(-2.8, 0.9)	0.314	
		Placebo	37	37 (100.0)	-3.9 (0.7)	(-5.2, -2.6)				
No	Week 12	CR845	195	167 (85.6)	-4.5 (0.3)	(-5.1, -4.0)	-1.2 (0.4)	(-2.0, -0.5)	0.002	*
		Placebo	199	183 (92.0)	-3.3 (0.3)	(-3.9, -2.8)				
Yes	Week 12	CR845	42	34 (81.0)	-5.2 (0.7)	(-6.5, -3.8)	-0.8 (1.0)	(-2.7, 1.1)	0.377	
		Placebo	37	36 (97.3)	-4.3 (0.7)	(-5.6, -3.0)				

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor previous use of anti-itch medication is also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DTC_ISCF: Change from baseline in 5-D total score - MMRM results by use of concomitant itch medication
ITT

Change from baseline in 5-D total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
F: Use of concomitant itch medication									0.889
No	Week 4	CR845	150	136 (90.7)	-3.8 (0.3)	(-4.4, -3.1)	-1.5 (0.4)	(-2.2, -0.7)	<0.001 *
		Placebo	151	146 (96.7)	-2.3 (0.3)	(-2.9, -1.6)			
Yes	Week 4	CR845	87	74 (85.1)	-4.0 (0.4)	(-4.8, -3.1)	-1.2 (0.6)	(-2.3, -0.1)	0.040 *
		Placebo	85	79 (92.9)	-2.8 (0.4)	(-3.7, -2.0)			
No	Week 8	CR845	150	134 (89.3)	-4.2 (0.3)	(-4.8, -3.5)	-0.9 (0.4)	(-1.7, -0.1)	0.028 *
		Placebo	151	142 (94.0)	-3.3 (0.3)	(-4.0, -2.7)			
Yes	Week 8	CR845	87	72 (82.8)	-4.8 (0.5)	(-5.7, -3.8)	-1.2 (0.6)	(-2.4, 0.1)	0.063
		Placebo	85	80 (94.1)	-3.6 (0.5)	(-4.5, -2.7)			
No	Week 10	CR845	150	130 (86.7)	-4.2 (0.3)	(-4.9, -3.6)	-1.0 (0.4)	(-1.8, -0.2)	0.020 *
		Placebo	151	140 (92.7)	-3.3 (0.3)	(-3.9, -2.6)			
Yes	Week 10	CR845	87	73 (83.9)	-5.2 (0.5)	(-6.2, -4.2)	-1.8 (0.6)	(-3.0, -0.5)	0.007 *
		Placebo	85	77 (90.6)	-3.4 (0.5)	(-4.4, -2.5)			
No	Week 12	CR845	150	131 (87.3)	-4.4 (0.4)	(-5.1, -3.7)	-1.0 (0.4)	(-1.9, -0.1)	0.024 *
		Placebo	151	141 (93.4)	-3.4 (0.4)	(-4.1, -2.7)			
Yes	Week 12	CR845	87	70 (80.5)	-5.3 (0.5)	(-6.3, -4.3)	-1.5 (0.7)	(-2.8, -0.2)	0.021 *
		Placebo	85	78 (91.8)	-3.8 (0.5)	(-4.8, -2.9)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor presence of medical condition is also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DTC_ISCG: Change from baseline in 5-D total score - MMRM results by region
ITT

Change from baseline in 5-D total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
G: Region									0.487
USA	Week 4	CR845	146	130 (89.0)	-3.4 (0.3)	(-4.1, -2.8)	-1.2 (0.4)	(-2.0, -0.4)	0.003 *
		Placebo	133	123 (92.5)	-2.2 (0.3)	(-2.9, -1.5)			
Asia	Week 4	CR845	8	8 (100.0)	-5.0 (1.0)	(-7.0, -2.9)	-1.2 (1.3)	(-4.0, 1.7)	0.396
		Placebo	12	12 (100.0)	-3.8 (0.8)	(-5.6, -2.1)			
Eastern Europe	Week 4	CR845	54	50 (92.6)	-4.1 (0.6)	(-5.2, -2.9)	-1.4 (0.6)	(-2.6, -0.1)	0.032 *
		Placebo	60	59 (98.3)	-2.7 (0.5)	(-3.8, -1.7)			
Western Europe/European origin	Week 4	CR845	29	22 (75.9)	-5.5 (0.9)	(-7.3, -3.6)	-2.3 (1.2)	(-4.7, 0.0)	0.050
		Placebo	31	31 (100.0)	-3.2 (0.8)	(-4.8, -1.5)			
USA	Week 8	CR845	146	128 (87.7)	-4.2 (0.3)	(-4.8, -3.5)	-0.6 (0.4)	(-1.4, 0.3)	0.198
		Placebo	133	125 (94.0)	-3.6 (0.4)	(-4.3, -2.9)			
Asia	Week 8	CR845	8	7 (87.5)	-4.6 (1.2)	(-7.1, -2.0)	-0.0 (1.6)	(-3.4, 3.4)	0.989
		Placebo	12	12 (100.0)	-4.6 (0.9)	(-6.6, -2.6)			
Eastern Europe	Week 8	CR845	54	48 (88.9)	-4.6 (0.6)	(-5.8, -3.3)	-1.5 (0.7)	(-2.9, -0.1)	0.040 *
		Placebo	60	59 (98.3)	-3.1 (0.6)	(-4.2, -1.9)			
Western Europe/European origin	Week 8	CR845	29	23 (79.3)	-5.6 (0.8)	(-7.2, -3.9)	-2.2 (1.1)	(-4.4, -0.0)	0.047 *
		Placebo	31	26 (83.9)	-3.4 (0.8)	(-4.9, -1.8)			
USA	Week 10	CR845	146	126 (86.3)	-4.3 (0.3)	(-5.0, -3.6)	-0.6 (0.4)	(-1.4, 0.3)	0.201
		Placebo	133	122 (91.7)	-3.7 (0.4)	(-4.4, -3.0)			
Asia	Week 10	CR845	8	7 (87.5)	-4.9 (1.2)	(-7.4, -2.3)	-0.1 (1.6)	(-3.4, 3.3)	0.974
		Placebo	12	11 (91.7)	-4.8 (1.0)	(-6.8, -2.8)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DTC_ISCG: Change from baseline in 5-D total score - MMRM results by region
ITT

Change from baseline in 5-D total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Eastern Europe	Week 10	CR845	54	48 (88.9)	-5.0 (0.6)	(-6.2, -3.8)	-2.4 (0.6)	(-3.7, -1.1)	<0.001 *
		Placebo	60	59 (98.3)	-2.6 (0.5)	(-3.7, -1.5)			
Western Europe/European origin	Week 10	CR845	29	22 (75.9)	-5.6 (1.0)	(-7.7, -3.6)	-2.5 (1.3)	(-5.1, 0.2)	0.066
		Placebo	31	25 (80.6)	-3.2 (0.9)	(-5.0, -1.3)			
USA	Week 12	CR845	146	125 (85.6)	-4.7 (0.4)	(-5.4, -4.0)	-0.9 (0.5)	(-1.8, 0.0)	0.050
		Placebo	133	125 (94.0)	-3.8 (0.4)	(-4.5, -3.0)			
Asia	Week 12	CR845	8	7 (87.5)	-4.3 (1.5)	(-7.5, -1.1)	1.0 (2.0)	(-3.1, 5.2)	0.609
		Placebo	12	11 (91.7)	-5.3 (1.2)	(-7.9, -2.8)			
Eastern Europe	Week 12	CR845	54	47 (87.0)	-5.1 (0.7)	(-6.4, -3.8)	-2.1 (0.7)	(-3.5, -0.6)	0.005 *
		Placebo	60	58 (96.7)	-3.0 (0.6)	(-4.2, -1.8)			
Western Europe/European origin	Week 12	CR845	29	22 (75.9)	-4.7 (1.0)	(-6.7, -2.8)	-1.0 (1.3)	(-3.5, 1.5)	0.427
		Placebo	31	25 (80.6)	-3.7 (0.9)	(-5.5, -1.9)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DTC_ISCH: Change from baseline in 5-D total score - MMRM results by dialysis method
ITT

Change from baseline in 5-D total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
H: Dialysis method									0.886
Hemodialysis (HD)	Week 4	CR845	222	197 (88.7)	-3.8 (0.3)	(-4.4, -3.3)	-1.4 (0.3)	(-2.0, -0.7)	<0.001 *
		Placebo	199	188 (94.5)	-2.5 (0.3)	(-3.0, -1.9)			
Hemodiafiltration (HDF)	Week 4	CR845	15	13 (86.7)	-4.5 (1.8)	(-8.2, -0.9)	-1.1 (1.3)	(-3.8, 1.5)	0.383
		Placebo	37	37 (100.0)	-3.4 (1.3)	(-5.9, -0.8)			
Hemodialysis (HD)	Week 8	CR845	222	193 (86.9)	-4.4 (0.3)	(-5.0, -3.9)	-1.0 (0.4)	(-1.7, -0.3)	0.005 *
		Placebo	199	187 (94.0)	-3.4 (0.3)	(-4.0, -2.8)			
Hemodiafiltration (HDF)	Week 8	CR845	15	13 (86.7)	-4.9 (1.8)	(-8.5, -1.3)	-0.6 (1.3)	(-3.2, 1.9)	0.627
		Placebo	37	35 (94.6)	-4.3 (1.3)	(-6.8, -1.7)			
Hemodialysis (HD)	Week 10	CR845	222	191 (86.0)	-4.6 (0.3)	(-5.1, -4.0)	-1.1 (0.4)	(-1.8, -0.4)	0.004 *
		Placebo	199	185 (93.0)	-3.5 (0.3)	(-4.1, -2.9)			
Hemodiafiltration (HDF)	Week 10	CR845	15	12 (80.0)	-5.8 (1.8)	(-9.5, -2.2)	-2.5 (1.4)	(-5.3, 0.2)	0.067
		Placebo	37	32 (86.5)	-3.3 (1.3)	(-5.9, -0.7)			
Hemodialysis (HD)	Week 12	CR845	222	188 (84.7)	-4.8 (0.3)	(-5.4, -4.2)	-1.1 (0.4)	(-1.9, -0.3)	0.005 *
		Placebo	199	185 (93.0)	-3.7 (0.3)	(-4.3, -3.1)			
Hemodiafiltration (HDF)	Week 12	CR845	15	13 (86.7)	-4.7 (1.8)	(-8.4, -1.1)	-1.1 (1.3)	(-3.8, 1.6)	0.412
		Placebo	37	34 (91.9)	-3.6 (1.3)	(-6.2, -1.0)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DDC_ISCA: Change from baseline in 5-D degree score - MMRM results by age
ITT

Change from baseline in 5-D degree score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
A: Age									0.516
< 65 years	Week 4	CR845	147	132 (89.8)	-0.8 (0.1)	(-0.9, -0.6)	-0.2 (0.1)	(-0.4, -0.0)	0.014 *
		Placebo	153	144 (94.1)	-0.5 (0.1)	(-0.7, -0.4)			
>= 65 years	Week 4	CR845	90	80 (88.9)	-0.8 (0.1)	(-1.0, -0.6)	-0.3 (0.1)	(-0.5, -0.0)	0.020 *
		Placebo	83	81 (97.6)	-0.5 (0.1)	(-0.7, -0.3)			
< 65 years	Week 8	CR845	147	130 (88.4)	-0.9 (0.1)	(-1.0, -0.7)	-0.1 (0.1)	(-0.3, 0.1)	0.224
		Placebo	153	143 (93.5)	-0.8 (0.1)	(-0.9, -0.6)			
>= 65 years	Week 8	CR845	90	78 (86.7)	-0.7 (0.1)	(-0.9, -0.5)	-0.2 (0.1)	(-0.5, 0.0)	0.087
		Placebo	83	79 (95.2)	-0.5 (0.1)	(-0.7, -0.3)			
< 65 years	Week 10	CR845	147	130 (88.4)	-0.9 (0.1)	(-1.1, -0.8)	-0.2 (0.1)	(-0.4, 0.0)	0.068
		Placebo	153	141 (92.2)	-0.8 (0.1)	(-0.9, -0.6)			
>= 65 years	Week 10	CR845	90	74 (82.2)	-0.8 (0.1)	(-1.0, -0.6)	-0.3 (0.1)	(-0.6, -0.0)	0.021 *
		Placebo	83	76 (91.6)	-0.5 (0.1)	(-0.7, -0.3)			
< 65 years	Week 12	CR845	147	129 (87.8)	-1.0 (0.1)	(-1.1, -0.8)	-0.1 (0.1)	(-0.3, 0.0)	0.136
		Placebo	153	142 (92.8)	-0.8 (0.1)	(-1.0, -0.7)			
>= 65 years	Week 12	CR845	90	74 (82.2)	-0.8 (0.1)	(-1.1, -0.6)	-0.2 (0.1)	(-0.4, 0.1)	0.226
		Placebo	83	77 (92.8)	-0.7 (0.1)	(-0.9, -0.5)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DDC_ISCB: Change from baseline in 5-D degree score - MMRM results by sex
ITT

Change from baseline in 5-D degree score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
B: Sex									<0.001 i
Male	Week 4	CR845	137	123 (89.8)	-0.5 (0.1)	(-0.6, -0.4)	-0.0 (0.1)	(-0.2, 0.2)	0.993
		Placebo	139	131 (94.2)	-0.5 (0.1)	(-0.6, -0.4)			
Female	Week 4	CR845	100	89 (89.0)	-1.1 (0.1)	(-1.2, -0.9)	-0.6 (0.1)	(-0.8, -0.4)	<0.001 *
		Placebo	97	94 (96.9)	-0.5 (0.1)	(-0.7, -0.3)			
Male	Week 8	CR845	137	122 (89.1)	-0.5 (0.1)	(-0.7, -0.4)	0.0 (0.1)	(-0.2, 0.2)	0.800
		Placebo	139	132 (95.0)	-0.6 (0.1)	(-0.7, -0.4)			
Female	Week 8	CR845	100	86 (86.0)	-1.2 (0.1)	(-1.4, -1.0)	-0.4 (0.1)	(-0.6, -0.1)	0.003 *
		Placebo	97	90 (92.8)	-0.8 (0.1)	(-1.0, -0.6)			
Male	Week 10	CR845	137	117 (85.4)	-0.6 (0.1)	(-0.8, -0.5)	0.0 (0.1)	(-0.1, 0.2)	0.669
		Placebo	139	127 (91.4)	-0.7 (0.1)	(-0.8, -0.5)			
Female	Week 10	CR845	100	87 (87.0)	-1.2 (0.1)	(-1.4, -1.0)	-0.6 (0.1)	(-0.8, -0.3)	<0.001 *
		Placebo	97	90 (92.8)	-0.7 (0.1)	(-0.9, -0.5)			
Male	Week 12	CR845	137	117 (85.4)	-0.6 (0.1)	(-0.8, -0.5)	0.0 (0.1)	(-0.2, 0.2)	0.749
		Placebo	139	127 (91.4)	-0.7 (0.1)	(-0.8, -0.5)			
Female	Week 12	CR845	100	86 (86.0)	-1.3 (0.1)	(-1.5, -1.1)	-0.4 (0.1)	(-0.7, -0.1)	0.003 *
		Placebo	97	92 (94.8)	-0.9 (0.1)	(-1.1, -0.7)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DDC_ISCC: Change from baseline in 5-D degree score - MMRM results by race
ITT

Change from baseline in 5-D degree score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
C: Race									0.740
Black/African American	Week 4	CR845	53	45 (84.9)	-0.7 (0.1)	(-0.9, -0.5)	-0.2 (0.2)	(-0.5, 0.2)	0.306
		Placebo	38	35 (92.1)	-0.5 (0.1)	(-0.8, -0.3)			
White	Week 4	CR845	164	150 (91.5)	-0.8 (0.1)	(-0.9, -0.6)	-0.3 (0.1)	(-0.4, -0.1)	<0.001 *
		Placebo	169	162 (95.9)	-0.5 (0.1)	(-0.6, -0.4)			
Other	Week 4	CR845	20	17 (85.0)	-0.9 (0.2)	(-1.3, -0.5)	-0.3 (0.2)	(-0.8, 0.1)	0.132
		Placebo	29	28 (96.6)	-0.6 (0.2)	(-0.9, -0.2)			
Black/African American	Week 8	CR845	53	45 (84.9)	-0.7 (0.1)	(-1.0, -0.5)	-0.0 (0.2)	(-0.4, 0.4)	0.928
		Placebo	38	37 (97.4)	-0.7 (0.2)	(-1.0, -0.4)			
White	Week 8	CR845	164	146 (89.0)	-0.8 (0.1)	(-1.0, -0.7)	-0.2 (0.1)	(-0.4, -0.0)	0.038 *
		Placebo	169	159 (94.1)	-0.6 (0.1)	(-0.8, -0.5)			
Other	Week 8	CR845	20	17 (85.0)	-1.1 (0.2)	(-1.5, -0.7)	-0.4 (0.2)	(-0.8, 0.1)	0.081
		Placebo	29	26 (89.7)	-0.7 (0.2)	(-1.1, -0.3)			
Black/African American	Week 10	CR845	53	42 (79.2)	-0.9 (0.1)	(-1.2, -0.6)	-0.2 (0.2)	(-0.6, 0.2)	0.436
		Placebo	38	36 (94.7)	-0.7 (0.1)	(-1.0, -0.4)			
White	Week 10	CR845	164	146 (89.0)	-0.9 (0.1)	(-1.1, -0.8)	-0.3 (0.1)	(-0.4, -0.1)	0.003 *
		Placebo	169	156 (92.3)	-0.7 (0.1)	(-0.8, -0.5)			
Other	Week 10	CR845	20	16 (80.0)	-0.8 (0.2)	(-1.3, -0.4)	-0.1 (0.3)	(-0.7, 0.4)	0.598
		Placebo	29	25 (86.2)	-0.7 (0.2)	(-1.1, -0.3)			
Black/African American	Week 12	CR845	53	43 (81.1)	-1.0 (0.1)	(-1.2, -0.8)	-0.2 (0.2)	(-0.5, 0.2)	0.326
		Placebo	38	37 (97.4)	-0.8 (0.1)	(-1.1, -0.6)			
White	Week 12	CR845	164	144 (87.8)	-0.9 (0.1)	(-1.1, -0.8)	-0.2 (0.1)	(-0.4, -0.0)	0.031 *
		Placebo	169	159 (94.1)	-0.7 (0.1)	(-0.9, -0.6)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DDC_ISCC: Change from baseline in 5-D degree score - MMRM results by race
ITT

Change from baseline in 5-D degree score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Other	Week 12	CR845	20	16 (80.0)	-0.8 (0.2)	(-1.3, -0.3)	0.2 (0.3)	(-0.4, 0.7)	0.598
		Placebo	29	23 (79.3)	-1.0 (0.2)	(-1.4, -0.5)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DDC_ISCD: Change from baseline in 5-D degree score - MMRM results by baseline WI-NRS
ITT

Change from baseline in 5-D degree score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
D: Baseline worst itching NRS score (WI-NRS)									0.731
>= 4 to < 7	Week 4	CR845	102	94 (92.2)	-0.6 (0.1)	(-0.8, -0.4)	-0.1 (0.1)	(-0.3, 0.1)	0.168
		Placebo	113	109 (96.5)	-0.5 (0.1)	(-0.6, -0.3)			
>= 7	Week 4	CR845	135	118 (87.4)	-0.9 (0.1)	(-1.1, -0.8)	-0.4 (0.1)	(-0.6, -0.2)	<0.001 *
		Placebo	123	116 (94.3)	-0.6 (0.1)	(-0.7, -0.4)			
>= 4 to < 7	Week 8	CR845	102	94 (92.2)	-0.7 (0.1)	(-0.9, -0.5)	-0.2 (0.1)	(-0.4, -0.0)	0.041 *
		Placebo	113	105 (92.9)	-0.5 (0.1)	(-0.7, -0.3)			
>= 7	Week 8	CR845	135	114 (84.4)	-0.9 (0.1)	(-1.1, -0.8)	-0.1 (0.1)	(-0.3, 0.1)	0.298
		Placebo	123	117 (95.1)	-0.8 (0.1)	(-1.0, -0.6)			
>= 4 to < 7	Week 10	CR845	102	91 (89.2)	-0.8 (0.1)	(-1.0, -0.6)	-0.3 (0.1)	(-0.5, -0.1)	0.005 *
		Placebo	113	102 (90.3)	-0.5 (0.1)	(-0.7, -0.4)			
>= 7	Week 10	CR845	135	113 (83.7)	-1.0 (0.1)	(-1.2, -0.8)	-0.2 (0.1)	(-0.4, 0.0)	0.115
		Placebo	123	115 (93.5)	-0.8 (0.1)	(-1.0, -0.6)			
>= 4 to < 7	Week 12	CR845	102	90 (88.2)	-0.9 (0.1)	(-1.0, -0.7)	-0.2 (0.1)	(-0.4, -0.0)	0.042 *
		Placebo	113	103 (91.2)	-0.6 (0.1)	(-0.8, -0.5)			
>= 7	Week 12	CR845	135	113 (83.7)	-1.0 (0.1)	(-1.2, -0.9)	-0.1 (0.1)	(-0.4, 0.1)	0.271
		Placebo	123	116 (94.3)	-0.9 (0.1)	(-1.1, -0.7)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DDC_ISCE: Change from baseline in 5-D degree score - MMRM results by specific medical condition
ITT

Change from baseline in 5-D degree score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
E: Presence of specific medical conditions									0.225
No	Week 4	CR845	195	174 (89.2)	-0.7 (0.1)	(-0.8, -0.6)	-0.2 (0.1)	(-0.4, -0.1)	0.008 *
		Placebo	199	191 (96.0)	-0.5 (0.1)	(-0.6, -0.4)			
Yes	Week 4	CR845	42	38 (90.5)	-1.0 (0.1)	(-1.2, -0.7)	-0.4 (0.2)	(-0.8, -0.1)	0.026 *
		Placebo	37	34 (91.9)	-0.6 (0.1)	(-0.8, -0.3)			
No	Week 8	CR845	195	172 (88.2)	-0.8 (0.1)	(-0.9, -0.7)	-0.1 (0.1)	(-0.3, 0.0)	0.148
		Placebo	199	185 (93.0)	-0.7 (0.1)	(-0.8, -0.5)			
Yes	Week 8	CR845	42	36 (85.7)	-0.9 (0.2)	(-1.2, -0.6)	-0.3 (0.2)	(-0.8, 0.1)	0.134
		Placebo	37	37 (100.0)	-0.6 (0.2)	(-0.9, -0.3)			
No	Week 10	CR845	195	169 (86.7)	-0.8 (0.1)	(-0.9, -0.7)	-0.2 (0.1)	(-0.4, -0.0)	0.030 *
		Placebo	199	180 (90.5)	-0.6 (0.1)	(-0.8, -0.5)			
Yes	Week 10	CR845	42	35 (83.3)	-1.1 (0.1)	(-1.4, -0.9)	-0.4 (0.2)	(-0.8, -0.0)	0.033 *
		Placebo	37	37 (100.0)	-0.7 (0.1)	(-1.0, -0.5)			
No	Week 12	CR845	195	168 (86.2)	-0.9 (0.1)	(-1.0, -0.8)	-0.2 (0.1)	(-0.3, 0.0)	0.082
		Placebo	199	183 (92.0)	-0.7 (0.1)	(-0.9, -0.6)			
Yes	Week 12	CR845	42	35 (83.3)	-1.0 (0.1)	(-1.3, -0.7)	-0.2 (0.2)	(-0.6, 0.2)	0.410
		Placebo	37	36 (97.3)	-0.8 (0.1)	(-1.1, -0.6)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor previous use of anti-itch medication is also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DDC_ISCF: Change from baseline in 5-D degree score - MMRM results by use of concomitant itch medication
ITT

Change from baseline in 5-D degree score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
F: Use of concomitant itch medication									0.538
No	Week 4	CR845	150	138 (92.0)	-0.8 (0.1)	(-0.9, -0.6)	-0.2 (0.1)	(-0.4, -0.1)	0.006 *
		Placebo	151	146 (96.7)	-0.5 (0.1)	(-0.7, -0.4)			
Yes	Week 4	CR845	87	74 (85.1)	-0.8 (0.1)	(-1.0, -0.6)	-0.3 (0.1)	(-0.5, -0.0)	0.035 *
		Placebo	85	79 (92.9)	-0.5 (0.1)	(-0.7, -0.3)			
No	Week 8	CR845	150	136 (90.7)	-0.8 (0.1)	(-0.9, -0.6)	-0.1 (0.1)	(-0.3, 0.0)	0.150
		Placebo	151	142 (94.0)	-0.7 (0.1)	(-0.8, -0.5)			
Yes	Week 8	CR845	87	72 (82.8)	-0.9 (0.1)	(-1.1, -0.7)	-0.2 (0.1)	(-0.5, 0.1)	0.152
		Placebo	85	80 (94.1)	-0.7 (0.1)	(-0.9, -0.5)			
No	Week 10	CR845	150	131 (87.3)	-0.8 (0.1)	(-1.0, -0.7)	-0.2 (0.1)	(-0.4, 0.0)	0.081
		Placebo	151	140 (92.7)	-0.7 (0.1)	(-0.8, -0.5)			
Yes	Week 10	CR845	87	73 (83.9)	-1.0 (0.1)	(-1.2, -0.8)	-0.3 (0.1)	(-0.6, -0.1)	0.019 *
		Placebo	85	77 (90.6)	-0.7 (0.1)	(-0.9, -0.5)			
No	Week 12	CR845	150	132 (88.0)	-0.9 (0.1)	(-1.0, -0.7)	-0.1 (0.1)	(-0.3, 0.1)	0.251
		Placebo	151	141 (93.4)	-0.8 (0.1)	(-0.9, -0.6)			
Yes	Week 12	CR845	87	71 (81.6)	-1.1 (0.1)	(-1.3, -0.8)	-0.2 (0.1)	(-0.5, 0.0)	0.092
		Placebo	85	78 (91.8)	-0.8 (0.1)	(-1.0, -0.6)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor presence of medical condition is also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DDC_ISCG: Change from baseline in 5-D degree score - MMRM results by region
ITT

Change from baseline in 5-D degree score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
G: Region									0.334
USA	Week 4	CR845	146	131 (89.7)	-0.7 (0.1)	(-0.8, -0.5)	-0.2 (0.1)	(-0.4, -0.1)	0.012 *
		Placebo	133	123 (92.5)	-0.4 (0.1)	(-0.6, -0.3)			
Asia	Week 4	CR845	8	8 (100.0)	-1.3 (0.2)	(-1.8, -0.8)	-0.8 (0.3)	(-1.4, -0.1)	0.019 *
		Placebo	12	12 (100.0)	-0.5 (0.2)	(-0.9, -0.2)			
Eastern Europe	Week 4	CR845	54	51 (94.4)	-0.7 (0.1)	(-1.0, -0.4)	-0.2 (0.1)	(-0.5, 0.1)	0.268
		Placebo	60	59 (98.3)	-0.5 (0.1)	(-0.8, -0.3)			
Western Europe/European origin	Week 4	CR845	29	22 (75.9)	-1.1 (0.2)	(-1.4, -0.7)	-0.2 (0.2)	(-0.7, 0.2)	0.321
		Placebo	31	31 (100.0)	-0.8 (0.2)	(-1.2, -0.5)			
USA	Week 8	CR845	146	129 (88.4)	-0.8 (0.1)	(-0.9, -0.6)	-0.1 (0.1)	(-0.3, 0.1)	0.517
		Placebo	133	125 (94.0)	-0.7 (0.1)	(-0.9, -0.5)			
Asia	Week 8	CR845	8	7 (87.5)	-1.3 (0.2)	(-1.7, -0.9)	-0.5 (0.2)	(-1.0, 0.1)	0.079
		Placebo	12	12 (100.0)	-0.8 (0.2)	(-1.1, -0.5)			
Eastern Europe	Week 8	CR845	54	49 (90.7)	-0.7 (0.1)	(-1.0, -0.4)	-0.1 (0.2)	(-0.4, 0.2)	0.368
		Placebo	60	59 (98.3)	-0.6 (0.1)	(-0.8, -0.3)			
Western Europe/European origin	Week 8	CR845	29	23 (79.3)	-1.1 (0.2)	(-1.5, -0.7)	-0.4 (0.2)	(-0.9, 0.1)	0.140
		Placebo	31	26 (83.9)	-0.7 (0.2)	(-1.1, -0.4)			
USA	Week 10	CR845	146	127 (87.0)	-0.8 (0.1)	(-1.0, -0.7)	-0.0 (0.1)	(-0.2, 0.1)	0.646
		Placebo	133	122 (91.7)	-0.8 (0.1)	(-0.9, -0.6)			
Asia	Week 10	CR845	8	7 (87.5)	-1.0 (0.3)	(-1.7, -0.3)	-0.1 (0.4)	(-1.0, 0.9)	0.874
		Placebo	12	11 (91.7)	-0.9 (0.3)	(-1.5, -0.3)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DDC_ISCG: Change from baseline in 5-D degree score - MMRM results by region
ITT

Change from baseline in 5-D degree score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Eastern Europe	Week 10	CR845	54	48 (88.9)	-0.9 (0.1)	(-1.2, -0.6)	-0.5 (0.2)	(-0.8, -0.2)	<0.001 *
		Placebo	60	59 (98.3)	-0.4 (0.1)	(-0.6, -0.1)			
Western Europe/European origin	Week 10	CR845	29	22 (75.9)	-1.1 (0.2)	(-1.5, -0.7)	-0.4 (0.3)	(-0.9, 0.2)	0.198
		Placebo	31	25 (80.6)	-0.8 (0.2)	(-1.2, -0.4)			
USA	Week 12	CR845	146	127 (87.0)	-0.9 (0.1)	(-1.0, -0.7)	-0.1 (0.1)	(-0.3, 0.1)	0.554
		Placebo	133	125 (94.0)	-0.8 (0.1)	(-1.0, -0.7)			
Asia	Week 12	CR845	8	7 (87.5)	-1.3 (0.3)	(-1.9, -0.6)	-0.1 (0.4)	(-0.9, 0.7)	0.803
		Placebo	12	11 (91.7)	-1.2 (0.2)	(-1.7, -0.7)			
Eastern Europe	Week 12	CR845	54	47 (87.0)	-1.0 (0.1)	(-1.3, -0.7)	-0.4 (0.2)	(-0.8, -0.1)	0.012 *
		Placebo	60	58 (96.7)	-0.5 (0.1)	(-0.8, -0.3)			
Western Europe/European origin	Week 12	CR845	29	22 (75.9)	-0.9 (0.2)	(-1.3, -0.5)	0.1 (0.3)	(-0.4, 0.7)	0.647
		Placebo	31	25 (80.6)	-1.0 (0.2)	(-1.4, -0.6)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DDC_ISCH: Change from baseline in 5-D degree score - MMRM results by dialysis method
ITT

Change from baseline in 5-D degree score					Repeated measures analysis					
					Change from Baseline		Treatment Difference			
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value	
H: Dialysis method									0.581	
Hemodialysis (HD)	Week 4	CR845	222	199 (89.6)	-0.8 (0.1)	(-0.9, -0.6)	-0.3 (0.1)	(-0.4, -0.1)	<0.001	*
		Placebo	199	188 (94.5)	-0.5 (0.1)	(-0.6, -0.4)				
Hemodiafiltration (HDF)	Week 4	CR845	15	13 (86.7)	-0.6 (0.4)	(-1.4, 0.1)	0.1 (0.3)	(-0.5, 0.7)	0.673	
		Placebo	37	37 (100.0)	-0.7 (0.3)	(-1.3, -0.2)				
Hemodialysis (HD)	Week 8	CR845	222	195 (87.8)	-0.8 (0.1)	(-0.9, -0.7)	-0.2 (0.1)	(-0.3, -0.0)	0.037	*
		Placebo	199	187 (94.0)	-0.6 (0.1)	(-0.8, -0.5)				
Hemodiafiltration (HDF)	Week 8	CR845	15	13 (86.7)	-0.7 (0.4)	(-1.4, 0.0)	0.1 (0.3)	(-0.5, 0.7)	0.671	
		Placebo	37	35 (94.6)	-0.8 (0.3)	(-1.4, -0.3)				
Hemodialysis (HD)	Week 10	CR845	222	192 (86.5)	-0.9 (0.1)	(-1.0, -0.8)	-0.2 (0.1)	(-0.3, -0.0)	0.039	*
		Placebo	199	185 (93.0)	-0.7 (0.1)	(-0.8, -0.6)				
Hemodiafiltration (HDF)	Week 10	CR845	15	12 (80.0)	-1.0 (0.4)	(-1.8, -0.3)	-0.5 (0.3)	(-1.1, 0.1)	0.103	
		Placebo	37	32 (86.5)	-0.5 (0.3)	(-1.1, 0.0)				
Hemodialysis (HD)	Week 12	CR845	222	190 (85.6)	-0.9 (0.1)	(-1.1, -0.8)	-0.1 (0.1)	(-0.3, 0.0)	0.094	
		Placebo	199	185 (93.0)	-0.8 (0.1)	(-0.9, -0.7)				
Hemodiafiltration (HDF)	Week 12	CR845	15	13 (86.7)	-0.9 (0.4)	(-1.6, -0.1)	-0.1 (0.3)	(-0.7, 0.6)	0.832	
		Placebo	37	34 (91.9)	-0.8 (0.3)	(-1.3, -0.2)				

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DLC_ISCA: Change from baseline in 5-D duration score - MMRM results by age
ITT

Change from baseline in 5-D duration score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
A: Age									0.678
< 65 years	Week 4	CR845	147	132 (89.8)	-0.6 (0.1)	(-0.8, -0.4)	-0.3 (0.1)	(-0.6, -0.0)	0.046 *
		Placebo	153	144 (94.1)	-0.3 (0.1)	(-0.6, -0.1)			
>= 65 years	Week 4	CR845	90	79 (87.8)	-0.7 (0.1)	(-1.0, -0.5)	-0.2 (0.2)	(-0.6, 0.2)	0.264
		Placebo	83	81 (97.6)	-0.5 (0.1)	(-0.8, -0.3)			
< 65 years	Week 8	CR845	147	129 (87.8)	-0.8 (0.1)	(-1.0, -0.6)	-0.1 (0.1)	(-0.3, 0.2)	0.504
		Placebo	153	143 (93.5)	-0.7 (0.1)	(-0.9, -0.5)			
>= 65 years	Week 8	CR845	90	78 (86.7)	-0.9 (0.1)	(-1.2, -0.7)	-0.3 (0.2)	(-0.6, 0.0)	0.085
		Placebo	83	79 (95.2)	-0.6 (0.1)	(-0.9, -0.4)			
< 65 years	Week 10	CR845	147	129 (87.8)	-0.7 (0.1)	(-1.0, -0.5)	-0.0 (0.1)	(-0.3, 0.2)	0.801
		Placebo	153	141 (92.2)	-0.7 (0.1)	(-0.9, -0.5)			
>= 65 years	Week 10	CR845	90	74 (82.2)	-0.8 (0.1)	(-1.1, -0.5)	-0.3 (0.2)	(-0.6, 0.1)	0.168
		Placebo	83	76 (91.6)	-0.6 (0.1)	(-0.8, -0.3)			
< 65 years	Week 12	CR845	147	128 (87.1)	-0.8 (0.1)	(-1.1, -0.6)	-0.2 (0.1)	(-0.5, 0.0)	0.094
		Placebo	153	142 (92.8)	-0.6 (0.1)	(-0.8, -0.4)			
>= 65 years	Week 12	CR845	90	74 (82.2)	-0.9 (0.1)	(-1.2, -0.6)	-0.3 (0.2)	(-0.6, 0.1)	0.115
		Placebo	83	77 (92.8)	-0.6 (0.1)	(-0.9, -0.3)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DLC_ISCB: Change from baseline in 5-D duration score - MMRM results by sex
ITT

Change from baseline in 5-D duration score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
B: Sex									<0.001 i
Male	Week 4	CR845	137	124 (90.5)	-0.4 (0.1)	(-0.6, -0.1)	0.0 (0.1)	(-0.3, 0.3)	0.989
		Placebo	139	131 (94.2)	-0.4 (0.1)	(-0.6, -0.2)			
Female	Week 4	CR845	100	87 (87.0)	-1.0 (0.1)	(-1.3, -0.8)	-0.6 (0.2)	(-0.9, -0.3)	<0.001 *
		Placebo	97	94 (96.9)	-0.4 (0.1)	(-0.7, -0.2)			
Male	Week 8	CR845	137	122 (89.1)	-0.6 (0.1)	(-0.8, -0.4)	0.1 (0.1)	(-0.2, 0.3)	0.548
		Placebo	139	132 (95.0)	-0.7 (0.1)	(-0.9, -0.5)			
Female	Week 8	CR845	100	85 (85.0)	-1.1 (0.1)	(-1.4, -0.9)	-0.5 (0.2)	(-0.8, -0.2)	0.004 *
		Placebo	97	90 (92.8)	-0.7 (0.1)	(-0.9, -0.4)			
Male	Week 10	CR845	137	117 (85.4)	-0.5 (0.1)	(-0.7, -0.3)	0.2 (0.1)	(-0.1, 0.5)	0.154
		Placebo	139	127 (91.4)	-0.7 (0.1)	(-0.9, -0.5)			
Female	Week 10	CR845	100	86 (86.0)	-1.1 (0.1)	(-1.4, -0.9)	-0.5 (0.2)	(-0.8, -0.2)	0.001 *
		Placebo	97	90 (92.8)	-0.6 (0.1)	(-0.9, -0.4)			
Male	Week 12	CR845	137	117 (85.4)	-0.7 (0.1)	(-0.9, -0.5)	-0.1 (0.1)	(-0.4, 0.2)	0.448
		Placebo	139	127 (91.4)	-0.6 (0.1)	(-0.8, -0.4)			
Female	Week 12	CR845	100	85 (85.0)	-1.1 (0.1)	(-1.3, -0.8)	-0.4 (0.2)	(-0.8, -0.1)	0.013 *
		Placebo	97	92 (94.8)	-0.6 (0.1)	(-0.9, -0.4)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DLC_ISCC: Change from baseline in 5-D duration score - MMRM results by race
ITT

Change from baseline in 5-D duration score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
C: Race									0.752
Black/African American	Week 4	CR845	53	45 (84.9)	-0.6 (0.2)	(-0.9, -0.2)	-0.0 (0.3)	(-0.5, 0.5)	0.989
		Placebo	38	35 (92.1)	-0.6 (0.2)	(-0.9, -0.2)			
White	Week 4	CR845	164	149 (90.9)	-0.7 (0.1)	(-0.9, -0.5)	-0.3 (0.1)	(-0.6, -0.1)	0.011 *
		Placebo	169	162 (95.9)	-0.4 (0.1)	(-0.6, -0.1)			
Other	Week 4	CR845	20	17 (85.0)	-0.7 (0.3)	(-1.2, -0.1)	-0.3 (0.3)	(-0.8, 0.3)	0.300
		Placebo	29	28 (96.6)	-0.4 (0.2)	(-0.9, 0.1)			
Black/African American	Week 8	CR845	53	45 (84.9)	-1.0 (0.2)	(-1.4, -0.6)	-0.4 (0.3)	(-1.0, 0.2)	0.152
		Placebo	38	37 (97.4)	-0.6 (0.2)	(-1.0, -0.1)			
White	Week 8	CR845	164	145 (88.4)	-0.8 (0.1)	(-1.0, -0.6)	-0.1 (0.1)	(-0.3, 0.2)	0.541
		Placebo	169	159 (94.1)	-0.7 (0.1)	(-0.9, -0.5)			
Other	Week 8	CR845	20	17 (85.0)	-1.1 (0.3)	(-1.6, -0.5)	-0.5 (0.3)	(-1.2, 0.1)	0.074
		Placebo	29	26 (89.7)	-0.5 (0.3)	(-1.0, -0.0)			
Black/African American	Week 10	CR845	53	42 (79.2)	-1.0 (0.2)	(-1.4, -0.6)	-0.5 (0.3)	(-1.0, 0.1)	0.095
		Placebo	38	36 (94.7)	-0.5 (0.2)	(-1.0, -0.1)			
White	Week 10	CR845	164	145 (88.4)	-0.7 (0.1)	(-0.9, -0.5)	-0.0 (0.1)	(-0.2, 0.2)	0.938
		Placebo	169	156 (92.3)	-0.7 (0.1)	(-0.9, -0.5)			
Other	Week 10	CR845	20	16 (80.0)	-0.9 (0.3)	(-1.5, -0.3)	-0.3 (0.3)	(-1.0, 0.3)	0.293
		Placebo	29	25 (86.2)	-0.5 (0.3)	(-1.0, 0.0)			
Black/African American	Week 12	CR845	53	43 (81.1)	-1.1 (0.2)	(-1.5, -0.8)	-0.4 (0.3)	(-0.9, 0.1)	0.106
		Placebo	38	37 (97.4)	-0.7 (0.2)	(-1.1, -0.3)			
White	Week 12	CR845	164	143 (87.2)	-0.8 (0.1)	(-1.0, -0.6)	-0.3 (0.1)	(-0.5, -0.0)	0.045 *
		Placebo	169	159 (94.1)	-0.6 (0.1)	(-0.8, -0.4)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DLC_ISCC: Change from baseline in 5-D duration score - MMRM results by race
ITT

Change from baseline in 5-D duration score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Other	Week 12	CR845	20	16 (80.0)	-0.5 (0.4)	(-1.3, 0.2)	-0.0 (0.4)	(-0.9, 0.9)	0.957
		Placebo	29	23 (79.3)	-0.5 (0.3)	(-1.1, 0.1)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DLC_ISCD: Change from baseline in 5-D duration score - MMRM results by baseline WI-NRS
ITT

Change from baseline in 5-D duration score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
D: Baseline worst itching NRS score (WI-NRS)									0.736
>= 4 to < 7	Week 4	CR845	102	94 (92.2)	-0.5 (0.1)	(-0.7, -0.2)	-0.2 (0.1)	(-0.5, 0.1)	0.211
		Placebo	113	109 (96.5)	-0.3 (0.1)	(-0.5, -0.0)			
>= 7	Week 4	CR845	135	117 (86.7)	-0.9 (0.1)	(-1.1, -0.6)	-0.3 (0.2)	(-0.6, 0.0)	0.050
		Placebo	123	116 (94.3)	-0.6 (0.1)	(-0.8, -0.3)			
>= 4 to < 7	Week 8	CR845	102	93 (91.2)	-0.7 (0.1)	(-0.9, -0.5)	-0.3 (0.1)	(-0.5, -0.0)	0.034 *
		Placebo	113	105 (92.9)	-0.4 (0.1)	(-0.7, -0.2)			
>= 7	Week 8	CR845	135	114 (84.4)	-1.0 (0.1)	(-1.2, -0.7)	-0.1 (0.2)	(-0.4, 0.2)	0.645
		Placebo	123	117 (95.1)	-0.9 (0.1)	(-1.1, -0.7)			
>= 4 to < 7	Week 10	CR845	102	90 (88.2)	-0.6 (0.1)	(-0.9, -0.4)	-0.2 (0.1)	(-0.5, 0.1)	0.165
		Placebo	113	102 (90.3)	-0.5 (0.1)	(-0.7, -0.2)			
>= 7	Week 10	CR845	135	113 (83.7)	-0.9 (0.1)	(-1.2, -0.7)	-0.1 (0.2)	(-0.4, 0.3)	0.731
		Placebo	123	115 (93.5)	-0.9 (0.1)	(-1.1, -0.6)			
>= 4 to < 7	Week 12	CR845	102	89 (87.3)	-0.6 (0.1)	(-0.9, -0.4)	-0.2 (0.2)	(-0.5, 0.1)	0.126
		Placebo	113	103 (91.2)	-0.4 (0.1)	(-0.7, -0.2)			
>= 7	Week 12	CR845	135	113 (83.7)	-1.1 (0.1)	(-1.3, -0.8)	-0.3 (0.2)	(-0.6, 0.0)	0.076
		Placebo	123	116 (94.3)	-0.8 (0.1)	(-1.0, -0.5)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DLC_ISCE: Change from baseline in 5-D duration score - MMRM results by specific medical condition
ITT

Change from baseline in 5-D duration score					Repeated measures analysis					
					Change from Baseline		Treatment Difference			
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value	
E: Presence of specific medical conditions									0.797	
No	Week 4	CR845	195	173 (88.7)	-0.6 (0.1)	(-0.8, -0.5)	-0.3 (0.1)	(-0.6, -0.1)	0.013	*
		Placebo	199	191 (96.0)	-0.3 (0.1)	(-0.5, -0.2)				
Yes	Week 4	CR845	42	38 (90.5)	-0.7 (0.2)	(-1.0, -0.3)	0.0 (0.2)	(-0.5, 0.5)	0.911	
		Placebo	37	34 (91.9)	-0.7 (0.2)	(-1.1, -0.4)				
No	Week 8	CR845	195	171 (87.7)	-0.8 (0.1)	(-0.9, -0.6)	-0.1 (0.1)	(-0.3, 0.1)	0.296	
		Placebo	199	185 (93.0)	-0.7 (0.1)	(-0.8, -0.5)				
Yes	Week 8	CR845	42	36 (85.7)	-1.1 (0.2)	(-1.4, -0.7)	-0.4 (0.3)	(-0.9, 0.1)	0.133	
		Placebo	37	37 (100.0)	-0.7 (0.2)	(-1.1, -0.3)				
No	Week 10	CR845	195	168 (86.2)	-0.8 (0.1)	(-0.9, -0.6)	-0.1 (0.1)	(-0.4, 0.1)	0.228	
		Placebo	199	180 (90.5)	-0.6 (0.1)	(-0.8, -0.5)				
Yes	Week 10	CR845	42	35 (83.3)	-0.8 (0.2)	(-1.2, -0.4)	0.0 (0.3)	(-0.6, 0.6)	0.976	
		Placebo	37	37 (100.0)	-0.8 (0.2)	(-1.2, -0.4)				
No	Week 12	CR845	195	167 (85.6)	-0.8 (0.1)	(-1.0, -0.6)	-0.3 (0.1)	(-0.5, -0.0)	0.028	*
		Placebo	199	183 (92.0)	-0.5 (0.1)	(-0.7, -0.4)				
Yes	Week 12	CR845	42	35 (83.3)	-1.0 (0.2)	(-1.3, -0.6)	-0.2 (0.2)	(-0.6, 0.3)	0.484	
		Placebo	37	36 (97.3)	-0.8 (0.2)	(-1.1, -0.5)				

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor previous use of anti-itch medication is also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DLC_ISCF: Change from baseline in 5-D duration score - MMRM results by use of concomitant itch medication
ITT

Change from baseline in 5-D duration score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
F: Use of concomitant itch medication									0.644
No	Week 4	CR845	150	137 (91.3)	-0.7 (0.1)	(-0.9, -0.4)	-0.3 (0.1)	(-0.6, -0.1)	0.018 *
		Placebo	151	146 (96.7)	-0.3 (0.1)	(-0.5, -0.1)			
Yes	Week 4	CR845	87	74 (85.1)	-0.7 (0.1)	(-0.9, -0.4)	-0.1 (0.2)	(-0.5, 0.2)	0.471
		Placebo	85	79 (92.9)	-0.5 (0.1)	(-0.8, -0.3)			
No	Week 8	CR845	150	135 (90.0)	-0.8 (0.1)	(-1.0, -0.6)	-0.2 (0.1)	(-0.4, 0.1)	0.180
		Placebo	151	142 (94.0)	-0.7 (0.1)	(-0.9, -0.5)			
Yes	Week 8	CR845	87	72 (82.8)	-0.8 (0.1)	(-1.1, -0.6)	-0.1 (0.2)	(-0.5, 0.2)	0.410
		Placebo	85	80 (94.1)	-0.7 (0.1)	(-0.9, -0.4)			
No	Week 10	CR845	150	130 (86.7)	-0.8 (0.1)	(-1.0, -0.6)	-0.1 (0.1)	(-0.4, 0.1)	0.382
		Placebo	151	140 (92.7)	-0.7 (0.1)	(-0.9, -0.4)			
Yes	Week 10	CR845	87	73 (83.9)	-0.8 (0.1)	(-1.1, -0.5)	-0.1 (0.2)	(-0.5, 0.2)	0.520
		Placebo	85	77 (90.6)	-0.7 (0.1)	(-0.9, -0.4)			
No	Week 12	CR845	150	131 (87.3)	-0.8 (0.1)	(-1.0, -0.6)	-0.3 (0.1)	(-0.5, -0.0)	0.048 *
		Placebo	151	141 (93.4)	-0.5 (0.1)	(-0.8, -0.3)			
Yes	Week 12	CR845	87	71 (81.6)	-0.9 (0.1)	(-1.2, -0.6)	-0.2 (0.2)	(-0.6, 0.1)	0.202
		Placebo	85	78 (91.8)	-0.7 (0.1)	(-0.9, -0.4)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor presence of medical condition is also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DLC_ISCG: Change from baseline in 5-D duration score - MMRM results by region
ITT

Change from baseline in 5-D duration score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
G: Region									0.539
USA	Week 4	CR845	146	130 (89.0)	-0.5 (0.1)	(-0.8, -0.3)	-0.2 (0.1)	(-0.5, 0.1)	0.199
		Placebo	133	123 (92.5)	-0.4 (0.1)	(-0.6, -0.1)			
Asia	Week 4	CR845	8	8 (100.0)	-1.6 (0.3)	(-2.1, -1.0)	-0.8 (0.3)	(-1.5, -0.1)	0.037 *
		Placebo	12	12 (100.0)	-0.8 (0.2)	(-1.3, -0.3)			
Eastern Europe	Week 4	CR845	54	51 (94.4)	-0.7 (0.2)	(-1.1, -0.4)	-0.2 (0.2)	(-0.7, 0.2)	0.258
		Placebo	60	59 (98.3)	-0.5 (0.2)	(-0.8, -0.1)			
Western Europe/European origin	Week 4	CR845	29	22 (75.9)	-1.0 (0.3)	(-1.5, -0.4)	-0.6 (0.3)	(-1.3, 0.1)	0.110
		Placebo	31	31 (100.0)	-0.4 (0.2)	(-0.9, 0.0)			
USA	Week 8	CR845	146	128 (87.7)	-0.8 (0.1)	(-1.0, -0.6)	-0.1 (0.1)	(-0.4, 0.2)	0.467
		Placebo	133	125 (94.0)	-0.7 (0.1)	(-0.9, -0.5)			
Asia	Week 8	CR845	8	7 (87.5)	-1.4 (0.3)	(-2.1, -0.8)	-0.6 (0.4)	(-1.5, 0.2)	0.135
		Placebo	12	12 (100.0)	-0.8 (0.3)	(-1.3, -0.3)			
Eastern Europe	Week 8	CR845	54	49 (90.7)	-0.8 (0.2)	(-1.1, -0.5)	-0.2 (0.2)	(-0.5, 0.2)	0.287
		Placebo	60	59 (98.3)	-0.6 (0.2)	(-0.9, -0.3)			
Western Europe/European origin	Week 8	CR845	29	23 (79.3)	-1.0 (0.2)	(-1.5, -0.5)	-0.3 (0.3)	(-0.9, 0.3)	0.387
		Placebo	31	26 (83.9)	-0.7 (0.2)	(-1.2, -0.3)			
USA	Week 10	CR845	146	126 (86.3)	-0.8 (0.1)	(-1.0, -0.5)	-0.0 (0.1)	(-0.3, 0.3)	0.858
		Placebo	133	122 (91.7)	-0.7 (0.1)	(-1.0, -0.5)			
Asia	Week 10	CR845	8	7 (87.5)	-1.4 (0.3)	(-2.0, -0.8)	-0.5 (0.4)	(-1.2, 0.3)	0.240
		Placebo	12	11 (91.7)	-1.0 (0.2)	(-1.5, -0.5)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DLC_ISCG: Change from baseline in 5-D duration score - MMRM results by region
ITT

Change from baseline in 5-D duration score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Eastern Europe	Week 10	CR845	54	48 (88.9)	-0.8 (0.2)	(-1.1, -0.5)	-0.3 (0.2)	(-0.7, 0.1)	0.103
		Placebo	60	59 (98.3)	-0.5 (0.2)	(-0.8, -0.2)			
Western Europe/European origin	Week 10	CR845	29	22 (75.9)	-0.8 (0.3)	(-1.4, -0.2)	-0.0 (0.4)	(-0.8, 0.7)	0.898
		Placebo	31	25 (80.6)	-0.7 (0.3)	(-1.3, -0.2)			
USA	Week 12	CR845	146	126 (86.3)	-0.9 (0.1)	(-1.1, -0.7)	-0.2 (0.1)	(-0.4, 0.1)	0.233
		Placebo	133	125 (94.0)	-0.7 (0.1)	(-1.0, -0.5)			
Asia	Week 12	CR845	8	7 (87.5)	-1.4 (0.4)	(-2.3, -0.6)	-0.6 (0.5)	(-1.7, 0.4)	0.222
		Placebo	12	11 (91.7)	-0.8 (0.3)	(-1.5, -0.1)			
Eastern Europe	Week 12	CR845	54	47 (87.0)	-0.8 (0.2)	(-1.2, -0.4)	-0.4 (0.2)	(-0.8, 0.0)	0.077
		Placebo	60	58 (96.7)	-0.4 (0.2)	(-0.7, -0.1)			
Western Europe/European origin	Week 12	CR845	29	22 (75.9)	-0.6 (0.3)	(-1.3, -0.0)	-0.3 (0.4)	(-1.1, 0.6)	0.545
		Placebo	31	25 (80.6)	-0.4 (0.3)	(-1.0, 0.2)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DLC_ISCH: Change from baseline in 5-D duration score - MMRM results by dialysis method
ITT

Change from baseline in 5-D duration score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
H: Dialysis method									0.809
Hemodialysis (HD)	Week 4	CR845	222	198 (89.2)	-0.7 (0.1)	(-0.9, -0.5)	-0.3 (0.1)	(-0.5, -0.0)	0.025 *
		Placebo	199	188 (94.5)	-0.4 (0.1)	(-0.6, -0.3)			
Hemodiafiltration (HDF)	Week 4	CR845	15	13 (86.7)	-0.1 (0.6)	(-1.2, 1.1)	-0.2 (0.5)	(-1.1, 0.8)	0.721
		Placebo	37	37 (100.0)	0.1 (0.4)	(-0.7, 0.9)			
Hemodialysis (HD)	Week 8	CR845	222	194 (87.4)	-0.9 (0.1)	(-1.0, -0.7)	-0.2 (0.1)	(-0.4, 0.0)	0.095
		Placebo	199	187 (94.0)	-0.7 (0.1)	(-0.9, -0.5)			
Hemodiafiltration (HDF)	Week 8	CR845	15	13 (86.7)	-0.1 (0.5)	(-1.2, 0.9)	0.1 (0.4)	(-0.7, 0.8)	0.838
		Placebo	37	35 (94.6)	-0.2 (0.4)	(-1.0, 0.5)			
Hemodialysis (HD)	Week 10	CR845	222	191 (86.0)	-0.8 (0.1)	(-1.0, -0.6)	-0.1 (0.1)	(-0.3, 0.1)	0.386
		Placebo	199	185 (93.0)	-0.7 (0.1)	(-0.9, -0.5)			
Hemodiafiltration (HDF)	Week 10	CR845	15	12 (80.0)	-0.3 (0.6)	(-1.4, 0.8)	-0.2 (0.4)	(-1.1, 0.6)	0.604
		Placebo	37	32 (86.5)	-0.1 (0.4)	(-0.9, 0.7)			
Hemodialysis (HD)	Week 12	CR845	222	189 (85.1)	-0.9 (0.1)	(-1.1, -0.7)	-0.2 (0.1)	(-0.4, 0.0)	0.064
		Placebo	199	185 (93.0)	-0.7 (0.1)	(-0.9, -0.5)			
Hemodiafiltration (HDF)	Week 12	CR845	15	13 (86.7)	-0.1 (0.6)	(-1.3, 1.1)	-0.3 (0.5)	(-1.3, 0.6)	0.499
		Placebo	37	34 (91.9)	0.2 (0.4)	(-0.6, 1.0)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DWC_ISCA: Change from baseline in 5-D direction score - MMRM results by age
ITT

Change from baseline in 5-D direction score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
A: Age									0.537
< 65 years	Week 4	CR845	147	133 (90.5)	-1.2 (0.1)	(-1.4, -1.1)	-0.5 (0.1)	(-0.6, -0.3)	<0.001 *
		Placebo	153	144 (94.1)	-0.8 (0.1)	(-1.0, -0.6)			
>= 65 years	Week 4	CR845	90	80 (88.9)	-1.1 (0.1)	(-1.3, -0.9)	-0.3 (0.1)	(-0.6, -0.1)	0.013 *
		Placebo	83	81 (97.6)	-0.7 (0.1)	(-1.0, -0.5)			
< 65 years	Week 8	CR845	147	129 (87.8)	-1.3 (0.1)	(-1.5, -1.1)	-0.3 (0.1)	(-0.5, -0.1)	0.002 *
		Placebo	153	143 (93.5)	-1.0 (0.1)	(-1.1, -0.8)			
>= 65 years	Week 8	CR845	90	78 (86.7)	-1.0 (0.1)	(-1.2, -0.8)	-0.1 (0.1)	(-0.4, 0.2)	0.489
		Placebo	83	79 (95.2)	-0.9 (0.1)	(-1.1, -0.7)			
< 65 years	Week 10	CR845	147	130 (88.4)	-1.3 (0.1)	(-1.5, -1.1)	-0.3 (0.1)	(-0.5, -0.1)	0.006 *
		Placebo	153	141 (92.2)	-1.0 (0.1)	(-1.2, -0.8)			
>= 65 years	Week 10	CR845	90	74 (82.2)	-1.2 (0.1)	(-1.4, -1.0)	-0.5 (0.1)	(-0.8, -0.2)	<0.001 *
		Placebo	83	76 (91.6)	-0.7 (0.1)	(-0.9, -0.5)			
< 65 years	Week 12	CR845	147	129 (87.8)	-1.3 (0.1)	(-1.5, -1.1)	-0.3 (0.1)	(-0.6, -0.1)	0.005 *
		Placebo	153	142 (92.8)	-0.9 (0.1)	(-1.1, -0.8)			
>= 65 years	Week 12	CR845	90	73 (81.1)	-1.1 (0.1)	(-1.3, -0.9)	-0.2 (0.2)	(-0.5, 0.1)	0.270
		Placebo	83	77 (92.8)	-0.9 (0.1)	(-1.2, -0.7)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DWC_ISCB: Change from baseline in 5-D direction score - MMRM results by sex
ITT

Change from baseline in 5-D direction score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
B: Sex									<0.001 i
Male	Week 4	CR845	137	124 (90.5)	-1.0 (0.1)	(-1.2, -0.9)	-0.2 (0.1)	(-0.4, -0.0)	0.019 *
		Placebo	139	131 (94.2)	-0.8 (0.1)	(-1.0, -0.6)			
Female	Week 4	CR845	100	89 (89.0)	-1.4 (0.1)	(-1.6, -1.2)	-0.6 (0.1)	(-0.9, -0.4)	<0.001 *
		Placebo	97	94 (96.9)	-0.7 (0.1)	(-0.9, -0.5)			
Male	Week 8	CR845	137	121 (88.3)	-0.9 (0.1)	(-1.1, -0.7)	-0.0 (0.1)	(-0.2, 0.2)	0.918
		Placebo	139	132 (95.0)	-0.9 (0.1)	(-1.1, -0.7)			
Female	Week 8	CR845	100	86 (86.0)	-1.6 (0.1)	(-1.7, -1.4)	-0.6 (0.1)	(-0.8, -0.3)	<0.001 *
		Placebo	97	90 (92.8)	-1.0 (0.1)	(-1.2, -0.8)			
Male	Week 10	CR845	137	117 (85.4)	-1.0 (0.1)	(-1.2, -0.9)	-0.1 (0.1)	(-0.3, 0.1)	0.180
		Placebo	139	127 (91.4)	-0.9 (0.1)	(-1.1, -0.7)			
Female	Week 10	CR845	100	87 (87.0)	-1.5 (0.1)	(-1.7, -1.3)	-0.7 (0.1)	(-1.0, -0.4)	<0.001 *
		Placebo	97	90 (92.8)	-0.8 (0.1)	(-1.1, -0.6)			
Male	Week 12	CR845	137	117 (85.4)	-1.0 (0.1)	(-1.2, -0.8)	-0.1 (0.1)	(-0.4, 0.1)	0.298
		Placebo	139	127 (91.4)	-0.9 (0.1)	(-1.1, -0.7)			
Female	Week 12	CR845	100	85 (85.0)	-1.5 (0.1)	(-1.7, -1.2)	-0.5 (0.1)	(-0.8, -0.2)	<0.001 *
		Placebo	97	92 (94.8)	-1.0 (0.1)	(-1.2, -0.8)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DWC_ISCC: Change from baseline in 5-D direction score - MMRM results by race
ITT

Change from baseline in 5-D direction score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
C: Race									0.817
Black/African American	Week 4	CR845	53	45 (84.9)	-1.1 (0.1)	(-1.3, -0.8)	-0.2 (0.2)	(-0.6, 0.1)	0.191
		Placebo	38	35 (92.1)	-0.8 (0.1)	(-1.1, -0.5)			
White	Week 4	CR845	164	151 (92.1)	-1.2 (0.1)	(-1.4, -1.0)	-0.4 (0.1)	(-0.6, -0.3)	<0.001 *
		Placebo	169	162 (95.9)	-0.8 (0.1)	(-0.9, -0.6)			
Other	Week 4	CR845	20	17 (85.0)	-1.3 (0.2)	(-1.7, -0.8)	-0.5 (0.3)	(-1.0, -0.0)	0.047 *
		Placebo	29	28 (96.6)	-0.7 (0.2)	(-1.1, -0.4)			
Black/African American	Week 8	CR845	53	45 (84.9)	-1.2 (0.1)	(-1.5, -1.0)	-0.1 (0.2)	(-0.5, 0.3)	0.533
		Placebo	38	37 (97.4)	-1.1 (0.1)	(-1.4, -0.8)			
White	Week 8	CR845	164	145 (88.4)	-1.2 (0.1)	(-1.4, -1.0)	-0.3 (0.1)	(-0.5, -0.1)	0.004 *
		Placebo	169	159 (94.1)	-0.9 (0.1)	(-1.1, -0.7)			
Other	Week 8	CR845	20	17 (85.0)	-1.1 (0.2)	(-1.5, -0.7)	-0.0 (0.2)	(-0.4, 0.4)	0.928
		Placebo	29	26 (89.7)	-1.1 (0.2)	(-1.4, -0.7)			
Black/African American	Week 10	CR845	53	42 (79.2)	-1.3 (0.1)	(-1.6, -1.0)	-0.3 (0.2)	(-0.7, 0.1)	0.135
		Placebo	38	36 (94.7)	-1.0 (0.2)	(-1.3, -0.7)			
White	Week 10	CR845	164	146 (89.0)	-1.2 (0.1)	(-1.4, -1.0)	-0.4 (0.1)	(-0.6, -0.2)	<0.001 *
		Placebo	169	156 (92.3)	-0.8 (0.1)	(-1.0, -0.7)			
Other	Week 10	CR845	20	16 (80.0)	-1.3 (0.2)	(-1.7, -0.9)	-0.3 (0.2)	(-0.8, 0.1)	0.152
		Placebo	29	25 (86.2)	-1.0 (0.2)	(-1.3, -0.6)			
Black/African American	Week 12	CR845	53	42 (79.2)	-1.4 (0.1)	(-1.7, -1.1)	-0.3 (0.2)	(-0.7, 0.1)	0.144
		Placebo	38	37 (97.4)	-1.1 (0.1)	(-1.4, -0.8)			
White	Week 12	CR845	164	144 (87.8)	-1.2 (0.1)	(-1.3, -1.0)	-0.3 (0.1)	(-0.5, -0.1)	0.014 *
		Placebo	169	159 (94.1)	-0.9 (0.1)	(-1.1, -0.7)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DWC_ISCC: Change from baseline in 5-D direction score - MMRM results by race
ITT

Change from baseline in 5-D direction score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Other	Week 12	CR845	20	16 (80.0)	-1.2 (0.2)	(-1.6, -0.7)	-0.1 (0.3)	(-0.7, 0.5)	0.753
		Placebo	29	23 (79.3)	-1.1 (0.2)	(-1.5, -0.6)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DWC_ISCD: Change from baseline in 5-D direction score - MMRM results by baseline WI-NRS
ITT

Change from baseline in 5-D direction score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
D: Baseline worst itching NRS score (WI-NRS)									0.706
>= 4 to < 7	Week 4	CR845	102	95 (93.1)	-1.1 (0.1)	(-1.3, -0.9)	-0.4 (0.1)	(-0.6, -0.2)	<0.001 *
		Placebo	113	109 (96.5)	-0.7 (0.1)	(-0.9, -0.5)			
>= 7	Week 4	CR845	135	118 (87.4)	-1.3 (0.1)	(-1.4, -1.1)	-0.4 (0.1)	(-0.7, -0.2)	<0.001 *
		Placebo	123	116 (94.3)	-0.8 (0.1)	(-1.0, -0.6)			
>= 4 to < 7	Week 8	CR845	102	94 (92.2)	-1.1 (0.1)	(-1.3, -0.9)	-0.4 (0.1)	(-0.6, -0.1)	0.002 *
		Placebo	113	105 (92.9)	-0.8 (0.1)	(-0.9, -0.6)			
>= 7	Week 8	CR845	135	113 (83.7)	-1.3 (0.1)	(-1.4, -1.1)	-0.1 (0.1)	(-0.4, 0.1)	0.220
		Placebo	123	117 (95.1)	-1.1 (0.1)	(-1.3, -0.9)			
>= 4 to < 7	Week 10	CR845	102	91 (89.2)	-1.2 (0.1)	(-1.4, -1.0)	-0.5 (0.1)	(-0.7, -0.2)	<0.001 *
		Placebo	113	102 (90.3)	-0.8 (0.1)	(-0.9, -0.6)			
>= 7	Week 10	CR845	135	113 (83.7)	-1.3 (0.1)	(-1.5, -1.1)	-0.3 (0.1)	(-0.5, -0.1)	0.008 *
		Placebo	123	115 (93.5)	-1.0 (0.1)	(-1.2, -0.8)			
>= 4 to < 7	Week 12	CR845	102	90 (88.2)	-1.1 (0.1)	(-1.3, -0.9)	-0.2 (0.1)	(-0.5, 0.0)	0.073
		Placebo	113	103 (91.2)	-0.9 (0.1)	(-1.1, -0.7)			
>= 7	Week 12	CR845	135	112 (83.0)	-1.3 (0.1)	(-1.5, -1.1)	-0.3 (0.1)	(-0.6, -0.1)	0.015 *
		Placebo	123	116 (94.3)	-1.0 (0.1)	(-1.2, -0.8)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DWC_ISCE: Change from baseline in 5-D direction score - MMRM results by specific medical condition
ITT

Change from baseline in 5-D direction score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
E: Presence of specific medical conditions									0.907
No	Week 4	CR845	195	175 (89.7)	-1.2 (0.1)	(-1.3, -1.0)	-0.4 (0.1)	(-0.6, -0.2)	<0.001 *
		Placebo	199	191 (96.0)	-0.8 (0.1)	(-0.9, -0.6)			
Yes	Week 4	CR845	42	38 (90.5)	-1.2 (0.1)	(-1.5, -0.9)	-0.5 (0.2)	(-0.8, -0.1)	0.018 *
		Placebo	37	34 (91.9)	-0.7 (0.1)	(-1.0, -0.5)			
No	Week 8	CR845	195	171 (87.7)	-1.1 (0.1)	(-1.2, -1.0)	-0.2 (0.1)	(-0.4, -0.0)	0.026 *
		Placebo	199	185 (93.0)	-0.9 (0.1)	(-1.0, -0.8)			
Yes	Week 8	CR845	42	36 (85.7)	-1.5 (0.1)	(-1.7, -1.2)	-0.4 (0.2)	(-0.8, -0.0)	0.041 *
		Placebo	37	37 (100.0)	-1.1 (0.1)	(-1.3, -0.8)			
No	Week 10	CR845	195	169 (86.7)	-1.2 (0.1)	(-1.4, -1.1)	-0.4 (0.1)	(-0.6, -0.2)	<0.001 *
		Placebo	199	180 (90.5)	-0.8 (0.1)	(-1.0, -0.7)			
Yes	Week 10	CR845	42	35 (83.3)	-1.3 (0.1)	(-1.5, -1.0)	-0.2 (0.2)	(-0.6, 0.2)	0.288
		Placebo	37	37 (100.0)	-1.1 (0.1)	(-1.3, -0.8)			
No	Week 12	CR845	195	168 (86.2)	-1.2 (0.1)	(-1.3, -1.0)	-0.3 (0.1)	(-0.5, -0.1)	0.004 *
		Placebo	199	183 (92.0)	-0.9 (0.1)	(-1.0, -0.7)			
Yes	Week 12	CR845	42	34 (81.0)	-1.3 (0.2)	(-1.6, -0.9)	-0.2 (0.2)	(-0.6, 0.3)	0.511
		Placebo	37	36 (97.3)	-1.1 (0.2)	(-1.4, -0.8)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor previous use of anti-itch medication is also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DWC_ISCF: Change from baseline in 5-D direction score - MMRM results by use of concomitant itch medication
ITT

Change from baseline in 5-D direction score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
F: Use of concomitant itch medication									0.218
No	Week 4	CR845	150	139 (92.7)	-1.2 (0.1)	(-1.4, -1.0)	-0.4 (0.1)	(-0.6, -0.2)	<0.001 *
		Placebo	151	146 (96.7)	-0.8 (0.1)	(-1.0, -0.7)			
Yes	Week 4	CR845	87	74 (85.1)	-1.2 (0.1)	(-1.4, -0.9)	-0.5 (0.1)	(-0.7, -0.2)	<0.001 *
		Placebo	85	79 (92.9)	-0.7 (0.1)	(-0.9, -0.5)			
No	Week 8	CR845	150	135 (90.0)	-1.2 (0.1)	(-1.3, -1.0)	-0.2 (0.1)	(-0.4, -0.0)	0.047 *
		Placebo	151	142 (94.0)	-1.0 (0.1)	(-1.1, -0.8)			
Yes	Week 8	CR845	87	72 (82.8)	-1.2 (0.1)	(-1.4, -1.0)	-0.3 (0.1)	(-0.6, -0.0)	0.041 *
		Placebo	85	80 (94.1)	-0.9 (0.1)	(-1.1, -0.7)			
No	Week 10	CR845	150	131 (87.3)	-1.2 (0.1)	(-1.3, -1.0)	-0.2 (0.1)	(-0.4, -0.0)	0.035 *
		Placebo	151	140 (92.7)	-0.9 (0.1)	(-1.1, -0.8)			
Yes	Week 10	CR845	87	73 (83.9)	-1.4 (0.1)	(-1.6, -1.2)	-0.6 (0.1)	(-0.9, -0.3)	<0.001 *
		Placebo	85	77 (90.6)	-0.8 (0.1)	(-1.0, -0.6)			
No	Week 12	CR845	150	132 (88.0)	-1.2 (0.1)	(-1.3, -1.0)	-0.2 (0.1)	(-0.5, 0.0)	0.064
		Placebo	151	141 (93.4)	-0.9 (0.1)	(-1.1, -0.8)			
Yes	Week 12	CR845	87	70 (80.5)	-1.3 (0.1)	(-1.5, -1.1)	-0.4 (0.2)	(-0.7, -0.1)	0.015 *
		Placebo	85	78 (91.8)	-0.9 (0.1)	(-1.2, -0.7)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor presence of medical condition is also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DWC_ISCG: Change from baseline in 5-D direction score - MMRM results by region
ITT

Change from baseline in 5-D direction score					Repeated measures analysis					
					Change from Baseline		Treatment Difference			
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value	
G: Region									0.553	
USA	Week 4	CR845	146	131 (89.7)	-1.1 (0.1)	(-1.3, -1.0)	-0.4 (0.1)	(-0.6, -0.2)	<0.001	*
		Placebo	133	123 (92.5)	-0.8 (0.1)	(-0.9, -0.6)				
Asia	Week 4	CR845	8	8 (100.0)	-1.3 (0.3)	(-1.9, -0.7)	-0.8 (0.4)	(-1.5, -0.0)	0.044	*
		Placebo	12	12 (100.0)	-0.5 (0.2)	(-1.0, -0.1)				
Eastern Europe	Week 4	CR845	54	52 (96.3)	-1.2 (0.2)	(-1.5, -0.8)	-0.4 (0.2)	(-0.8, -0.1)	0.017	*
		Placebo	60	59 (98.3)	-0.7 (0.1)	(-1.0, -0.4)				
Western Europe/European origin	Week 4	CR845	29	22 (75.9)	-1.4 (0.2)	(-1.9, -0.9)	-0.6 (0.3)	(-1.2, 0.0)	0.057	
		Placebo	31	31 (100.0)	-0.8 (0.2)	(-1.2, -0.4)				
USA	Week 8	CR845	146	129 (88.4)	-1.2 (0.1)	(-1.4, -1.1)	-0.2 (0.1)	(-0.4, 0.0)	0.096	
		Placebo	133	125 (94.0)	-1.1 (0.1)	(-1.2, -0.9)				
Asia	Week 8	CR845	8	7 (87.5)	-1.0 (0.2)	(-1.4, -0.5)	-0.0 (0.3)	(-0.7, 0.6)	0.885	
		Placebo	12	12 (100.0)	-0.9 (0.2)	(-1.3, -0.6)				
Eastern Europe	Week 8	CR845	54	48 (88.9)	-1.1 (0.2)	(-1.4, -0.8)	-0.4 (0.2)	(-0.7, -0.0)	0.040	*
		Placebo	60	59 (98.3)	-0.7 (0.1)	(-1.0, -0.4)				
Western Europe/European origin	Week 8	CR845	29	23 (79.3)	-1.2 (0.2)	(-1.6, -0.7)	-0.3 (0.3)	(-0.9, 0.3)	0.276	
		Placebo	31	26 (83.9)	-0.8 (0.2)	(-1.3, -0.4)				
USA	Week 10	CR845	146	127 (87.0)	-1.3 (0.1)	(-1.4, -1.1)	-0.2 (0.1)	(-0.4, -0.0)	0.022	*
		Placebo	133	122 (91.7)	-1.0 (0.1)	(-1.2, -0.9)				
Asia	Week 10	CR845	8	7 (87.5)	-1.4 (0.2)	(-1.9, -0.9)	-0.6 (0.3)	(-1.3, 0.1)	0.079	
		Placebo	12	11 (91.7)	-0.8 (0.2)	(-1.2, -0.4)				

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DWC_ISCG: Change from baseline in 5-D direction score - MMRM results by region
ITT

Change from baseline in 5-D direction score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Eastern Europe	Week 10	CR845	54	48 (88.9)	-1.1 (0.2)	(-1.4, -0.8)	-0.5 (0.2)	(-0.9, -0.1)	0.011 *
		Placebo	60	59 (98.3)	-0.6 (0.2)	(-0.9, -0.3)			
Western Europe/European origin	Week 10	CR845	29	22 (75.9)	-1.3 (0.2)	(-1.7, -0.8)	-0.7 (0.3)	(-1.3, -0.1)	0.021 *
		Placebo	31	25 (80.6)	-0.6 (0.2)	(-1.0, -0.1)			
USA	Week 12	CR845	146	126 (86.3)	-1.2 (0.1)	(-1.4, -1.1)	-0.2 (0.1)	(-0.5, 0.0)	0.050
		Placebo	133	125 (94.0)	-1.0 (0.1)	(-1.2, -0.8)			
Asia	Week 12	CR845	8	7 (87.5)	-1.4 (0.3)	(-2.1, -0.7)	-0.5 (0.4)	(-1.4, 0.4)	0.258
		Placebo	12	11 (91.7)	-0.9 (0.3)	(-1.5, -0.4)			
Eastern Europe	Week 12	CR845	54	47 (87.0)	-1.1 (0.2)	(-1.4, -0.7)	-0.3 (0.2)	(-0.7, 0.1)	0.129
		Placebo	60	58 (96.7)	-0.8 (0.2)	(-1.1, -0.5)			
Western Europe/European origin	Week 12	CR845	29	22 (75.9)	-1.1 (0.2)	(-1.6, -0.7)	-0.3 (0.3)	(-1.0, 0.3)	0.307
		Placebo	31	25 (80.6)	-0.8 (0.2)	(-1.3, -0.4)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DWC_ISCH: Change from baseline in 5-D direction score - MMRM results by dialysis method
ITT

Change from baseline in 5-D direction score					Repeated measures analysis					
					Change from Baseline		Treatment Difference			
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value	
H: Dialysis method									0.399	
Hemodialysis (HD)	Week 4	CR845	222	200 (90.1)	-1.2 (0.1)	(-1.3, -1.0)	-0.4 (0.1)	(-0.6, -0.3)	<0.001	*
		Placebo	199	188 (94.5)	-0.7 (0.1)	(-0.9, -0.6)				
Hemodiafiltration (HDF)	Week 4	CR845	15	13 (86.7)	-1.4 (0.4)	(-2.3, -0.5)	-0.4 (0.3)	(-1.0, 0.3)	0.282	
		Placebo	37	37 (100.0)	-1.0 (0.3)	(-1.6, -0.4)				
Hemodialysis (HD)	Week 8	CR845	222	194 (87.4)	-1.2 (0.1)	(-1.3, -1.1)	-0.3 (0.1)	(-0.4, -0.1)	0.002	*
		Placebo	199	187 (94.0)	-0.9 (0.1)	(-1.1, -0.8)				
Hemodiafiltration (HDF)	Week 8	CR845	15	13 (86.7)	-1.0 (0.4)	(-1.9, -0.1)	0.2 (0.3)	(-0.5, 0.9)	0.535	
		Placebo	37	35 (94.6)	-1.2 (0.3)	(-1.8, -0.6)				
Hemodialysis (HD)	Week 10	CR845	222	192 (86.5)	-1.2 (0.1)	(-1.4, -1.1)	-0.3 (0.1)	(-0.5, -0.2)	<0.001	*
		Placebo	199	185 (93.0)	-0.9 (0.1)	(-1.0, -0.8)				
Hemodiafiltration (HDF)	Week 10	CR845	15	12 (80.0)	-1.4 (0.5)	(-2.3, -0.5)	-0.6 (0.4)	(-1.3, 0.2)	0.135	
		Placebo	37	32 (86.5)	-0.8 (0.3)	(-1.5, -0.2)				
Hemodialysis (HD)	Week 12	CR845	222	189 (85.1)	-1.2 (0.1)	(-1.4, -1.1)	-0.3 (0.1)	(-0.5, -0.1)	0.006	*
		Placebo	199	185 (93.0)	-0.9 (0.1)	(-1.1, -0.8)				
Hemodiafiltration (HDF)	Week 12	CR845	15	13 (86.7)	-0.9 (0.4)	(-1.8, -0.0)	0.0 (0.4)	(-0.7, 0.8)	0.925	
		Placebo	37	34 (91.9)	-1.0 (0.3)	(-1.6, -0.3)				

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DNC_ISCA: Change from baseline in 5-D disability score - MMRM results by age
ITT

Change from baseline in 5-D disability score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
A: Age									0.496
< 65 years	Week 4	CR845	147	133 (90.5)	-0.7 (0.1)	(-0.9, -0.5)	-0.1 (0.1)	(-0.4, 0.2)	0.405
		Placebo	153	144 (94.1)	-0.6 (0.1)	(-0.8, -0.4)			
>= 65 years	Week 4	CR845	90	80 (88.9)	-0.5 (0.1)	(-0.8, -0.3)	-0.1 (0.2)	(-0.4, 0.2)	0.542
		Placebo	83	81 (97.6)	-0.4 (0.1)	(-0.7, -0.2)			
< 65 years	Week 8	CR845	147	130 (88.4)	-1.0 (0.1)	(-1.2, -0.7)	-0.0 (0.1)	(-0.3, 0.3)	0.942
		Placebo	153	143 (93.5)	-0.9 (0.1)	(-1.2, -0.7)			
>= 65 years	Week 8	CR845	90	78 (86.7)	-0.9 (0.1)	(-1.1, -0.6)	-0.4 (0.2)	(-0.8, -0.1)	0.019 *
		Placebo	83	79 (95.2)	-0.4 (0.1)	(-0.7, -0.2)			
< 65 years	Week 10	CR845	147	130 (88.4)	-1.1 (0.1)	(-1.3, -0.8)	-0.1 (0.1)	(-0.4, 0.2)	0.556
		Placebo	153	141 (92.2)	-1.0 (0.1)	(-1.2, -0.8)			
>= 65 years	Week 10	CR845	90	74 (82.2)	-1.0 (0.1)	(-1.3, -0.7)	-0.5 (0.2)	(-0.8, -0.1)	0.008 *
		Placebo	83	76 (91.6)	-0.5 (0.1)	(-0.8, -0.2)			
< 65 years	Week 12	CR845	147	129 (87.8)	-1.2 (0.1)	(-1.4, -0.9)	-0.2 (0.1)	(-0.5, 0.1)	0.198
		Placebo	153	142 (92.8)	-1.0 (0.1)	(-1.2, -0.8)			
>= 65 years	Week 12	CR845	90	74 (82.2)	-0.9 (0.1)	(-1.1, -0.6)	0.0 (0.2)	(-0.4, 0.4)	0.999
		Placebo	83	77 (92.8)	-0.9 (0.1)	(-1.1, -0.6)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DNC_ISCB: Change from baseline in 5-D disability score - MMRM results by sex
ITT

Change from baseline in 5-D disability score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
B: Sex									0.006 i
Male	Week 4	CR845	137	124 (90.5)	-0.5 (0.1)	(-0.7, -0.3)	0.1 (0.1)	(-0.2, 0.3)	0.466
		Placebo	139	131 (94.2)	-0.6 (0.1)	(-0.8, -0.4)			
Female	Week 4	CR845	100	89 (89.0)	-0.8 (0.1)	(-1.1, -0.6)	-0.4 (0.2)	(-0.7, -0.0)	0.025 *
		Placebo	97	94 (96.9)	-0.5 (0.1)	(-0.7, -0.2)			
Male	Week 8	CR845	137	122 (89.1)	-0.7 (0.1)	(-0.9, -0.5)	0.1 (0.1)	(-0.2, 0.4)	0.515
		Placebo	139	132 (95.0)	-0.8 (0.1)	(-1.0, -0.6)			
Female	Week 8	CR845	100	86 (86.0)	-1.2 (0.1)	(-1.5, -0.9)	-0.5 (0.2)	(-0.9, -0.2)	0.004 *
		Placebo	97	90 (92.8)	-0.7 (0.1)	(-0.9, -0.4)			
Male	Week 10	CR845	137	117 (85.4)	-0.9 (0.1)	(-1.1, -0.6)	-0.0 (0.1)	(-0.3, 0.2)	0.764
		Placebo	139	127 (91.4)	-0.8 (0.1)	(-1.0, -0.6)			
Female	Week 10	CR845	100	87 (87.0)	-1.3 (0.1)	(-1.5, -1.0)	-0.5 (0.2)	(-0.8, -0.1)	0.006 *
		Placebo	97	90 (92.8)	-0.8 (0.1)	(-1.0, -0.5)			
Male	Week 12	CR845	137	117 (85.4)	-0.9 (0.1)	(-1.1, -0.7)	0.0 (0.1)	(-0.3, 0.3)	0.824
		Placebo	139	127 (91.4)	-0.9 (0.1)	(-1.2, -0.7)			
Female	Week 12	CR845	100	86 (86.0)	-1.2 (0.1)	(-1.5, -1.0)	-0.3 (0.2)	(-0.7, 0.0)	0.077
		Placebo	97	92 (94.8)	-0.9 (0.1)	(-1.2, -0.6)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DNC_ISCC: Change from baseline in 5-D disability score - MMRM results by race
ITT

Change from baseline in 5-D disability score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
C: Race									0.178
Black/African American	Week 4	CR845	53	45 (84.9)	-0.5 (0.2)	(-0.9, -0.2)	0.3 (0.2)	(-0.2, 0.8)	0.218
		Placebo	38	35 (92.1)	-0.8 (0.2)	(-1.2, -0.5)			
White	Week 4	CR845	164	151 (92.1)	-0.7 (0.1)	(-0.9, -0.5)	-0.2 (0.1)	(-0.5, 0.0)	0.060
		Placebo	169	162 (95.9)	-0.5 (0.1)	(-0.7, -0.3)			
Other	Week 4	CR845	20	17 (85.0)	-0.7 (0.3)	(-1.3, -0.2)	-0.0 (0.3)	(-0.6, 0.5)	0.891
		Placebo	29	28 (96.6)	-0.7 (0.2)	(-1.2, -0.2)			
Black/African American	Week 8	CR845	53	45 (84.9)	-0.8 (0.2)	(-1.2, -0.5)	0.1 (0.3)	(-0.5, 0.6)	0.758
		Placebo	38	37 (97.4)	-0.9 (0.2)	(-1.3, -0.5)			
White	Week 8	CR845	164	146 (89.0)	-1.0 (0.1)	(-1.2, -0.7)	-0.2 (0.1)	(-0.5, 0.0)	0.085
		Placebo	169	159 (94.1)	-0.7 (0.1)	(-0.9, -0.5)			
Other	Week 8	CR845	20	17 (85.0)	-1.0 (0.3)	(-1.6, -0.4)	-0.2 (0.3)	(-0.9, 0.4)	0.516
		Placebo	29	26 (89.7)	-0.8 (0.3)	(-1.3, -0.2)			
Black/African American	Week 10	CR845	53	42 (79.2)	-1.0 (0.2)	(-1.4, -0.6)	0.1 (0.3)	(-0.5, 0.6)	0.849
		Placebo	38	36 (94.7)	-1.1 (0.2)	(-1.5, -0.6)			
White	Week 10	CR845	164	146 (89.0)	-1.0 (0.1)	(-1.2, -0.8)	-0.3 (0.1)	(-0.6, -0.1)	0.013 *
		Placebo	169	156 (92.3)	-0.7 (0.1)	(-0.9, -0.5)			
Other	Week 10	CR845	20	16 (80.0)	-1.3 (0.3)	(-1.9, -0.6)	-0.3 (0.3)	(-1.0, 0.4)	0.389
		Placebo	29	25 (86.2)	-1.0 (0.3)	(-1.5, -0.4)			
Black/African American	Week 12	CR845	53	43 (81.1)	-0.9 (0.2)	(-1.3, -0.5)	0.2 (0.3)	(-0.4, 0.8)	0.501
		Placebo	38	37 (97.4)	-1.1 (0.2)	(-1.6, -0.7)			
White	Week 12	CR845	164	144 (87.8)	-1.1 (0.1)	(-1.3, -0.9)	-0.2 (0.1)	(-0.4, 0.1)	0.140
		Placebo	169	159 (94.1)	-0.9 (0.1)	(-1.1, -0.7)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DNC_ISCC: Change from baseline in 5-D disability score - MMRM results by race
ITT

Change from baseline in 5-D disability score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Other	Week 12	CR845	20	16 (80.0)	-1.2 (0.4)	(-1.9, -0.5)	-0.3 (0.4)	(-1.1, 0.6)	0.523
		Placebo	29	23 (79.3)	-0.9 (0.3)	(-1.6, -0.3)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DNC_ISCD: Change from baseline in 5-D disability score - MMRM results by baseline WI-NRS
ITT

Change from baseline in 5-D disability score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
D: Baseline worst itching NRS score (WI-NRS)									0.555
>= 4 to < 7	Week 4	CR845	102	95 (93.1)	-0.6 (0.1)	(-0.9, -0.4)	-0.1 (0.1)	(-0.4, 0.2)	0.469
		Placebo	113	109 (96.5)	-0.5 (0.1)	(-0.7, -0.3)			
>= 7	Week 4	CR845	135	118 (87.4)	-0.7 (0.1)	(-1.0, -0.5)	-0.1 (0.1)	(-0.4, 0.1)	0.307
		Placebo	123	116 (94.3)	-0.6 (0.1)	(-0.8, -0.4)			
>= 4 to < 7	Week 8	CR845	102	94 (92.2)	-0.9 (0.1)	(-1.2, -0.6)	-0.3 (0.2)	(-0.6, 0.0)	0.061
		Placebo	113	105 (92.9)	-0.6 (0.1)	(-0.8, -0.3)			
>= 7	Week 8	CR845	135	114 (84.4)	-1.0 (0.1)	(-1.2, -0.8)	-0.1 (0.1)	(-0.4, 0.2)	0.666
		Placebo	123	117 (95.1)	-0.9 (0.1)	(-1.1, -0.7)			
>= 4 to < 7	Week 10	CR845	102	91 (89.2)	-1.0 (0.1)	(-1.3, -0.8)	-0.4 (0.2)	(-0.6, -0.1)	0.021 *
		Placebo	113	102 (90.3)	-0.7 (0.1)	(-0.9, -0.4)			
>= 7	Week 10	CR845	135	113 (83.7)	-1.1 (0.1)	(-1.3, -0.9)	-0.2 (0.2)	(-0.5, 0.2)	0.318
		Placebo	123	115 (93.5)	-0.9 (0.1)	(-1.2, -0.7)			
>= 4 to < 7	Week 12	CR845	102	90 (88.2)	-1.0 (0.1)	(-1.3, -0.8)	-0.2 (0.2)	(-0.5, 0.1)	0.179
		Placebo	113	103 (91.2)	-0.8 (0.1)	(-1.1, -0.6)			
>= 7	Week 12	CR845	135	113 (83.7)	-1.1 (0.1)	(-1.4, -0.9)	-0.1 (0.2)	(-0.4, 0.3)	0.709
		Placebo	123	116 (94.3)	-1.1 (0.1)	(-1.3, -0.8)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DNC_ISCE: Change from baseline in 5-D disability score - MMRM results by specific medical condition
ITT

Change from baseline in 5-D disability score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
E: Presence of specific medical conditions									0.983
No	Week 4	CR845	195	175 (89.7)	-0.6 (0.1)	(-0.8, -0.4)	-0.1 (0.1)	(-0.3, 0.1)	0.312
		Placebo	199	191 (96.0)	-0.5 (0.1)	(-0.7, -0.3)			
Yes	Week 4	CR845	42	38 (90.5)	-0.8 (0.2)	(-1.1, -0.5)	-0.1 (0.2)	(-0.6, 0.4)	0.793
		Placebo	37	34 (91.9)	-0.7 (0.2)	(-1.1, -0.4)			
No	Week 8	CR845	195	172 (88.2)	-0.9 (0.1)	(-1.0, -0.7)	-0.1 (0.1)	(-0.3, 0.1)	0.330
		Placebo	199	185 (93.0)	-0.8 (0.1)	(-0.9, -0.6)			
Yes	Week 8	CR845	42	36 (85.7)	-1.1 (0.2)	(-1.5, -0.7)	-0.4 (0.3)	(-1.0, 0.2)	0.166
		Placebo	37	37 (100.0)	-0.7 (0.2)	(-1.1, -0.3)			
No	Week 10	CR845	195	169 (86.7)	-1.0 (0.1)	(-1.2, -0.8)	-0.3 (0.1)	(-0.5, -0.0)	0.033 *
		Placebo	199	180 (90.5)	-0.8 (0.1)	(-0.9, -0.6)			
Yes	Week 10	CR845	42	35 (83.3)	-1.1 (0.2)	(-1.5, -0.7)	-0.2 (0.3)	(-0.7, 0.4)	0.617
		Placebo	37	37 (100.0)	-1.0 (0.2)	(-1.4, -0.6)			
No	Week 12	CR845	195	168 (86.2)	-1.0 (0.1)	(-1.2, -0.8)	-0.1 (0.1)	(-0.4, 0.1)	0.291
		Placebo	199	183 (92.0)	-0.9 (0.1)	(-1.0, -0.7)			
Yes	Week 12	CR845	42	35 (83.3)	-1.3 (0.2)	(-1.7, -0.9)	-0.0 (0.3)	(-0.6, 0.5)	0.875
		Placebo	37	36 (97.3)	-1.2 (0.2)	(-1.6, -0.8)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor previous use of anti-itch medication is also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DNC_ISCF: Change from baseline in 5-D disability score - MMRM results by use of concomitant itch medication
ITT

Change from baseline in 5-D disability score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
F: Use of concomitant itch medication									0.974
No	Week 4	CR845	150	139 (92.7)	-0.6 (0.1)	(-0.8, -0.4)	-0.2 (0.1)	(-0.4, 0.1)	0.132
		Placebo	151	146 (96.7)	-0.4 (0.1)	(-0.6, -0.2)			
Yes	Week 4	CR845	87	74 (85.1)	-0.7 (0.1)	(-1.0, -0.4)	0.0 (0.2)	(-0.3, 0.4)	0.817
		Placebo	85	79 (92.9)	-0.8 (0.1)	(-1.0, -0.5)			
No	Week 8	CR845	150	136 (90.7)	-0.8 (0.1)	(-1.0, -0.6)	-0.1 (0.1)	(-0.4, 0.1)	0.356
		Placebo	151	142 (94.0)	-0.7 (0.1)	(-0.9, -0.5)			
Yes	Week 8	CR845	87	72 (82.8)	-1.0 (0.2)	(-1.3, -0.7)	-0.2 (0.2)	(-0.6, 0.2)	0.233
		Placebo	85	80 (94.1)	-0.8 (0.1)	(-1.1, -0.5)			
No	Week 10	CR845	150	131 (87.3)	-0.9 (0.1)	(-1.2, -0.7)	-0.2 (0.1)	(-0.4, 0.1)	0.171
		Placebo	151	140 (92.7)	-0.8 (0.1)	(-1.0, -0.6)			
Yes	Week 10	CR845	87	73 (83.9)	-1.2 (0.1)	(-1.5, -0.9)	-0.3 (0.2)	(-0.7, 0.1)	0.097
		Placebo	85	77 (90.6)	-0.9 (0.1)	(-1.2, -0.6)			
No	Week 12	CR845	150	132 (88.0)	-1.0 (0.1)	(-1.2, -0.8)	-0.1 (0.1)	(-0.3, 0.2)	0.592
		Placebo	151	141 (93.4)	-0.9 (0.1)	(-1.1, -0.7)			
Yes	Week 12	CR845	87	71 (81.6)	-1.2 (0.1)	(-1.5, -0.9)	-0.2 (0.2)	(-0.6, 0.2)	0.293
		Placebo	85	78 (91.8)	-1.0 (0.1)	(-1.3, -0.7)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor presence of medical condition is also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DNC_ISCG: Change from baseline in 5-D disability score - MMRM results by region
ITT

Change from baseline in 5-D disability score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
G: Region									0.501
USA	Week 4	CR845	146	131 (89.7)	-0.6 (0.1)	(-0.8, -0.4)	-0.1 (0.1)	(-0.4, 0.1)	0.256
		Placebo	133	123 (92.5)	-0.5 (0.1)	(-0.7, -0.2)			
Asia	Week 4	CR845	8	8 (100.0)	-0.9 (0.3)	(-1.6, -0.2)	-0.2 (0.4)	(-1.1, 0.7)	0.634
		Placebo	12	12 (100.0)	-0.7 (0.3)	(-1.2, -0.1)			
Eastern Europe	Week 4	CR845	54	52 (96.3)	-0.6 (0.2)	(-1.0, -0.2)	0.1 (0.2)	(-0.3, 0.5)	0.683
		Placebo	60	59 (98.3)	-0.7 (0.2)	(-1.1, -0.4)			
Western Europe/European origin	Week 4	CR845	29	22 (75.9)	-1.1 (0.3)	(-1.7, -0.5)	-0.4 (0.4)	(-1.1, 0.4)	0.339
		Placebo	31	31 (100.0)	-0.8 (0.3)	(-1.3, -0.2)			
USA	Week 8	CR845	146	129 (88.4)	-0.8 (0.1)	(-1.0, -0.6)	0.0 (0.1)	(-0.3, 0.3)	0.937
		Placebo	133	125 (94.0)	-0.8 (0.1)	(-1.0, -0.6)			
Asia	Week 8	CR845	8	7 (87.5)	-1.2 (0.4)	(-2.1, -0.4)	-0.5 (0.5)	(-1.6, 0.6)	0.338
		Placebo	12	12 (100.0)	-0.7 (0.3)	(-1.4, -0.1)			
Eastern Europe	Week 8	CR845	54	49 (90.7)	-1.0 (0.2)	(-1.4, -0.6)	-0.3 (0.2)	(-0.7, 0.1)	0.172
		Placebo	60	59 (98.3)	-0.7 (0.2)	(-1.1, -0.4)			
Western Europe/European origin	Week 8	CR845	29	23 (79.3)	-1.4 (0.3)	(-1.9, -0.9)	-0.6 (0.3)	(-1.3, 0.0)	0.062
		Placebo	31	26 (83.9)	-0.7 (0.2)	(-1.2, -0.2)			
USA	Week 10	CR845	146	127 (87.0)	-0.9 (0.1)	(-1.1, -0.7)	0.0 (0.1)	(-0.3, 0.3)	0.923
		Placebo	133	122 (91.7)	-0.9 (0.1)	(-1.1, -0.7)			
Asia	Week 10	CR845	8	7 (87.5)	-1.4 (0.4)	(-2.2, -0.6)	-0.5 (0.5)	(-1.6, 0.6)	0.329
		Placebo	12	11 (91.7)	-0.9 (0.3)	(-1.5, -0.2)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DNC_ISCG: Change from baseline in 5-D disability score - MMRM results by region
ITT

Change from baseline in 5-D disability score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Eastern Europe	Week 10	CR845	54	48 (88.9)	-1.2 (0.2)	(-1.6, -0.9)	-0.5 (0.2)	(-0.9, -0.1)	0.015 *
		Placebo	60	59 (98.3)	-0.7 (0.2)	(-1.1, -0.4)			
Western Europe/European origin	Week 10	CR845	29	22 (75.9)	-1.4 (0.3)	(-2.0, -0.8)	-0.8 (0.4)	(-1.6, -0.0)	0.041 *
		Placebo	31	25 (80.6)	-0.6 (0.3)	(-1.2, -0.0)			
USA	Week 12	CR845	146	127 (87.0)	-1.0 (0.1)	(-1.3, -0.8)	-0.1 (0.1)	(-0.4, 0.2)	0.570
		Placebo	133	125 (94.0)	-1.0 (0.1)	(-1.2, -0.7)			
Asia	Week 12	CR845	8	7 (87.5)	-0.8 (0.5)	(-1.8, 0.2)	0.4 (0.6)	(-0.9, 1.7)	0.534
		Placebo	12	11 (91.7)	-1.2 (0.4)	(-2.0, -0.4)			
Eastern Europe	Week 12	CR845	54	47 (87.0)	-1.2 (0.2)	(-1.5, -0.8)	-0.3 (0.2)	(-0.7, 0.1)	0.203
		Placebo	60	58 (96.7)	-0.9 (0.2)	(-1.2, -0.5)			
Western Europe/European origin	Week 12	CR845	29	22 (75.9)	-1.1 (0.3)	(-1.8, -0.5)	-0.1 (0.4)	(-1.0, 0.7)	0.727
		Placebo	31	25 (80.6)	-1.0 (0.3)	(-1.6, -0.4)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DNC_ISCH: Change from baseline in 5-D disability score - MMRM results by dialysis method
ITT

Change from baseline in 5-D disability score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
H: Dialysis method									0.385
Hemodialysis (HD)	Week 4	CR845	222	200 (90.1)	-0.6 (0.1)	(-0.8, -0.5)	-0.1 (0.1)	(-0.3, 0.1)	0.267
		Placebo	199	188 (94.5)	-0.5 (0.1)	(-0.7, -0.3)			
Hemodiafiltration (HDF)	Week 4	CR845	15	13 (86.7)	-1.1 (0.5)	(-2.2, -0.0)	-0.3 (0.4)	(-1.1, 0.5)	0.473
		Placebo	37	37 (100.0)	-0.8 (0.4)	(-1.6, -0.1)			
Hemodialysis (HD)	Week 8	CR845	222	195 (87.8)	-0.9 (0.1)	(-1.1, -0.7)	-0.2 (0.1)	(-0.4, 0.1)	0.187
		Placebo	199	187 (94.0)	-0.7 (0.1)	(-0.9, -0.6)			
Hemodiafiltration (HDF)	Week 8	CR845	15	13 (86.7)	-1.4 (0.5)	(-2.4, -0.3)	-0.4 (0.4)	(-1.2, 0.4)	0.274
		Placebo	37	35 (94.6)	-0.9 (0.4)	(-1.7, -0.2)			
Hemodialysis (HD)	Week 10	CR845	222	192 (86.5)	-1.0 (0.1)	(-1.2, -0.8)	-0.2 (0.1)	(-0.4, 0.0)	0.069
		Placebo	199	185 (93.0)	-0.8 (0.1)	(-1.0, -0.6)			
Hemodiafiltration (HDF)	Week 10	CR845	15	12 (80.0)	-1.4 (0.5)	(-2.5, -0.3)	-0.5 (0.4)	(-1.4, 0.3)	0.215
		Placebo	37	32 (86.5)	-0.9 (0.4)	(-1.7, -0.1)			
Hemodialysis (HD)	Week 12	CR845	222	190 (85.6)	-1.0 (0.1)	(-1.2, -0.9)	-0.1 (0.1)	(-0.3, 0.1)	0.410
		Placebo	199	185 (93.0)	-0.9 (0.1)	(-1.1, -0.8)			
Hemodiafiltration (HDF)	Week 12	CR845	15	13 (86.7)	-1.3 (0.5)	(-2.4, -0.2)	-0.3 (0.4)	(-1.1, 0.5)	0.465
		Placebo	37	34 (91.9)	-1.0 (0.4)	(-1.7, -0.2)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DVC_ISCA: Change from baseline in 5-D distribution score - MMRM results by age
ITT

Change from baseline in 5-D distribution score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
A: Age									0.574
< 65 years	Week 4	CR845	147	133 (90.5)	-0.5 (0.1)	(-0.7, -0.4)	-0.2 (0.1)	(-0.4, 0.0)	0.060
		Placebo	153	144 (94.1)	-0.3 (0.1)	(-0.5, -0.2)			
>= 65 years	Week 4	CR845	90	80 (88.9)	-0.4 (0.1)	(-0.7, -0.2)	-0.2 (0.2)	(-0.5, 0.1)	0.162
		Placebo	83	81 (97.6)	-0.2 (0.1)	(-0.5, 0.0)			
< 65 years	Week 8	CR845	147	130 (88.4)	-0.7 (0.1)	(-0.9, -0.4)	-0.2 (0.1)	(-0.4, 0.1)	0.155
		Placebo	153	143 (93.5)	-0.5 (0.1)	(-0.7, -0.3)			
>= 65 years	Week 8	CR845	90	78 (86.7)	-0.4 (0.1)	(-0.7, -0.2)	-0.1 (0.2)	(-0.4, 0.2)	0.439
		Placebo	83	79 (95.2)	-0.3 (0.1)	(-0.6, -0.1)			
< 65 years	Week 10	CR845	147	130 (88.4)	-0.7 (0.1)	(-0.9, -0.5)	-0.3 (0.1)	(-0.6, -0.1)	0.009 *
		Placebo	153	141 (92.2)	-0.3 (0.1)	(-0.5, -0.2)			
>= 65 years	Week 10	CR845	90	74 (82.2)	-0.4 (0.1)	(-0.6, -0.1)	0.0 (0.2)	(-0.3, 0.4)	0.855
		Placebo	83	76 (91.6)	-0.4 (0.1)	(-0.7, -0.2)			
< 65 years	Week 12	CR845	147	129 (87.8)	-0.7 (0.1)	(-0.9, -0.5)	-0.3 (0.1)	(-0.6, -0.1)	0.007 *
		Placebo	153	142 (92.8)	-0.4 (0.1)	(-0.6, -0.2)			
>= 65 years	Week 12	CR845	90	74 (82.2)	-0.4 (0.1)	(-0.7, -0.2)	-0.2 (0.2)	(-0.5, 0.2)	0.322
		Placebo	83	77 (92.8)	-0.3 (0.1)	(-0.5, -0.0)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DVC_ISCB: Change from baseline in 5-D distribution score - MMRM results by sex
ITT

Change from baseline in 5-D distribution score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
B: Sex									0.009 i
Male	Week 4	CR845	137	124 (90.5)	-0.3 (0.1)	(-0.5, -0.1)	0.0 (0.1)	(-0.2, 0.2)	0.977
		Placebo	139	131 (94.2)	-0.3 (0.1)	(-0.5, -0.1)			
Female	Week 4	CR845	100	89 (89.0)	-0.7 (0.1)	(-1.0, -0.5)	-0.5 (0.1)	(-0.8, -0.3)	<0.001 *
		Placebo	97	94 (96.9)	-0.2 (0.1)	(-0.4, -0.0)			
Male	Week 8	CR845	137	122 (89.1)	-0.4 (0.1)	(-0.6, -0.2)	-0.0 (0.1)	(-0.3, 0.2)	0.683
		Placebo	139	132 (95.0)	-0.4 (0.1)	(-0.6, -0.2)			
Female	Week 8	CR845	100	86 (86.0)	-0.7 (0.1)	(-1.0, -0.5)	-0.3 (0.2)	(-0.7, 0.0)	0.060
		Placebo	97	90 (92.8)	-0.4 (0.1)	(-0.7, -0.1)			
Male	Week 10	CR845	137	117 (85.4)	-0.4 (0.1)	(-0.6, -0.2)	-0.1 (0.1)	(-0.3, 0.2)	0.513
		Placebo	139	127 (91.4)	-0.3 (0.1)	(-0.5, -0.1)			
Female	Week 10	CR845	100	87 (87.0)	-0.8 (0.1)	(-1.0, -0.5)	-0.4 (0.2)	(-0.7, -0.1)	0.023 *
		Placebo	97	90 (92.8)	-0.4 (0.1)	(-0.6, -0.2)			
Male	Week 12	CR845	137	117 (85.4)	-0.4 (0.1)	(-0.6, -0.2)	-0.2 (0.1)	(-0.4, 0.1)	0.193
		Placebo	139	127 (91.4)	-0.3 (0.1)	(-0.5, -0.1)			
Female	Week 12	CR845	100	86 (86.0)	-0.9 (0.1)	(-1.1, -0.6)	-0.4 (0.2)	(-0.8, -0.1)	0.008 *
		Placebo	97	92 (94.8)	-0.4 (0.1)	(-0.7, -0.2)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DVC_ISCC: Change from baseline in 5-D distribution score - MMRM results by race
ITT

Change from baseline in 5-D distribution score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
C: Race									0.259
Black/African American	Week 4	CR845	53	45 (84.9)	-0.5 (0.1)	(-0.8, -0.2)	-0.1 (0.2)	(-0.4, 0.3)	0.783
		Placebo	38	35 (92.1)	-0.5 (0.2)	(-0.8, -0.2)			
White	Week 4	CR845	164	151 (92.1)	-0.6 (0.1)	(-0.7, -0.4)	-0.3 (0.1)	(-0.5, -0.1)	0.003 *
		Placebo	169	162 (95.9)	-0.2 (0.1)	(-0.4, -0.1)			
Other	Week 4	CR845	20	17 (85.0)	-0.4 (0.3)	(-1.0, 0.3)	-0.0 (0.3)	(-0.7, 0.6)	0.923
		Placebo	29	28 (96.6)	-0.3 (0.3)	(-0.9, 0.2)			
Black/African American	Week 8	CR845	53	45 (84.9)	-0.5 (0.2)	(-0.8, -0.2)	-0.1 (0.2)	(-0.6, 0.4)	0.606
		Placebo	38	37 (97.4)	-0.4 (0.2)	(-0.7, -0.0)			
White	Week 8	CR845	164	146 (89.0)	-0.6 (0.1)	(-0.8, -0.4)	-0.3 (0.1)	(-0.5, -0.0)	0.037 *
		Placebo	169	159 (94.1)	-0.4 (0.1)	(-0.6, -0.2)			
Other	Week 8	CR845	20	17 (85.0)	-0.5 (0.3)	(-1.0, 0.0)	0.0 (0.3)	(-0.5, 0.6)	0.884
		Placebo	29	26 (89.7)	-0.5 (0.2)	(-1.0, -0.1)			
Black/African American	Week 10	CR845	53	42 (79.2)	-0.4 (0.2)	(-0.7, -0.0)	-0.0 (0.2)	(-0.5, 0.4)	0.925
		Placebo	38	36 (94.7)	-0.3 (0.2)	(-0.7, 0.0)			
White	Week 10	CR845	164	146 (89.0)	-0.7 (0.1)	(-0.8, -0.5)	-0.3 (0.1)	(-0.5, -0.1)	0.011 *
		Placebo	169	156 (92.3)	-0.4 (0.1)	(-0.5, -0.2)			
Other	Week 10	CR845	20	16 (80.0)	-0.5 (0.3)	(-1.1, 0.1)	-0.2 (0.3)	(-0.8, 0.4)	0.598
		Placebo	29	25 (86.2)	-0.3 (0.3)	(-0.8, 0.2)			
Black/African American	Week 12	CR845	53	43 (81.1)	-0.5 (0.2)	(-0.8, -0.1)	-0.2 (0.2)	(-0.6, 0.2)	0.360
		Placebo	38	37 (97.4)	-0.3 (0.2)	(-0.6, 0.1)			
White	Week 12	CR845	164	144 (87.8)	-0.7 (0.1)	(-0.9, -0.5)	-0.4 (0.1)	(-0.7, -0.2)	<0.001 *
		Placebo	169	159 (94.1)	-0.3 (0.1)	(-0.5, -0.1)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DVC_ISCC: Change from baseline in 5-D distribution score - MMRM results by race
ITT

Change from baseline in 5-D distribution score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Other	Week 12	CR845	20	16 (80.0)	-0.2 (0.3)	(-0.8, 0.4)	0.4 (0.3)	(-0.2, 1.0)	0.204
		Placebo	29	23 (79.3)	-0.6 (0.3)	(-1.1, -0.1)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DVC_ISCD: Change from baseline in 5-D distribution score - MMRM results by baseline WI-NRS
ITT

Change from baseline in 5-D distribution score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
D: Baseline worst itching NRS score (WI-NRS)									0.567
>= 4 to < 7	Week 4	CR845	102	95 (93.1)	-0.5 (0.1)	(-0.7, -0.3)	-0.3 (0.1)	(-0.6, -0.1)	0.012 *
		Placebo	113	109 (96.5)	-0.2 (0.1)	(-0.4, 0.0)			
>= 7	Week 4	CR845	135	118 (87.4)	-0.5 (0.1)	(-0.7, -0.3)	-0.1 (0.1)	(-0.4, 0.1)	0.277
		Placebo	123	116 (94.3)	-0.4 (0.1)	(-0.6, -0.2)			
>= 4 to < 7	Week 8	CR845	102	94 (92.2)	-0.5 (0.1)	(-0.7, -0.2)	-0.2 (0.1)	(-0.4, 0.1)	0.185
		Placebo	113	105 (92.9)	-0.3 (0.1)	(-0.5, -0.1)			
>= 7	Week 8	CR845	135	114 (84.4)	-0.7 (0.1)	(-0.9, -0.5)	-0.2 (0.1)	(-0.4, 0.1)	0.288
		Placebo	123	117 (95.1)	-0.5 (0.1)	(-0.7, -0.3)			
>= 4 to < 7	Week 10	CR845	102	91 (89.2)	-0.5 (0.1)	(-0.7, -0.2)	-0.2 (0.1)	(-0.5, 0.1)	0.155
		Placebo	113	102 (90.3)	-0.3 (0.1)	(-0.5, -0.1)			
>= 7	Week 10	CR845	135	113 (83.7)	-0.7 (0.1)	(-0.9, -0.4)	-0.2 (0.1)	(-0.5, 0.1)	0.140
		Placebo	123	115 (93.5)	-0.4 (0.1)	(-0.7, -0.2)			
>= 4 to < 7	Week 12	CR845	102	90 (88.2)	-0.6 (0.1)	(-0.8, -0.4)	-0.3 (0.1)	(-0.5, 0.0)	0.062
		Placebo	113	103 (91.2)	-0.4 (0.1)	(-0.6, -0.1)			
>= 7	Week 12	CR845	135	113 (83.7)	-0.6 (0.1)	(-0.9, -0.4)	-0.3 (0.1)	(-0.6, -0.0)	0.032 *
		Placebo	123	116 (94.3)	-0.3 (0.1)	(-0.6, -0.1)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DVC_ISCE: Change from baseline in 5-D distribution score - MMRM results by specific medical condition
ITT

Change from baseline in 5-D distribution score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
E: Presence of specific medical conditions									0.617
No	Week 4	CR845	195	175 (89.7)	-0.5 (0.1)	(-0.6, -0.3)	-0.2 (0.1)	(-0.4, -0.0)	0.036 *
		Placebo	199	191 (96.0)	-0.3 (0.1)	(-0.4, -0.1)			
Yes	Week 4	CR845	42	38 (90.5)	-0.6 (0.2)	(-0.9, -0.3)	-0.3 (0.2)	(-0.8, 0.1)	0.161
		Placebo	37	34 (91.9)	-0.3 (0.2)	(-0.6, 0.0)			
No	Week 8	CR845	195	172 (88.2)	-0.5 (0.1)	(-0.7, -0.4)	-0.2 (0.1)	(-0.4, 0.1)	0.173
		Placebo	199	185 (93.0)	-0.4 (0.1)	(-0.5, -0.2)			
Yes	Week 8	CR845	42	36 (85.7)	-0.6 (0.2)	(-1.0, -0.3)	-0.3 (0.2)	(-0.7, 0.2)	0.254
		Placebo	37	37 (100.0)	-0.4 (0.2)	(-0.7, -0.1)			
No	Week 10	CR845	195	169 (86.7)	-0.5 (0.1)	(-0.7, -0.4)	-0.2 (0.1)	(-0.4, 0.0)	0.102
		Placebo	199	180 (90.5)	-0.3 (0.1)	(-0.5, -0.2)			
Yes	Week 10	CR845	42	35 (83.3)	-0.7 (0.2)	(-1.0, -0.4)	-0.3 (0.2)	(-0.8, 0.1)	0.172
		Placebo	37	37 (100.0)	-0.4 (0.2)	(-0.7, -0.0)			
No	Week 12	CR845	195	168 (86.2)	-0.6 (0.1)	(-0.7, -0.4)	-0.3 (0.1)	(-0.5, -0.0)	0.024 *
		Placebo	199	183 (92.0)	-0.3 (0.1)	(-0.5, -0.2)			
Yes	Week 12	CR845	42	35 (83.3)	-0.8 (0.2)	(-1.1, -0.4)	-0.4 (0.2)	(-0.9, 0.0)	0.055
		Placebo	37	36 (97.3)	-0.3 (0.2)	(-0.6, -0.0)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor previous use of anti-itch medication is also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DVC_ISCF: Change from baseline in 5-D distribution score - MMRM results by use of concomitant itch medication
ITT

Change from baseline in 5-D distribution score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
F: Use of concomitant itch medication									0.933
No	Week 4	CR845	150	139 (92.7)	-0.4 (0.1)	(-0.6, -0.3)	-0.3 (0.1)	(-0.5, -0.0)	0.017 *
		Placebo	151	146 (96.7)	-0.2 (0.1)	(-0.4, -0.0)			
Yes	Week 4	CR845	87	74 (85.1)	-0.6 (0.1)	(-0.8, -0.3)	-0.2 (0.2)	(-0.5, 0.2)	0.350
		Placebo	85	79 (92.9)	-0.4 (0.1)	(-0.7, -0.2)			
No	Week 8	CR845	150	136 (90.7)	-0.4 (0.1)	(-0.6, -0.3)	-0.2 (0.1)	(-0.4, 0.1)	0.155
		Placebo	151	142 (94.0)	-0.3 (0.1)	(-0.5, -0.1)			
Yes	Week 8	CR845	87	72 (82.8)	-0.7 (0.1)	(-1.0, -0.5)	-0.1 (0.2)	(-0.5, 0.2)	0.404
		Placebo	85	80 (94.1)	-0.6 (0.1)	(-0.8, -0.3)			
No	Week 10	CR845	150	131 (87.3)	-0.4 (0.1)	(-0.6, -0.2)	-0.2 (0.1)	(-0.4, 0.1)	0.140
		Placebo	151	140 (92.7)	-0.2 (0.1)	(-0.4, -0.1)			
Yes	Week 10	CR845	87	73 (83.9)	-0.8 (0.1)	(-1.0, -0.5)	-0.2 (0.2)	(-0.6, 0.1)	0.152
		Placebo	85	77 (90.6)	-0.5 (0.1)	(-0.8, -0.3)			
No	Week 12	CR845	150	132 (88.0)	-0.5 (0.1)	(-0.7, -0.3)	-0.2 (0.1)	(-0.5, -0.0)	0.047 *
		Placebo	151	141 (93.4)	-0.2 (0.1)	(-0.4, -0.1)			
Yes	Week 12	CR845	87	71 (81.6)	-0.8 (0.1)	(-1.1, -0.5)	-0.4 (0.2)	(-0.7, -0.0)	0.043 *
		Placebo	85	78 (91.8)	-0.5 (0.1)	(-0.7, -0.2)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor presence of medical condition is also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DVC_ISCG: Change from baseline in 5-D distribution score - MMRM results by region
ITT

Change from baseline in 5-D distribution score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
G: Region									0.346
USA	Week 4	CR845	146	131 (89.7)	-0.4 (0.1)	(-0.6, -0.3)	-0.1 (0.1)	(-0.4, 0.1)	0.275
		Placebo	133	123 (92.5)	-0.3 (0.1)	(-0.5, -0.1)			
Asia	Week 4	CR845	8	8 (100.0)	-0.6 (0.4)	(-1.5, 0.3)	0.0 (0.6)	(-1.2, 1.3)	0.940
		Placebo	12	12 (100.0)	-0.6 (0.4)	(-1.4, 0.1)			
Eastern Europe	Week 4	CR845	54	52 (96.3)	-0.8 (0.2)	(-1.1, -0.5)	-0.5 (0.2)	(-0.9, -0.2)	0.004 *
		Placebo	60	59 (98.3)	-0.3 (0.2)	(-0.6, 0.0)			
Western Europe/European origin	Week 4	CR845	29	22 (75.9)	-0.6 (0.2)	(-1.0, -0.3)	-0.4 (0.3)	(-0.9, 0.1)	0.087
		Placebo	31	31 (100.0)	-0.2 (0.2)	(-0.6, 0.1)			
USA	Week 8	CR845	146	129 (88.4)	-0.5 (0.1)	(-0.7, -0.3)	-0.1 (0.1)	(-0.4, 0.2)	0.457
		Placebo	133	125 (94.0)	-0.4 (0.1)	(-0.6, -0.2)			
Asia	Week 8	CR845	8	7 (87.5)	-0.5 (0.4)	(-1.2, 0.3)	0.2 (0.5)	(-0.9, 1.2)	0.743
		Placebo	12	12 (100.0)	-0.6 (0.3)	(-1.3, -0.0)			
Eastern Europe	Week 8	CR845	54	49 (90.7)	-0.9 (0.2)	(-1.2, -0.5)	-0.4 (0.2)	(-0.8, 0.0)	0.071
		Placebo	60	59 (98.3)	-0.5 (0.2)	(-0.8, -0.1)			
Western Europe/European origin	Week 8	CR845	29	23 (79.3)	-0.7 (0.2)	(-1.1, -0.3)	-0.4 (0.3)	(-1.0, 0.1)	0.107
		Placebo	31	26 (83.9)	-0.3 (0.2)	(-0.6, 0.1)			
USA	Week 10	CR845	146	127 (87.0)	-0.5 (0.1)	(-0.7, -0.3)	-0.1 (0.1)	(-0.4, 0.1)	0.292
		Placebo	133	122 (91.7)	-0.3 (0.1)	(-0.5, -0.1)			
Asia	Week 10	CR845	8	7 (87.5)	-0.5 (0.4)	(-1.2, 0.3)	0.1 (0.5)	(-1.0, 1.1)	0.910
		Placebo	12	11 (91.7)	-0.5 (0.3)	(-1.2, 0.1)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DVC_ISCG: Change from baseline in 5-D distribution score - MMRM results by region
ITT

Change from baseline in 5-D distribution score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Eastern Europe	Week 10	CR845	54	48 (88.9)	-0.9 (0.2)	(-1.3, -0.5)	-0.5 (0.2)	(-0.9, -0.1)	0.020 *
		Placebo	60	59 (98.3)	-0.4 (0.2)	(-0.8, -0.1)			
Western Europe/European origin	Week 10	CR845	29	22 (75.9)	-0.8 (0.2)	(-1.2, -0.4)	-0.3 (0.3)	(-0.9, 0.3)	0.292
		Placebo	31	25 (80.6)	-0.5 (0.2)	(-0.9, -0.1)			
USA	Week 12	CR845	146	127 (87.0)	-0.6 (0.1)	(-0.8, -0.4)	-0.2 (0.1)	(-0.5, 0.0)	0.090
		Placebo	133	125 (94.0)	-0.3 (0.1)	(-0.5, -0.1)			
Asia	Week 12	CR845	8	7 (87.5)	-0.2 (0.4)	(-1.0, 0.6)	0.4 (0.5)	(-0.7, 1.4)	0.486
		Placebo	12	11 (91.7)	-0.6 (0.3)	(-1.2, 0.0)			
Eastern Europe	Week 12	CR845	54	47 (87.0)	-1.0 (0.2)	(-1.4, -0.6)	-0.6 (0.2)	(-1.0, -0.2)	0.002 *
		Placebo	60	58 (96.7)	-0.4 (0.2)	(-0.7, -0.1)			
Western Europe/European origin	Week 12	CR845	29	22 (75.9)	-0.7 (0.2)	(-1.1, -0.3)	-0.3 (0.3)	(-0.9, 0.2)	0.263
		Placebo	31	25 (80.6)	-0.4 (0.2)	(-0.8, -0.0)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DVC_ISCH: Change from baseline in 5-D distribution score - MMRM results by dialysis method
ITT

Change from baseline in 5-D distribution score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
H: Dialysis method									0.604
Hemodialysis (HD)	Week 4	CR845	222	200 (90.1)	-0.5 (0.1)	(-0.7, -0.4)	-0.2 (0.1)	(-0.4, -0.0)	0.037 *
		Placebo	199	188 (94.5)	-0.3 (0.1)	(-0.5, -0.2)			
Hemodiafiltration (HDF)	Week 4	CR845	15	13 (86.7)	-0.1 (0.4)	(-0.8, 0.7)	0.0 (0.3)	(-0.5, 0.6)	0.858
		Placebo	37	37 (100.0)	-0.1 (0.3)	(-0.6, 0.4)			
Hemodialysis (HD)	Week 8	CR845	222	195 (87.8)	-0.6 (0.1)	(-0.7, -0.4)	-0.1 (0.1)	(-0.4, 0.1)	0.186
		Placebo	199	187 (94.0)	-0.4 (0.1)	(-0.6, -0.3)			
Hemodiafiltration (HDF)	Week 8	CR845	15	13 (86.7)	-0.4 (0.4)	(-1.2, 0.4)	-0.1 (0.3)	(-0.8, 0.5)	0.661
		Placebo	37	35 (94.6)	-0.3 (0.3)	(-0.9, 0.3)			
Hemodialysis (HD)	Week 10	CR845	222	192 (86.5)	-0.6 (0.1)	(-0.7, -0.4)	-0.2 (0.1)	(-0.4, 0.0)	0.100
		Placebo	199	185 (93.0)	-0.4 (0.1)	(-0.6, -0.2)			
Hemodiafiltration (HDF)	Week 10	CR845	15	12 (80.0)	-0.4 (0.4)	(-1.2, 0.4)	-0.2 (0.3)	(-0.9, 0.5)	0.556
		Placebo	37	32 (86.5)	-0.2 (0.3)	(-0.8, 0.4)			
Hemodialysis (HD)	Week 12	CR845	222	190 (85.6)	-0.6 (0.1)	(-0.8, -0.5)	-0.3 (0.1)	(-0.5, -0.1)	0.009 *
		Placebo	199	185 (93.0)	-0.4 (0.1)	(-0.5, -0.2)			
Hemodiafiltration (HDF)	Week 12	CR845	15	13 (86.7)	-0.3 (0.4)	(-1.1, 0.5)	0.0 (0.3)	(-0.6, 0.6)	0.965
		Placebo	37	34 (91.9)	-0.3 (0.3)	(-0.9, 0.3)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived, created on: 17FEB2022

Table BT2DTCD5_ISPA: Decrease of 5-D total score of at least 5 points by age
ITT

Decrease of 5-D total score of at least 5 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	A: Age										0.593
	< 65 years	147	128 (87.1)	67 (45.6) [37.4, 54.0]	153	142 (92.8)	59 (38.6) [30.8, 46.8]	1.182 [0.905, 1.543]	1.334 [0.843, 2.113]	7.0 [-4.8, 18.8]	0.219
	>= 65 years	90	73 (81.1)	35 (38.9) [28.8, 49.7]	83	77 (92.8)	31 (37.3) [27.0, 48.7]	1.041 [0.712, 1.523]	1.067 [0.577, 1.973]	1.5 [-14.1, 17.2]	0.836

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DTCD5_ISPB: Decrease of 5-D total score of at least 5 points by sex
ITT

Decrease of 5-D total score of at least 5 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	B: Sex										0.636
	Male	137	117 (85.4)	54 (39.4) [31.2, 48.1]	139	127 (91.4)	51 (36.7) [28.7, 45.3]	1.074 [0.795, 1.452]	1.123 [0.690, 1.826]	2.7 [-9.5, 14.9]	0.642
	Female	100	84 (84.0)	48 (48.0) [37.9, 58.2]	97	92 (94.8)	39 (40.2) [30.4, 50.7]	1.194 [0.869, 1.639]	1.373 [0.781, 2.414]	7.8 [-7.0, 22.6]	0.272

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DTCD5_ISPC: Decrease of 5-D total score of at least 5 points by race
ITT

Decrease of 5-D total score of at least 5 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	C: Race										0.274
	Black/African American	53	42 (79.2)	22 (41.5) [28.1, 55.9]	38	37 (97.4)	16 (42.1) [26.3, 59.2]	0.986 [0.603, 1.611]	0.976 [0.419, 2.271]	-0.6 [-23.4, 22.2]	0.955
	White	164	143 (87.2)	74 (45.1) [37.4, 53.1]	169	159 (94.1)	61 (36.1) [28.9, 43.8]	1.250 [0.962, 1.625]	1.456 [0.938, 2.259]	9.0 [-2.1, 20.1]	0.094
	Other	20	16 (80.0)	6 (30.0) [11.9, 54.3]	29	23 (79.3)	13 (44.8) [26.4, 64.3]	0.669 [0.306, 1.463]	0.527 [0.158, 1.759]	-14.8 [-46.1, 16.4]	0.300

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DTCD5_ISPD: Decrease of 5-D total score of at least 5 points by baseline WI-NRS
ITT

Decrease of 5-D total score of at least 5 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.149
	>= 4 to < 7	102	89 (87.3)	43 (42.2) [32.4, 52.3]	113	103 (91.2)	35 (31.0) [22.6, 40.4]	1.361 [0.952, 1.945]	1.624 [0.928, 2.843]	11.2 [-2.6, 24.9]	0.089
	>= 7	135	112 (83.0)	59 (43.7) [35.2, 52.5]	123	116 (94.3)	55 (44.7) [35.7, 53.9]	0.977 [0.743, 1.286]	0.960 [0.587, 1.570]	-1.0 [-13.9, 11.9]	0.870

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DTCD5_ISPE: Decrease of 5-D total score of at least 5 points by specific medical condition
ITT

Decrease of 5-D total score of at least 5 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	E: Presence of specific medical conditions										0.064
	No	195	167 (85.6)	85 (43.6) [36.5, 50.9]	199	183 (92.0)	70 (35.2) [28.6, 42.2]	1.239 [0.968, 1.587]	1.424 [0.949, 2.137]	8.4 [-1.7, 18.5]	0.088
	Yes	42	34 (81.0)	17 (40.5) [25.6, 56.7]	37	36 (97.3)	20 (54.1) [36.9, 70.5]	0.749 [0.467, 1.200]	0.578 [0.237, 1.412]	-13.6 [-38.0, 10.8]	0.230

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DTCD5_ISPF: Decrease of 5-D total score of at least 5 points by use of concomitant itch medication
ITT

Decrease of 5-D total score of at least 5 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	F: Use of concomitant itch medication										0.880
	No	150	131 (87.3)	67 (44.7) [36.6, 53.0]	151	141 (93.4)	59 (39.1) [31.2, 47.3]	1.143 [0.875, 1.493]	1.259 [0.796, 1.991]	5.6 [-6.2, 17.4]	0.326
	Yes	87	70 (80.5)	35 (40.2) [29.9, 51.3]	85	78 (91.8)	31 (36.5) [26.3, 47.6]	1.103 [0.754, 1.613]	1.172 [0.634, 2.169]	3.8 [-11.9, 19.4]	0.613

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DTCD5_ISPG: Decrease of 5-D total score of at least 5 points by region
ITT

Decrease of 5-D total score of at least 5 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	G: Region										0.290	
	USA	146	125 (85.6)	65 (44.5) [36.3, 53.0]	133	125 (94.0)	50 (37.6) [29.3, 46.4]	1.184 [0.891, 1.573]	1.332 [0.825, 2.151]	6.9 [-5.3, 19.2]	0.241	
	Asia	8	7 (87.5)	3 (37.5) [8.5, 75.5]	12	11 (91.7)	8 (66.7) [34.9, 90.1]	0.563 [0.211, 1.499]	0.300 [0.046, 1.943]	-29.2 [-82.4, 24.1]	0.362	#
	Eastern Europe	54	47 (87.0)	25 (46.3) [32.6, 60.4]	60	58 (96.7)	20 (33.3) [21.7, 46.7]	1.389 [0.878, 2.198]	1.724 [0.808, 3.679]	13.0 [-6.7, 32.6]	0.159	
	Western Europe/European origin	29	22 (75.9)	9 (31.0) [15.3, 50.8]	31	25 (80.6)	12 (38.7) [21.8, 57.8]	0.802 [0.398, 1.615]	0.713 [0.245, 2.074]	-7.7 [-35.0, 19.7]	0.537	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DTCD5_ISPH: Decrease of 5-D total score of at least 5 points by dialysis method
ITT

Decrease of 5-D total score of at least 5 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	H: Dialysis method										0.970
	Hemodialysis (HD)	222	188 (84.7)	95 (42.8) [36.2, 49.6]	199	185 (93.0)	75 (37.7) [30.9, 44.8]	1.135 [0.898, 1.436]	1.237 [0.837, 1.828]	5.1 [-4.7, 14.9]	0.287
	Hemodiafiltration (HDF)	15	13 (86.7)	7 (46.7) [21.3, 73.4]	37	34 (91.9)	15 (40.5) [24.8, 57.9]	1.151 [0.591, 2.243]	1.283 [0.383, 4.296]	6.1 [-28.4, 40.6]	0.688

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DDCD1_ISPA: Decrease of 5-D degree score of at least 1 point by age
ITT

Decrease of 5-D degree score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	A: Age										0.820
	< 65 years	147	129 (87.8)	90 (61.2) [52.8, 69.1]	153	142 (92.8)	92 (60.1) [51.9, 67.9]	1.018 [0.849, 1.222]	1.047 [0.659, 1.664]	1.1 [-10.6, 12.8]	0.847
	>= 65 years	90	74 (82.2)	46 (51.1) [40.3, 61.8]	83	77 (92.8)	40 (48.2) [37.1, 59.4]	1.061 [0.785, 1.433]	1.124 [0.619, 2.041]	2.9 [-13.1, 19.0]	0.702

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DDCD1_ISPB: Decrease of 5-D degree score of at least 1 point by sex
ITT

Decrease of 5-D degree score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	B: Sex										0.208
	Male	137	117 (85.4)	70 (51.1) [42.4, 59.7]	139	127 (91.4)	76 (54.7) [46.0, 63.1]	0.934 [0.748, 1.168]	0.866 [0.540, 1.390]	-3.6 [-16.1, 8.9]	0.552
	Female	100	86 (86.0)	66 (66.0) [55.8, 75.2]	97	92 (94.8)	56 (57.7) [47.3, 67.7]	1.143 [0.917, 1.426]	1.421 [0.798, 2.532]	8.3 [-6.3, 22.8]	0.233

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DDCD1_ISPC: Decrease of 5-D degree score of at least 1 point by race
ITT

Decrease of 5-D degree score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	C: Race										0.749
	Black/African American	53	43 (81.1)	33 (62.3) [47.9, 75.2]	38	37 (97.4)	24 (63.2) [46.0, 78.2]	0.986 [0.715, 1.359]	0.963 [0.407, 2.279]	-0.9 [-23.3, 21.5]	0.931
	White	164	144 (87.8)	93 (56.7) [48.8, 64.4]	169	159 (94.1)	91 (53.8) [46.0, 61.5]	1.053 [0.868, 1.278]	1.123 [0.729, 1.730]	2.9 [-8.4, 14.1]	0.600
	Other	20	16 (80.0)	10 (50.0) [27.2, 72.8]	29	23 (79.3)	17 (58.6) [38.9, 76.5]	0.853 [0.500, 1.455]	0.706 [0.224, 2.221]	-8.6 [-41.2, 23.9]	0.555

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DDCD1_ISPD: Decrease of 5-D degree score of at least 1 point by baseline WI-NRS
ITT

Decrease of 5-D degree score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.047	i
	>= 4 to < 7	102	90 (88.2)	60 (58.8) [48.6, 68.5]	113	103 (91.2)	54 (47.8) [38.3, 57.4]	1.231 [0.957, 1.584]	1.561 [0.909, 2.679]	11.0 [-3.2, 25.2]	0.106	
	>= 7	135	113 (83.7)	76 (56.3) [47.5, 64.8]	123	116 (94.3)	78 (63.4) [54.3, 71.9]	0.888 [0.727, 1.085]	0.743 [0.451, 1.226]	-7.1 [-19.8, 5.6]	0.245	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DDCD1_ISPE: Decrease of 5-D degree score of at least 1 point by specific medical condition
ITT

Decrease of 5-D degree score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	E: Presence of specific medical conditions										0.253
	No	195	168 (86.2)	113 (57.9) [50.7, 65.0]	199	183 (92.0)	108 (54.3) [47.1, 61.3]	1.068 [0.897, 1.272]	1.161 [0.780, 1.729]	3.7 [-6.6, 14.0]	0.463
	Yes	42	35 (83.3)	23 (54.8) [38.7, 70.2]	37	36 (97.3)	24 (64.9) [47.5, 79.8]	0.844 [0.587, 1.214]	0.656 [0.264, 1.626]	-10.1 [-34.2, 14.0]	0.364

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DDCD1_ISPF: Decrease of 5-D degree score of at least 1 point by use of concomitant itch medication
ITT

Decrease of 5-D degree score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	F: Use of concomitant itch medication										0.946
	No	150	132 (88.0)	87 (58.0) [49.7, 66.0]	151	141 (93.4)	85 (56.3) [48.0, 64.3]	1.030 [0.847, 1.253]	1.072 [0.679, 1.693]	1.7 [-10.1, 13.6]	0.765
	Yes	87	71 (81.6)	49 (56.3) [45.3, 66.9]	85	78 (91.8)	47 (55.3) [44.1, 66.1]	1.019 [0.781, 1.329]	1.043 [0.571, 1.903]	1.0 [-15.0, 17.0]	0.892

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DDCD1_ISPG: Decrease of 5-D degree score of at least 1 point by region
ITT

Decrease of 5-D degree score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	G: Region										0.537	
	USA	146	127 (87.0)	90 (61.6) [53.2, 69.6]	133	125 (94.0)	76 (57.1) [48.3, 65.7]	1.079 [0.888, 1.311]	1.205 [0.747, 1.946]	4.5 [-7.7, 16.7]	0.445	
	Asia	8	7 (87.5)	6 (75.0) [34.9, 96.8]	12	11 (91.7)	8 (66.7) [34.9, 90.1]	1.125 [0.639, 1.981]	1.500 [0.203, 11.088]	8.3 [-42.2, 58.9]	1.000	#
	Eastern Europe	54	47 (87.0)	27 (50.0) [36.1, 63.9]	60	58 (96.7)	29 (48.3) [35.2, 61.6]	1.034 [0.712, 1.503]	1.069 [0.512, 2.230]	1.7 [-18.5, 21.8]	0.860	
	Western Europe/European origin	29	22 (75.9)	13 (44.8) [26.4, 64.3]	31	25 (80.6)	19 (61.3) [42.2, 78.2]	0.731 [0.448, 1.195]	0.513 [0.183, 1.435]	-16.5 [-44.7, 11.8]	0.205	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DDCD1_ISPH: Decrease of 5-D degree score of at least 1 point by dialysis method
ITT

Decrease of 5-D degree score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	H: Dialysis method										0.603
	Hemodialysis (HD)	222	190 (85.6)	128 (57.7) [50.9, 64.2]	199	185 (93.0)	110 (55.3) [48.1, 62.3]	1.043 [0.882, 1.234]	1.102 [0.749, 1.621]	2.4 [-7.6, 12.3]	0.623
	Hemodiafiltration (HDF)	15	13 (86.7)	8 (53.3) [26.6, 78.7]	37	34 (91.9)	22 (59.5) [42.1, 75.2]	0.897 [0.521, 1.544]	0.779 [0.233, 2.608]	-6.1 [-40.6, 28.4]	0.688

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DLCD1_ISPA: Decrease of 5-D duration score of at least 1 point by age
ITT

Decrease of 5-D duration score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	A: Age										0.986
	< 65 years	147	128 (87.1)	74 (50.3) [42.0, 58.7]	153	142 (92.8)	69 (45.1) [37.1, 53.3]	1.116 [0.880, 1.415]	1.234 [0.784, 1.943]	5.2 [-6.7, 17.2]	0.364
	>= 65 years	90	74 (82.2)	41 (45.6) [35.0, 56.4]	83	77 (92.8)	34 (41.0) [30.3, 52.3]	1.112 [0.789, 1.567]	1.206 [0.660, 2.204]	4.6 [-11.3, 20.5]	0.544

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DLCD1_ISPB: Decrease of 5-D duration score of at least 1 point by sex
ITT

Decrease of 5-D duration score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	B: Sex										0.304
	Male	137	117 (85.4)	61 (44.5) [36.0, 53.3]	139	127 (91.4)	61 (43.9) [35.5, 52.5]	1.015 [0.778, 1.323]	1.026 [0.638, 1.651]	0.6 [-11.8, 13.1]	0.915
	Female	100	85 (85.0)	54 (54.0) [43.7, 64.0]	97	92 (94.8)	42 (43.3) [33.3, 53.7]	1.247 [0.932, 1.668]	1.537 [0.876, 2.697]	10.7 [-4.2, 25.6]	0.134

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DLCD1_ISPC: Decrease of 5-D duration score of at least 1 point by race
ITT

Decrease of 5-D duration score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	C: Race										0.602
	Black/African American	53	43 (81.1)	28 (52.8) [38.6, 66.7]	38	37 (97.4)	17 (44.7) [28.6, 61.7]	1.181 [0.764, 1.825]	1.384 [0.599, 3.194]	8.1 [-14.9, 31.1]	0.449
	White	164	143 (87.2)	80 (48.8) [40.9, 56.7]	169	159 (94.1)	73 (43.2) [35.6, 51.0]	1.129 [0.894, 1.426]	1.252 [0.813, 1.929]	5.6 [-5.7, 16.9]	0.307
	Other	20	16 (80.0)	7 (35.0) [15.4, 59.2]	29	23 (79.3)	13 (44.8) [26.4, 64.3]	0.781 [0.380, 1.606]	0.663 [0.205, 2.145]	-9.8 [-41.7, 22.0]	0.496

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DLCD1_ISPD: Decrease of 5-D duration score of at least 1 point by baseline WI-NRS
ITT

Decrease of 5-D duration score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.419
	>= 4 to < 7	102	89 (87.3)	45 (44.1) [34.3, 54.3]	113	103 (91.2)	41 (36.3) [27.4, 45.9]	1.216 [0.876, 1.687]	1.386 [0.802, 2.397]	7.8 [-6.2, 21.9]	0.243
	>= 7	135	113 (83.7)	70 (51.9) [43.1, 60.5]	123	116 (94.3)	62 (50.4) [41.2, 59.5]	1.029 [0.810, 1.306]	1.060 [0.650, 1.727]	1.4 [-11.5, 14.4]	0.817

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DLCD1_ISPE: Decrease of 5-D duration score of at least 1 point by specific medical condition
ITT

Decrease of 5-D duration score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	E: Presence of specific medical conditions										0.277
	No	195	167 (85.6)	96 (49.2) [42.0, 56.5]	199	183 (92.0)	84 (42.2) [35.3, 49.4]	1.166 [0.940, 1.448]	1.328 [0.892, 1.975]	7.0 [-3.3, 17.3]	0.162
	Yes	42	35 (83.3)	19 (45.2) [29.8, 61.3]	37	36 (97.3)	19 (51.4) [34.4, 68.1]	0.881 [0.558, 1.392]	0.783 [0.323, 1.898]	-6.1 [-30.7, 18.5]	0.590

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DLCD1_ISPF: Decrease of 5-D duration score of at least 1 point by use of concomitant itch medication
ITT

Decrease of 5-D duration score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	F: Use of concomitant itch medication										0.323
	No	150	131 (87.3)	75 (50.0) [41.7, 58.3]	151	141 (93.4)	63 (41.7) [33.8, 50.0]	1.198 [0.936, 1.535]	1.397 [0.886, 2.202]	8.3 [-3.6, 20.2]	0.150
	Yes	87	71 (81.6)	40 (46.0) [35.2, 57.0]	85	78 (91.8)	40 (47.1) [36.1, 58.2]	0.977 [0.709, 1.346]	0.957 [0.526, 1.743]	-1.1 [-17.2, 15.0]	0.887

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DLCD1_ISPG: Decrease of 5-D duration score of at least 1 point by region
ITT

Decrease of 5-D duration score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	G: Region										0.693	
	USA	146	126 (86.3)	75 (51.4) [43.0, 59.7]	133	125 (94.0)	62 (46.6) [37.9, 55.5]	1.102 [0.866, 1.402]	1.210 [0.756, 1.936]	4.8 [-7.7, 17.2]	0.428	
	Asia	8	7 (87.5)	3 (37.5) [8.5, 75.5]	12	11 (91.7)	7 (58.3) [27.7, 84.8]	0.643 [0.233, 1.773]	0.429 [0.068, 2.684]	-20.8 [-74.9, 33.2]	0.650	#
	Eastern Europe	54	47 (87.0)	27 (50.0) [36.1, 63.9]	60	58 (96.7)	24 (40.0) [27.6, 53.5]	1.250 [0.831, 1.881]	1.500 [0.714, 3.152]	10.0 [-10.0, 30.0]	0.286	
	Western Europe/European origin	29	22 (75.9)	10 (34.5) [17.9, 54.3]	31	25 (80.6)	10 (32.3) [16.7, 51.4]	1.069 [0.523, 2.186]	1.105 [0.378, 3.235]	2.2 [-25.0, 29.4]	0.856	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DLCD1_ISPH: Decrease of 5-D duration score of at least 1 point by dialysis method
ITT

Decrease of 5-D duration score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	H: Dialysis method										0.734
	Hemodialysis (HD)	222	189 (85.1)	109 (49.1) [42.3, 55.9]	199	185 (93.0)	91 (45.7) [38.7, 52.9]	1.074 [0.877, 1.314]	1.145 [0.780, 1.680]	3.4 [-6.7, 13.4]	0.490
	Hemodiafiltration (HDF)	15	13 (86.7)	6 (40.0) [16.3, 67.7]	37	34 (91.9)	12 (32.4) [18.0, 49.8]	1.233 [0.568, 2.677]	1.389 [0.401, 4.806]	7.6 [-26.1, 41.3]	0.607

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DNCD1_ISPA: Decrease of 5-D disability score of at least 1 point by age
ITT

Decrease of 5-D disability score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	A: Age										0.901
	< 65 years	147	129 (87.8)	88 (59.9) [51.5, 67.9]	153	142 (92.8)	91 (59.5) [51.3, 67.3]	1.007 [0.836, 1.212]	1.016 [0.641, 1.612]	0.4 [-11.4, 12.2]	0.946
	>= 65 years	90	74 (82.2)	47 (52.2) [41.4, 62.9]	83	77 (92.8)	44 (53.0) [41.7, 64.1]	0.985 [0.742, 1.307]	0.969 [0.533, 1.761]	-0.8 [-16.8, 15.3]	0.917

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DNCD1_ISPB: Decrease of 5-D disability score of at least 1 point by sex
ITT

Decrease of 5-D disability score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	B: Sex										0.398
	Male	137	117 (85.4)	79 (57.7) [48.9, 66.1]	139	127 (91.4)	76 (54.7) [46.0, 63.1]	1.055 [0.856, 1.299]	1.129 [0.702, 1.817]	3.0 [-9.4, 15.4]	0.618
	Female	100	86 (86.0)	56 (56.0) [45.7, 65.9]	97	92 (94.8)	59 (60.8) [50.4, 70.6]	0.921 [0.727, 1.166]	0.820 [0.465, 1.446]	-4.8 [-19.6, 9.9]	0.493

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DNCD1_ISPC: Decrease of 5-D disability score of at least 1 point by race
ITT

Decrease of 5-D disability score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	C: Race										0.112
	Black/African American	53	43 (81.1)	25 (47.2) [33.3, 61.4]	38	37 (97.4)	24 (63.2) [46.0, 78.2]	0.747 [0.514, 1.086]	0.521 [0.222, 1.221]	-16.0 [-38.6, 6.7]	0.133
	White	164	144 (87.8)	97 (59.1) [51.2, 66.7]	169	159 (94.1)	98 (58.0) [50.2, 65.5]	1.020 [0.851, 1.222]	1.049 [0.678, 1.622]	1.2 [-10.0, 12.3]	0.830
	Other	20	16 (80.0)	13 (65.0) [40.8, 84.6]	29	23 (79.3)	13 (44.8) [26.4, 64.3]	1.450 [0.865, 2.430]	2.286 [0.706, 7.399]	20.2 [-11.7, 52.0]	0.169

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DNCD1_ISPD: Decrease of 5-D disability score of at least 1 point by baseline WI-NRS
ITT

Decrease of 5-D disability score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.052
	>= 4 to < 7	102	90 (88.2)	59 (57.8) [47.7, 67.6]	113	103 (91.2)	55 (48.7) [39.2, 58.3]	1.188 [0.924, 1.528]	1.447 [0.844, 2.480]	9.2 [-5.1, 23.4]	0.180
	>= 7	135	113 (83.7)	76 (56.3) [47.5, 64.8]	123	116 (94.3)	80 (65.0) [55.9, 73.4]	0.866 [0.711, 1.054]	0.692 [0.419, 1.145]	-8.7 [-21.4, 3.9]	0.152

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DNCD1_ISPE: Decrease of 5-D disability score of at least 1 point by specific medical condition
ITT

Decrease of 5-D disability score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	E: Presence of specific medical conditions										0.217
	No	195	168 (86.2)	112 (57.4) [50.2, 64.5]	199	183 (92.0)	110 (55.3) [48.1, 62.3]	1.039 [0.873, 1.236]	1.092 [0.733, 1.626]	2.2 [-8.1, 12.5]	0.666
	Yes	42	35 (83.3)	23 (54.8) [38.7, 70.2]	37	36 (97.3)	25 (67.6) [50.2, 82.0]	0.810 [0.569, 1.155]	0.581 [0.232, 1.455]	-12.8 [-36.7, 11.0]	0.248

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DNCD1_ISPF: Decrease of 5-D disability score of at least 1 point by use of concomitant itch medication
ITT

Decrease of 5-D disability score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	F: Use of concomitant itch medication										0.329
	No	150	132 (88.0)	83 (55.3) [47.0, 63.4]	151	141 (93.4)	89 (58.9) [50.7, 66.9]	0.939 [0.772, 1.142]	0.863 [0.546, 1.363]	-3.6 [-15.4, 8.2]	0.528
	Yes	87	71 (81.6)	52 (59.8) [48.7, 70.1]	85	78 (91.8)	46 (54.1) [43.0, 65.0]	1.104 [0.851, 1.434]	1.260 [0.688, 2.306]	5.7 [-10.3, 21.6]	0.455

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DNCD1_ISPG: Decrease of 5-D disability score of at least 1 point by region
ITT

Decrease of 5-D disability score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	G: Region										0.870	
	USA	146	127 (87.0)	85 (58.2) [49.8, 66.3]	133	125 (94.0)	74 (55.6) [46.8, 64.2]	1.046 [0.853, 1.284]	1.111 [0.691, 1.786]	2.6 [-9.8, 14.9]	0.664	
	Asia	8	7 (87.5)	5 (62.5) [24.5, 91.5]	12	11 (91.7)	7 (58.3) [27.7, 84.8]	1.071 [0.522, 2.199]	1.190 [0.190, 7.456]	4.2 [-49.9, 58.2]	1.000	#
	Eastern Europe	54	47 (87.0)	30 (55.6) [41.4, 69.1]	60	58 (96.7)	37 (61.7) [48.2, 73.9]	0.901 [0.660, 1.230]	0.777 [0.368, 1.641]	-6.1 [-26.0, 13.7]	0.510	
	Western Europe/European origin	29	22 (75.9)	15 (51.7) [32.5, 70.6]	31	25 (80.6)	17 (54.8) [36.0, 72.7]	0.943 [0.587, 1.517]	0.882 [0.320, 2.435]	-3.1 [-31.7, 25.5]	0.811	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DNCD1_ISPH: Decrease of 5-D disability score of at least 1 point by dialysis method
ITT

Decrease of 5-D disability score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	H: Dialysis method										0.867
	Hemodialysis (HD)	222	190 (85.6)	126 (56.8) [50.0, 63.4]	199	185 (93.0)	112 (56.3) [49.1, 63.3]	1.008 [0.853, 1.193]	1.020 [0.693, 1.500]	0.5 [-9.5, 10.4]	0.922
	Hemodiafiltration (HDF)	15	13 (86.7)	9 (60.0) [32.3, 83.7]	37	34 (91.9)	23 (62.2) [44.8, 77.5]	0.965 [0.595, 1.566]	0.913 [0.267, 3.118]	-2.2 [-36.2, 31.8]	0.886

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DVCD1_ISPA: Decrease of 5-D distribution score of at least 1 point by age
ITT

Decrease of 5-D distribution score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	A: Age										0.831
	< 65 years	147	129 (87.8)	62 (42.2) [34.1, 50.6]	153	142 (92.8)	55 (35.9) [28.4, 44.1]	1.173 [0.883, 1.558]	1.300 [0.816, 2.069]	6.2 [-5.5, 17.9]	0.270
	>= 65 years	90	74 (82.2)	35 (38.9) [28.8, 49.7]	83	77 (92.8)	29 (34.9) [24.8, 46.2]	1.113 [0.752, 1.646]	1.185 [0.638, 2.201]	3.9 [-11.6, 19.5]	0.592

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DVCD1_ISPB: Decrease of 5-D distribution score of at least 1 point by sex
ITT

Decrease of 5-D distribution score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	B: Sex										0.995
	Male	137	117 (85.4)	52 (38.0) [29.8, 46.6]	139	127 (91.4)	46 (33.1) [25.4, 41.6]	1.147 [0.834, 1.578]	1.237 [0.755, 2.027]	4.9 [-7.1, 16.9]	0.399
	Female	100	86 (86.0)	45 (45.0) [35.0, 55.3]	97	92 (94.8)	38 (39.2) [29.4, 49.6]	1.149 [0.826, 1.597]	1.270 [0.721, 2.239]	5.8 [-9.0, 20.6]	0.409

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DVCD1_ISPC: Decrease of 5-D distribution score of at least 1 point by race
ITT

Decrease of 5-D distribution score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	C: Race										0.127	
	Black/African American	53	43 (81.1)	13 (24.5) [13.8, 38.3]	38	37 (97.4)	13 (34.2) [19.6, 51.4]	0.717 [0.376, 1.368]	0.625 [0.250, 1.563]	-9.7 [-31.0, 11.6]	0.316	
	White	164	144 (87.8)	78 (47.6) [39.7, 55.5]	169	159 (94.1)	60 (35.5) [28.3, 43.2]	1.340 [1.034, 1.736]	1.648 [1.062, 2.557]	12.1 [0.9, 23.2]	0.026	*
	Other	20	16 (80.0)	6 (30.0) [11.9, 54.3]	29	23 (79.3)	11 (37.9) [20.7, 57.7]	0.791 [0.350, 1.788]	0.701 [0.208, 2.365]	-7.9 [-38.9, 23.0]	0.570	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DVCD1_ISPD: Decrease of 5-D distribution score of at least 1 point by baseline WI-NRS
ITT

Decrease of 5-D distribution score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.674
	>= 4 to < 7	102	90 (88.2)	45 (44.1) [34.3, 54.3]	113	103 (91.2)	41 (36.3) [27.4, 45.9]	1.216 [0.876, 1.687]	1.386 [0.802, 2.397]	7.8 [-6.2, 21.9]	0.243
	>= 7	135	113 (83.7)	52 (38.5) [30.3, 47.3]	123	116 (94.3)	43 (35.0) [26.6, 44.1]	1.102 [0.799, 1.520]	1.166 [0.702, 1.936]	3.6 [-9.0, 16.1]	0.555

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DVCD1_ISPE: Decrease of 5-D distribution score of at least 1 point by specific medical condition
ITT

Decrease of 5-D distribution score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	E: Presence of specific medical conditions										0.463
	No	195	168 (86.2)	82 (42.1) [35.0, 49.3]	199	183 (92.0)	70 (35.2) [28.6, 42.2]	1.195 [0.931, 1.536]	1.337 [0.890, 2.009]	6.9 [-3.2, 17.0]	0.162
	Yes	42	35 (83.3)	15 (35.7) [21.6, 52.0]	37	36 (97.3)	14 (37.8) [22.5, 55.2]	0.944 [0.529, 1.684]	0.913 [0.365, 2.282]	-2.1 [-26.0, 21.7]	0.846

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DVCD1_ISPF: Decrease of 5-D distribution score of at least 1 point by use of concomitant itch medication
ITT

Decrease of 5-D distribution score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	F: Use of concomitant itch medication										0.652
	No	150	132 (88.0)	63 (42.0) [34.0, 50.3]	151	141 (93.4)	53 (35.1) [27.5, 43.3]	1.197 [0.898, 1.594]	1.339 [0.841, 2.133]	6.9 [-4.7, 18.5]	0.219
	Yes	87	71 (81.6)	34 (39.1) [28.8, 50.1]	85	78 (91.8)	31 (36.5) [26.3, 47.6]	1.072 [0.730, 1.573]	1.117 [0.603, 2.071]	2.6 [-13.0, 18.3]	0.725

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DVCD1_ISPG: Decrease of 5-D distribution score of at least 1 point by region
ITT

Decrease of 5-D distribution score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	G: Region										0.558	
	USA	146	127 (87.0)	57 (39.0) [31.1, 47.5]	133	125 (94.0)	48 (36.1) [27.9, 44.9]	1.082 [0.798, 1.466]	1.134 [0.698, 1.843]	3.0 [-9.1, 15.0]	0.612	
	Asia	8	7 (87.5)	1 (12.5) [0.3, 52.7]	12	11 (91.7)	4 (33.3) [9.9, 65.1]	0.375 [0.051, 2.772]	0.286 [0.026, 3.196]	-20.8 [-66.4, 24.7]	0.603	#
	Eastern Europe	54	47 (87.0)	26 (48.1) [34.3, 62.2]	60	58 (96.7)	21 (35.0) [23.1, 48.4]	1.376 [0.884, 2.141]	1.724 [0.812, 3.660]	13.1 [-6.6, 32.9]	0.156	
	Western Europe/European origin	29	22 (75.9)	13 (44.8) [26.4, 64.3]	31	25 (80.6)	11 (35.5) [19.2, 54.6]	1.263 [0.677, 2.356]	1.477 [0.523, 4.170]	9.3 [-18.7, 37.4]	0.464	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DVCD1_ISPH: Decrease of 5-D distribution score of at least 1 point by dialysis method
ITT

Decrease of 5-D distribution score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	H: Dialysis method										0.497	
	Hemodialysis (HD)	222	190 (85.6)	91 (41.0) [34.5, 47.8]	199	185 (93.0)	74 (37.2) [30.5, 44.3]	1.102 [0.867, 1.401]	1.173 [0.792, 1.738]	3.8 [-6.0, 13.6]	0.425	
	Hemodiafiltration (HDF)	15	13 (86.7)	6 (40.0) [16.3, 67.7]	37	34 (91.9)	10 (27.0) [13.8, 44.1]	1.480 [0.655, 3.344]	1.800 [0.509, 6.361]	13.0 [-20.3, 46.3]	0.508	#

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DWCD1_ISPA: Decrease of 5-D direction score of at least 1 point by age
ITT

Decrease of 5-D direction score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	A: Age										0.106	
	< 65 years	147	129 (87.8)	105 (71.4) [63.4, 78.6]	153	142 (92.8)	88 (57.5) [49.3, 65.5]	1.242 [1.047, 1.472]	1.847 [1.142, 2.985]	13.9 [2.5, 25.3]	0.012	*
	>= 65 years	90	73 (81.1)	50 (55.6) [44.7, 66.0]	83	77 (92.8)	48 (57.8) [46.5, 68.6]	0.961 [0.740, 1.247]	0.911 [0.499, 1.664]	-2.3 [-18.2, 13.7]	0.763	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DWCD1_ISPB: Decrease of 5-D direction score of at least 1 point by sex
ITT

Decrease of 5-D direction score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	B: Sex										0.424
	Male	137	117 (85.4)	85 (62.0) [53.4, 70.2]	139	127 (91.4)	80 (57.6) [48.9, 65.9]	1.078 [0.888, 1.308]	1.206 [0.745, 1.952]	4.5 [-7.8, 16.8]	0.448
	Female	100	85 (85.0)	70 (70.0) [60.0, 78.8]	97	92 (94.8)	56 (57.7) [47.3, 67.7]	1.213 [0.980, 1.501]	1.708 [0.949, 3.074]	12.3 [-2.1, 26.6]	0.074

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DWCD1_ISPC: Decrease of 5-D direction score of at least 1 point by race
ITT

Decrease of 5-D direction score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	C: Race										0.767
	Black/African American	53	42 (79.2)	36 (67.9) [53.7, 80.1]	38	37 (97.4)	22 (57.9) [40.8, 73.7]	1.173 [0.845, 1.629]	1.540 [0.649, 3.656]	10.0 [-12.3, 32.4]	0.329
	White	164	144 (87.8)	107 (65.2) [57.4, 72.5]	169	159 (94.1)	96 (56.8) [49.0, 64.4]	1.149 [0.967, 1.365]	1.427 [0.917, 2.222]	8.4 [-2.6, 19.5]	0.115
	Other	20	16 (80.0)	12 (60.0) [36.1, 80.9]	29	23 (79.3)	18 (62.1) [42.3, 79.3]	0.967 [0.612, 1.527]	0.917 [0.285, 2.946]	-2.1 [-34.1, 30.0]	0.885

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DWCD1_ISPD: Decrease of 5-D direction score of at least 1 point by baseline WI-NRS
ITT

Decrease of 5-D direction score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.310
	>= 4 to < 7	102	90 (88.2)	70 (68.6) [58.7, 77.5]	113	103 (91.2)	63 (55.8) [46.1, 65.1]	1.231 [0.998, 1.519]	1.736 [0.992, 3.037]	12.9 [-0.9, 26.7]	0.053
	>= 7	135	112 (83.0)	85 (63.0) [54.2, 71.1]	123	116 (94.3)	73 (59.3) [50.1, 68.1]	1.061 [0.873, 1.290]	1.164 [0.705, 1.923]	3.6 [-9.1, 16.3]	0.553

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DWCD1_ISPE: Decrease of 5-D direction score of at least 1 point by specific medical condition
ITT

Decrease of 5-D direction score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	E: Presence of specific medical conditions										0.027	i
	No	195	168 (86.2)	130 (66.7) [59.6, 73.2]	199	183 (92.0)	109 (54.8) [47.6, 61.8]	1.217 [1.037, 1.429]	1.651 [1.098, 2.484]	11.9 [1.8, 22.0]	0.016	*
	Yes	42	34 (81.0)	25 (59.5) [43.3, 74.4]	37	36 (97.3)	27 (73.0) [55.9, 86.2]	0.816 [0.594, 1.120]	0.545 [0.210, 1.411]	-13.4 [-36.6, 9.7]	0.211	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DWCD1_ISPF: Decrease of 5-D direction score of at least 1 point by use of concomitant itch medication
ITT

Decrease of 5-D direction score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	F: Use of concomitant itch medication										0.867
	No	150	132 (88.0)	99 (66.0) [57.8, 73.5]	151	141 (93.4)	87 (57.6) [49.3, 65.6]	1.146 [0.958, 1.370]	1.428 [0.895, 2.278]	8.4 [-3.2, 20.0]	0.135
	Yes	87	70 (80.5)	56 (64.4) [53.4, 74.4]	85	78 (91.8)	49 (57.6) [46.4, 68.3]	1.117 [0.878, 1.420]	1.327 [0.718, 2.454]	6.7 [-9.0, 22.4]	0.368

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DWCD1_ISPG: Decrease of 5-D direction score of at least 1 point by region
ITT

Decrease of 5-D direction score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	G: Region										0.891	
	USA	146	126 (86.3)	100 (68.5) [60.3, 75.9]	133	125 (94.0)	80 (60.2) [51.3, 68.5]	1.139 [0.954, 1.359]	1.440 [0.880, 2.356]	8.3 [-3.6, 20.3]	0.146	
	Asia	8	7 (87.5)	6 (75.0) [34.9, 96.8]	12	11 (91.7)	8 (66.7) [34.9, 90.1]	1.125 [0.639, 1.981]	1.500 [0.203, 11.088]	8.3 [-42.2, 58.9]	1.000	#
	Eastern Europe	54	47 (87.0)	35 (64.8) [50.6, 77.3]	60	58 (96.7)	37 (61.7) [48.2, 73.9]	1.051 [0.794, 1.391]	1.145 [0.534, 2.457]	3.1 [-16.3, 22.6]	0.729	
	Western Europe/European origin	29	22 (75.9)	14 (48.3) [29.4, 67.5]	31	25 (80.6)	11 (35.5) [19.2, 54.6]	1.361 [0.742, 2.494]	1.697 [0.603, 4.778]	12.8 [-15.3, 40.9]	0.319	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2DWCD1_ISPH: Decrease of 5-D direction score of at least 1 point by dialysis method
ITT

Decrease of 5-D direction score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	H: Dialysis method										0.496
	Hemodialysis (HD)	222	189 (85.1)	147 (66.2) [59.6, 72.4]	199	185 (93.0)	115 (57.8) [50.6, 64.7]	1.146 [0.985, 1.333]	1.432 [0.964, 2.126]	8.4 [-1.3, 18.2]	0.075
	Hemodiafiltration (HDF)	15	13 (86.7)	8 (53.3) [26.6, 78.7]	37	34 (91.9)	21 (56.8) [39.5, 72.9]	0.940 [0.542, 1.630]	0.871 [0.261, 2.905]	-3.4 [-38.0, 31.1]	0.824

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived, created on: 17FEB2022

Table BT2PGI_ISPA: Relevant improvement in PGIC by age
ITT

		CR845			Placebo						
Relevant improvement in PGIC		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	A: Age										0.732
	< 65 years	147	139 (94.6)	73 (49.7) [41.3, 58.0]	153	146 (95.4)	63 (41.2) [33.3, 49.4]	1.206 [0.940, 1.548]	1.409 [0.893, 2.224]	8.5 [-3.4, 20.4]	0.141
	>= 65 years	90	84 (93.3)	41 (45.6) [35.0, 56.4]	83	80 (96.4)	29 (34.9) [24.8, 46.2]	1.304 [0.900, 1.888]	1.558 [0.844, 2.876]	10.6 [-5.1, 26.3]	0.156

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. PGIC = patient global impression of change.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: apgic, created on: 17FEB2022

Table BT2PGI_ISPB: Relevant improvement in PGIC by sex
ITT

		CR845			Placebo						
Relevant improvement in PGIC		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	B: Sex										0.747
	Male	137	130 (94.9)	60 (43.8) [35.3, 52.5]	139	133 (95.7)	51 (36.7) [28.7, 45.3]	1.194 [0.894, 1.594]	1.345 [0.830, 2.178]	7.1 [-5.2, 19.4]	0.230
	Female	100	93 (93.0)	54 (54.0) [43.7, 64.0]	97	93 (95.9)	41 (42.3) [32.3, 52.7]	1.278 [0.952, 1.715]	1.603 [0.913, 2.815]	11.7 [-3.1, 26.6]	0.100

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. PGIC = patient global impression of change.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: apgic, created on: 17FEB2022

Table BT2PGI_ISPC: Relevant improvement in PGIC by race
ITT

Relevant improvement in PGIC		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	C: Race										0.064	
	Black/African American	53	49 (92.5)	30 (56.6) [42.3, 70.2]	38	36 (94.7)	12 (31.6) [17.5, 48.7]	1.792 [1.061, 3.027]	2.826 [1.180, 6.769]	25.0 [2.9, 47.2]	0.019	*
	White	164	155 (94.5)	76 (46.3) [38.5, 54.3]	169	164 (97.0)	63 (37.3) [30.0, 45.0]	1.243 [0.963, 1.605]	1.453 [0.938, 2.251]	9.1 [-2.1, 20.2]	0.094	
	Other	20	19 (95.0)	8 (40.0) [19.1, 63.9]	29	26 (89.7)	17 (58.6) [38.9, 76.5]	0.682 [0.368, 1.266]	0.471 [0.147, 1.502]	-18.6 [-50.8, 13.6]	0.205	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. PGIC = patient global impression of change.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: apgic, created on: 17FEB2022

Table BT2PGI_ISPD: Relevant improvement in PGIC by baseline WI-NRS
ITT

		CR845			Placebo						
Relevant improvement in PGIC		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.666
	>= 4 to < 7	102	97 (95.1)	59 (57.8) [47.7, 67.6]	113	107 (94.7)	50 (44.2) [34.9, 53.9]	1.307 [1.003, 1.704]	1.729 [1.007, 2.968]	13.6 [-0.6, 27.8]	0.047 *
	>= 7	135	126 (93.3)	55 (40.7) [32.4, 49.5]	123	119 (96.7)	42 (34.1) [25.8, 43.2]	1.193 [0.867, 1.641]	1.326 [0.799, 2.201]	6.6 [-6.0, 19.2]	0.276

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. PGIC = patient global impression of change.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: apgic, created on: 17FEB2022

Table BT2PGI_ISPE: Relevant improvement in PGIC by specific medical condition
ITT

		CR845			Placebo						
Relevant improvement in PGIC		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	E: Presence of specific medical conditions										0.437
	No	195	186 (95.4)	92 (47.2) [40.0, 54.4]	199	191 (96.0)	79 (39.7) [32.8, 46.9]	1.188 [0.947, 1.491]	1.357 [0.910, 2.023]	7.5 [-2.8, 17.8]	0.135
	Yes	42	37 (88.1)	22 (52.4) [36.4, 68.0]	37	35 (94.6)	13 (35.1) [20.2, 52.5]	1.491 [0.883, 2.518]	2.031 [0.820, 5.029]	17.2 [-6.9, 41.3]	0.126

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. PGIC = patient global impression of change.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: apgic, created on: 17FEB2022

Table BT2PGI_ISPF: Relevant improvement in PGIC by use of concomitant itch medication
ITT

		CR845			Placebo						
Relevant improvement in PGIC		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	F: Use of concomitant itch medication										0.807
	No	150	143 (95.3)	70 (46.7) [38.5, 55.0]	151	145 (96.0)	56 (37.1) [29.4, 45.3]	1.258 [0.961, 1.647]	1.484 [0.937, 2.352]	9.6 [-2.2, 21.3]	0.093
	Yes	87	80 (92.0)	44 (50.6) [39.6, 61.5]	85	81 (95.3)	36 (42.4) [31.7, 53.6]	1.194 [0.864, 1.650]	1.393 [0.763, 2.541]	8.2 [-7.8, 24.2]	0.281

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. PGIC = patient global impression of change.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: apgic, created on: 17FEB2022

Table BT2PGI_ISPG: Relevant improvement in PGIC by region
ITT

		CR845			Placebo						
Relevant improvement in PGIC		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	G: Region										0.758
	USA	146	136 (93.2)	67 (45.9) [37.6, 54.3]	133	127 (95.5)	53 (39.8) [31.5, 48.7]	1.152 [0.876, 1.513]	1.280 [0.795, 2.060]	6.0 [-6.3, 18.4]	0.310
	Asia	8	7 (87.5)	5 (62.5) [24.5, 91.5]	12	12 (100.0)	7 (58.3) [27.7, 84.8]	1.071 [0.522, 2.199]	1.190 [0.190, 7.456]	4.2 [-49.9, 58.2]	1.000 #
	Eastern Europe	54	52 (96.3)	29 (53.7) [39.6, 67.4]	60	59 (98.3)	22 (36.7) [24.6, 50.1]	1.465 [0.968, 2.217]	2.004 [0.947, 4.240]	17.0 [-2.8, 36.8]	0.069
	Western Europe/European origin	29	28 (96.6)	13 (44.8) [26.4, 64.3]	31	28 (90.3)	10 (32.3) [16.7, 51.4]	1.390 [0.725, 2.663]	1.706 [0.597, 4.876]	12.6 [-15.2, 40.4]	0.321

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. PGIC = patient global impression of change.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: apgic, created on: 17FEB2022

Table BT2PGI_ISPH: Relevant improvement in PGIC by dialysis method
ITT

		CR845			Placebo						
Relevant improvement in PGIC		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	H: Dialysis method										0.994
	Hemodialysis (HD)	222	209 (94.1)	107 (48.2) [41.5, 55.0]	199	190 (95.5)	78 (39.2) [32.4, 46.3]	1.230 [0.987, 1.533]	1.443 [0.980, 2.127]	9.0 [-0.9, 18.9]	0.063
	Hemodiafiltration (HDF)	15	14 (93.3)	7 (46.7) [21.3, 73.4]	37	36 (97.3)	14 (37.8) [22.5, 55.2]	1.233 [0.624, 2.436]	1.438 [0.428, 4.833]	8.8 [-25.5, 43.2]	0.560

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. PGIC = patient global impression of change.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: apgic, created on: 17FEB2022

Table BT2STC_ISHA: Change from baseline in Skindex-10 total score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
< 65 years	Skindex-10 total score	Baseline	CR845	147	143 (97.3)	36.1 (14.9)	0	39.0	60	
			Placebo	153	149 (97.4)	34.7 (14.8)	3	35.0	60	
		Week 4	CR845	147	134 (91.2)	24.8 (16.1)	0	22.0	60	
			Placebo	153	139 (90.8)	26.7 (15.6)	2	25.0	60	
		Week 8	CR845	147	128 (87.1)	22.4 (17.1)	0	20.5	60	
			Placebo	153	142 (92.8)	22.0 (15.4)	0	19.0	60	
		Week 10	CR845	147	130 (88.4)	20.2 (16.6)	0	17.0	60	
			Placebo	153	138 (90.2)	22.2 (15.9)	0	19.0	60	
		Week 12	CR845	147	129 (87.8)	20.2 (16.9)	0	17.0	60	
			Placebo	153	139 (90.8)	20.5 (15.7)	0	16.0	60	
	Change from baseline in Skindex-10 total score	Week 4	CR845	147	131 (89.1)	-11.0 (14.6)	-51	-12.0	29	-0.23 [-0.47, 0.01]
			Placebo	153	136 (88.9)	-7.4 (16.2)	-55	-6.0	52	
		Week 8	CR845	147	125 (85.0)	-13.8 (16.3)	-51	-13.0	30	-0.09 [-0.33, 0.15]
			Placebo	153	139 (90.8)	-12.4 (15.6)	-57	-10.0	40	
		Week 10	CR845	147	128 (87.1)	-15.7 (16.1)	-55	-14.0	31	-0.22 [-0.46, 0.03]
			Placebo	153	135 (88.2)	-12.2 (16.4)	-57	-9.0	41	
		Week 12	CR845	147	127 (86.4)	-16.0 (16.9)	-58	-17.0	39	-0.12 [-0.36, 0.13]
			Placebo	153	137 (89.5)	-14.1 (17.1)	-59	-11.0	41	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2STC_ISHA: Change from baseline in Skindex-10 total score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 65 years	Skindex-10 total score	Baseline	CR845	90	88 (97.8)	34.4 (15.3)	1	35.5	60	
			Placebo	83	81 (97.6)	33.4 (14.4)	0	35.0	59	
		Week 4	CR845	90	77 (85.6)	23.6 (16.6)	0	21.0	60	
			Placebo	83	76 (91.6)	23.4 (15.6)	0	22.0	60	
		Week 8	CR845	90	74 (82.2)	21.4 (17.3)	0	15.5	60	
			Placebo	83	75 (90.4)	22.6 (15.6)	0	22.0	59	
		Week 10	CR845	90	73 (81.1)	18.3 (16.9)	0	14.0	60	
			Placebo	83	73 (88.0)	21.6 (15.1)	0	22.0	60	
		Week 12	CR845	90	73 (81.1)	18.4 (16.2)	0	14.0	60	
			Placebo	83	75 (90.4)	21.0 (15.2)	0	19.0	58	
	Change from baseline in Skindex-10 total score	Week 4	CR845	90	76 (84.4)	-11.1 (16.6)	-56	-7.0	40	-0.10 [-0.42, 0.21]
			Placebo	83	75 (90.4)	-9.5 (15.0)	-49	-8.0	23	
		Week 8	CR845	90	73 (81.1)	-13.3 (15.9)	-53	-13.0	43	-0.15 [-0.47, 0.17]
			Placebo	83	74 (89.2)	-11.0 (14.8)	-50	-10.0	44	
		Week 10	CR845	90	72 (80.0)	-15.5 (14.7)	-56	-14.5	17	-0.32 [-0.65, 0.01]
			Placebo	83	71 (85.5)	-10.9 (14.2)	-42	-10.0	32	
		Week 12	CR845	90	72 (80.0)	-15.3 (14.8)	-56	-15.0	21	-0.20 [-0.53, 0.13]
			Placebo	83	73 (88.0)	-12.3 (14.8)	-46	-11.0	26	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2STC_ISHB: Change from baseline in Skindex-10 total score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Male	Skindex-10 total score	Baseline	CR845	137	134 (97.8)	35.0 (14.9)	0	36.0	60	
			Placebo	139	135 (97.1)	33.2 (14.9)	0	35.0	60	
		Week 4	CR845	137	123 (89.8)	25.1 (15.5)	0	23.0	60	
			Placebo	139	126 (90.6)	23.4 (15.1)	0	23.0	60	
		Week 8	CR845	137	120 (87.6)	24.2 (17.2)	0	23.0	60	
			Placebo	139	130 (93.5)	20.4 (14.3)	0	18.0	60	
		Week 10	CR845	137	117 (85.4)	21.7 (17.0)	0	17.0	60	
			Placebo	139	123 (88.5)	19.8 (14.6)	0	19.0	60	
		Week 12	CR845	137	116 (84.7)	21.5 (16.6)	0	19.5	60	
			Placebo	139	125 (89.9)	19.0 (13.8)	0	16.0	60	
	Change from baseline in Skindex-10 total score	Week 4	CR845	137	121 (88.3)	-9.5 (13.5)	-43	-9.0	40	-0.02 [-0.27, 0.23]
			Placebo	139	122 (87.8)	-9.3 (17.6)	-55	-7.0	52	
		Week 8	CR845	137	118 (86.1)	-10.9 (14.8)	-50	-11.5	43	0.12 [-0.13, 0.38]
			Placebo	139	127 (91.4)	-12.8 (15.3)	-57	-10.0	40	
		Week 10	CR845	137	115 (83.9)	-13.0 (12.8)	-49	-12.0	18	-0.03 [-0.28, 0.23]
			Placebo	139	120 (86.3)	-12.6 (16.9)	-57	-10.0	41	
		Week 12	CR845	137	114 (83.2)	-13.3 (13.3)	-45	-14.0	21	0.03 [-0.22, 0.29]
			Placebo	139	122 (87.8)	-13.8 (16.9)	-56	-12.0	41	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2STC_ISHB: Change from baseline in Skindex-10 total score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Female	Skindex-10 total score	Baseline	CR845	100	97 (97.0)	36.1 (15.3)	1	40.0	60	
			Placebo	97	95 (97.9)	35.7 (14.2)	5	36.0	60	
		Week 4	CR845	100	88 (88.0)	23.3 (17.3)	0	20.5	60	
			Placebo	97	89 (91.8)	28.6 (15.9)	2	26.0	60	
		Week 8	CR845	100	82 (82.0)	18.8 (16.7)	0	15.0	60	
			Placebo	97	87 (89.7)	24.8 (16.8)	0	25.0	59	
		Week 10	CR845	100	86 (86.0)	16.6 (15.9)	0	10.0	60	
			Placebo	97	88 (90.7)	25.0 (16.5)	0	23.0	60	
		Week 12	CR845	100	86 (86.0)	17.0 (16.3)	0	12.5	60	
			Placebo	97	89 (91.8)	23.0 (17.5)	0	21.0	60	
	Change from baseline in Skindex-10 total score	Week 4	CR845	100	86 (86.0)	-13.2 (17.4)	-56	-13.0	29	-0.43 [-0.73, -0.13]
			Placebo	97	89 (91.8)	-6.6 (12.8)	-43	-6.0	18	
		Week 8	CR845	100	80 (80.0)	-17.6 (17.3)	-53	-18.0	30	-0.43 [-0.74, -0.12]
			Placebo	97	86 (88.7)	-10.6 (15.3)	-51	-9.5	44	
		Week 10	CR845	100	85 (85.0)	-19.2 (18.2)	-56	-18.0	31	-0.54 [-0.84, -0.23]
			Placebo	97	86 (88.7)	-10.6 (13.7)	-51	-9.0	19	
		Week 12	CR845	100	85 (85.0)	-19.1 (18.8)	-58	-20.0	39	-0.35 [-0.65, -0.05]
			Placebo	97	88 (90.7)	-13.0 (15.6)	-59	-10.0	14	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2STC_ISHC: Change from baseline in Skindex-10 total score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Black/African American	Skindex-10 total score	Baseline	CR845	53	50 (94.3)	35.4 (14.0)	5	35.0	60	
			Placebo	38	37 (97.4)	37.4 (16.7)	7	38.0	60	
		Week 4	CR845	53	45 (84.9)	27.8 (14.9)	0	24.0	60	
			Placebo	38	32 (84.2)	25.8 (14.7)	2	23.5	60	
		Week 8	CR845	53	46 (86.8)	24.6 (17.6)	0	25.0	60	
			Placebo	38	35 (92.1)	25.9 (16.2)	0	30.0	56	
		Week 10	CR845	53	44 (83.0)	23.6 (17.7)	0	19.0	60	
			Placebo	38	33 (86.8)	24.5 (17.9)	2	21.0	60	
		Week 12	CR845	53	43 (81.1)	21.0 (17.2)	0	21.0	60	
			Placebo	38	36 (94.7)	21.3 (17.9)	0	14.5	60	
	Change from baseline in Skindex-10 total score	Week 4	CR845	53	43 (81.1)	-7.9 (13.3)	-39	-6.0	29	0.15 [-0.32, 0.61]
			Placebo	38	31 (81.6)	-9.8 (13.2)	-43	-7.0	9	
		Week 8	CR845	53	44 (83.0)	-11.6 (14.7)	-48	-13.5	19	0.05 [-0.40, 0.50]
			Placebo	38	34 (89.5)	-12.3 (12.2)	-51	-10.5	5	
		Week 10	CR845	53	42 (79.2)	-12.4 (12.6)	-42	-12.0	12	0.09 [-0.37, 0.55]
			Placebo	38	32 (84.2)	-13.7 (15.4)	-54	-10.0	19	
		Week 12	CR845	53	41 (77.4)	-14.2 (13.3)	-36	-16.0	20	0.24 [-0.21, 0.70]
			Placebo	38	35 (92.1)	-17.8 (15.9)	-56	-13.0	5	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2STC_ISHC: Change from baseline in Skindex-10 total score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
White	Skindex-10 total score	Baseline	CR845	164	161 (98.2)	35.1 (15.6)	0	37.0	60	
			Placebo	169	167 (98.8)	33.5 (14.2)	0	34.0	60	
		Week 4	CR845	164	149 (90.9)	22.9 (16.4)	0	21.0	60	
			Placebo	169	157 (92.9)	25.8 (16.3)	0	24.0	60	
		Week 8	CR845	164	139 (84.8)	20.8 (17.3)	0	15.0	60	
			Placebo	169	157 (92.9)	21.6 (15.5)	0	19.0	60	
		Week 10	CR845	164	143 (87.2)	18.3 (16.0)	0	16.0	60	
			Placebo	169	154 (91.1)	21.5 (15.1)	0	19.0	60	
		Week 12	CR845	164	143 (87.2)	18.7 (16.3)	0	15.0	60	
			Placebo	169	155 (91.7)	20.9 (15.0)	0	18.0	60	
	Change from baseline in Skindex-10 total score	Week 4	CR845	164	147 (89.6)	-12.1 (15.9)	-56	-12.0	40	-0.28 [-0.51, -0.06]
			Placebo	169	155 (91.7)	-7.5 (16.5)	-55	-6.0	52	
		Week 8	CR845	164	137 (83.5)	-14.1 (16.7)	-53	-13.0	43	-0.16 [-0.40, 0.07]
			Placebo	169	155 (91.7)	-11.4 (15.9)	-57	-10.0	44	
		Week 10	CR845	164	142 (86.6)	-16.1 (16.0)	-56	-15.0	31	-0.32 [-0.55, -0.09]
			Placebo	169	152 (89.9)	-11.1 (15.7)	-57	-9.5	41	
		Week 12	CR845	164	142 (86.6)	-16.2 (16.7)	-58	-16.0	39	-0.24 [-0.47, -0.02]
			Placebo	169	153 (90.5)	-12.2 (16.3)	-59	-10.0	41	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2STC_ISHC: Change from baseline in Skindex-10 total score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Other	Skindex-10 total score	Baseline	CR845	20	20 (100.0)	38.8 (13.4)	15	39.0	60	
			Placebo	29	26 (89.7)	34.5 (14.4)	10	36.5	57	
		Week 4	CR845	20	17 (85.0)	28.1 (17.2)	0	28.0	60	
			Placebo	29	26 (89.7)	23.5 (13.2)	3	24.0	57	
		Week 8	CR845	20	17 (85.0)	25.1 (14.4)	2	23.0	48	
			Placebo	29	25 (86.2)	20.3 (13.4)	2	17.0	59	
		Week 10	CR845	20	16 (80.0)	19.1 (18.6)	0	14.0	51	
			Placebo	29	24 (82.8)	21.5 (15.5)	0	21.5	60	
		Week 12	CR845	20	16 (80.0)	23.5 (18.2)	0	20.5	51	
			Placebo	29	23 (79.3)	18.0 (15.2)	0	13.0	49	
	Change from baseline in Skindex-10 total score	Week 4	CR845	20	17 (85.0)	-10.1 (14.4)	-31	-13.0	22	0.01 [-0.61, 0.62]
			Placebo	29	25 (86.2)	-10.2 (13.8)	-35	-7.0	13	
		Week 8	CR845	20	17 (85.0)	-14.8 (15.4)	-42	-19.0	15	-0.02 [-0.64, 0.60]
			Placebo	29	24 (82.8)	-14.5 (15.5)	-44	-10.0	7	
		Week 10	CR845	20	16 (80.0)	-20.1 (18.7)	-55	-19.5	18	-0.37 [-1.02, 0.27]
			Placebo	29	22 (75.9)	-13.7 (16.0)	-43	-16.0	15	
		Week 12	CR845	20	16 (80.0)	-15.9 (18.1)	-55	-17.0	18	-0.01 [-0.66, 0.63]
			Placebo	29	22 (75.9)	-15.7 (16.3)	-46	-11.0	8	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2STC_ISHD: Change from baseline in Skindex-10 total score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 4 to < 7	Skindex-10 total score	Baseline	CR845	102	101 (99.0)	30.4 (14.6)	0	30.0	60	
			Placebo	113	111 (98.2)	29.2 (14.8)	0	27.0	60	
		Week 4	CR845	102	95 (93.1)	18.2 (12.8)	0	18.0	57	
			Placebo	113	106 (93.8)	20.8 (13.9)	0	19.0	60	
		Week 8	CR845	102	93 (91.2)	16.3 (13.2)	0	13.0	60	
			Placebo	113	105 (92.9)	19.0 (14.6)	0	15.0	60	
		Week 10	CR845	102	91 (89.2)	14.2 (13.0)	0	11.0	60	
			Placebo	113	101 (89.4)	17.9 (14.6)	0	15.0	60	
		Week 12	CR845	102	91 (89.2)	14.3 (13.3)	0	10.0	60	
			Placebo	113	102 (90.3)	17.9 (14.2)	0	15.0	56	
	Change from baseline in Skindex-10 total score	Week 4	CR845	102	94 (92.2)	-11.8 (14.2)	-47	-12.5	27	-0.27 [-0.55, 0.01]
			Placebo	113	104 (92.0)	-7.6 (17.0)	-49	-7.5	52	
		Week 8	CR845	102	92 (90.2)	-13.7 (16.2)	-48	-14.0	30	-0.25 [-0.53, 0.04]
			Placebo	113	104 (92.0)	-9.7 (15.7)	-51	-9.0	44	
		Week 10	CR845	102	90 (88.2)	-15.5 (15.2)	-50	-15.0	31	-0.29 [-0.57, -0.00]
			Placebo	113	100 (88.5)	-10.8 (16.8)	-54	-9.0	41	
		Week 12	CR845	102	90 (88.2)	-16.0 (16.1)	-56	-18.0	39	-0.31 [-0.60, -0.03]
			Placebo	113	101 (89.4)	-11.0 (16.4)	-56	-9.0	41	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2STC_ISHD: Change from baseline in Skindex-10 total score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 7	Skindex-10 total score	Baseline	CR845	135	130 (96.3)	39.4 (14.2)	0	41.5	60	
			Placebo	123	119 (96.7)	38.9 (12.9)	10	39.0	60	
		Week 4	CR845	135	116 (85.9)	29.4 (17.0)	0	30.0	60	
			Placebo	123	109 (88.6)	30.1 (16.0)	3	27.0	60	
		Week 8	CR845	135	109 (80.7)	26.9 (18.6)	0	28.0	60	
			Placebo	123	112 (91.1)	25.1 (15.7)	0	23.5	59	
		Week 10	CR845	135	112 (83.0)	23.8 (18.1)	0	24.0	60	
			Placebo	123	110 (89.4)	25.8 (15.6)	0	25.0	60	
		Week 12	CR845	135	111 (82.2)	23.9 (17.8)	0	24.0	60	
			Placebo	123	112 (91.1)	23.2 (16.3)	0	20.0	60	
	Change from baseline in Skindex-10 total score	Week 4	CR845	135	113 (83.7)	-10.4 (16.3)	-56	-9.0	40	-0.11 [-0.38, 0.15]
			Placebo	123	107 (87.0)	-8.7 (14.5)	-55	-5.0	17	
		Week 8	CR845	135	106 (78.5)	-13.6 (16.1)	-53	-13.0	43	0.03 [-0.24, 0.29]
			Placebo	123	109 (88.6)	-14.0 (14.6)	-57	-11.0	12	
		Week 10	CR845	135	110 (81.5)	-15.8 (16.0)	-56	-13.5	18	-0.21 [-0.47, 0.06]
			Placebo	123	106 (86.2)	-12.6 (14.5)	-57	-10.0	19	
		Week 12	CR845	135	109 (80.7)	-15.5 (16.2)	-58	-14.0	21	0.02 [-0.25, 0.28]
			Placebo	123	109 (88.6)	-15.8 (16.0)	-59	-14.0	14	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2STC_ISHE: Change from baseline in Skindex-10 total score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	Skindex-10 total score	Baseline	CR845	195	189 (96.9)	35.6 (15.2)	0	37.0	60	
			Placebo	199	194 (97.5)	33.0 (14.6)	0	34.0	60	
		Week 4	CR845	195	174 (89.2)	24.7 (16.0)	0	22.0	60	
			Placebo	199	185 (93.0)	25.3 (15.7)	0	24.0	60	
		Week 8	CR845	195	169 (86.7)	22.2 (17.0)	0	19.0	60	
			Placebo	199	182 (91.5)	21.4 (15.2)	0	18.0	59	
		Week 10	CR845	195	169 (86.7)	19.9 (16.6)	0	17.0	60	
			Placebo	199	177 (88.9)	21.1 (15.4)	0	19.0	60	
		Week 12	CR845	195	167 (85.6)	19.7 (16.7)	0	16.0	60	
			Placebo	199	179 (89.9)	20.2 (15.1)	0	16.0	60	
	Change from baseline in Skindex-10 total score	Week 4	CR845	195	170 (87.2)	-10.9 (14.7)	-56	-11.0	29	-0.24 [-0.45, -0.03]
			Placebo	199	182 (91.5)	-7.3 (15.4)	-55	-6.0	52	
		Week 8	CR845	195	165 (84.6)	-13.7 (15.0)	-53	-13.0	30	-0.16 [-0.37, 0.06]
			Placebo	199	179 (89.9)	-11.3 (15.4)	-57	-10.0	44	
		Week 10	CR845	195	166 (85.1)	-15.4 (14.7)	-56	-14.0	30	-0.26 [-0.48, -0.05]
			Placebo	199	173 (86.9)	-11.4 (15.9)	-57	-9.0	41	
		Week 12	CR845	195	164 (84.1)	-15.8 (15.1)	-58	-16.0	30	-0.20 [-0.41, 0.02]
			Placebo	199	176 (88.4)	-12.7 (16.3)	-59	-10.5	41	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2STC_ISHE: Change from baseline in Skindex-10 total score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	Skindex-10 total score	Baseline	CR845	42	42 (100.0)	34.6 (14.5)	5	35.0	60	
			Placebo	37	36 (97.3)	40.6 (13.5)	10	40.0	60	
		Week 4	CR845	42	37 (88.1)	22.8 (17.7)	0	20.0	60	
			Placebo	37	30 (81.1)	26.7 (15.5)	0	24.5	60	
		Week 8	CR845	42	33 (78.6)	21.3 (17.9)	0	20.0	60	
			Placebo	37	35 (94.6)	26.1 (16.0)	0	26.0	60	
		Week 10	CR845	42	34 (81.0)	17.3 (17.0)	0	14.0	60	
			Placebo	37	34 (91.9)	26.4 (15.9)	2	25.0	60	
		Week 12	CR845	42	35 (83.3)	19.1 (16.4)	0	16.0	60	
			Placebo	37	35 (94.6)	23.3 (17.5)	0	25.0	56	
	Change from baseline in Skindex-10 total score	Week 4	CR845	42	37 (88.1)	-11.7 (18.2)	-51	-8.0	40	0.09 [-0.39, 0.58]
			Placebo	37	29 (78.4)	-13.3 (17.3)	-49	-8.0	11	
		Week 8	CR845	42	33 (78.6)	-13.1 (21.1)	-51	-11.0	43	0.10 [-0.38, 0.58]
			Placebo	37	34 (91.9)	-14.9 (14.8)	-51	-12.0	8	
		Week 10	CR845	42	34 (81.0)	-16.8 (19.5)	-55	-14.5	31	-0.17 [-0.65, 0.31]
			Placebo	37	33 (89.2)	-13.8 (14.4)	-54	-11.0	5	
		Week 12	CR845	42	35 (83.3)	-15.6 (20.4)	-56	-15.0	39	0.09 [-0.38, 0.57]
			Placebo	37	34 (91.9)	-17.3 (16.4)	-56	-13.5	4	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2STC_ISHF: Change from baseline in Skindex-10 total score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	Skindex-10 total score	Baseline	CR845	150	146 (97.3)	34.2 (15.2)	0	36.0	60	
			Placebo	151	147 (97.4)	33.7 (14.9)	0	34.0	60	
		Week 4	CR845	150	138 (92.0)	23.9 (15.5)	0	22.0	60	
			Placebo	151	141 (93.4)	24.9 (15.5)	0	23.0	60	
		Week 8	CR845	150	135 (90.0)	21.5 (16.7)	0	16.0	60	
			Placebo	151	139 (92.1)	21.0 (14.5)	0	19.0	60	
		Week 10	CR845	150	131 (87.3)	19.1 (16.4)	0	16.0	60	
			Placebo	151	136 (90.1)	21.4 (14.8)	0	19.0	60	
		Week 12	CR845	150	132 (88.0)	19.1 (16.8)	0	14.0	60	
			Placebo	151	140 (92.7)	20.0 (14.9)	0	17.0	60	
	Change from baseline in Skindex-10 total score	Week 4	CR845	150	135 (90.0)	-10.1 (16.1)	-56	-10.0	40	-0.11 [-0.34, 0.13]
			Placebo	151	138 (91.4)	-8.4 (15.9)	-55	-6.0	52	
		Week 8	CR845	150	132 (88.0)	-12.8 (15.8)	-53	-13.0	43	-0.02 [-0.26, 0.21]
			Placebo	151	137 (90.7)	-12.4 (15.8)	-57	-10.0	44	
		Week 10	CR845	150	128 (85.3)	-14.5 (15.1)	-56	-13.0	31	-0.16 [-0.40, 0.08]
			Placebo	151	133 (88.1)	-11.9 (17.1)	-57	-10.0	41	
		Week 12	CR845	150	129 (86.0)	-14.5 (16.3)	-56	-15.0	39	-0.04 [-0.28, 0.20]
			Placebo	151	137 (90.7)	-13.8 (17.0)	-59	-10.0	41	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2STC_ISHF: Change from baseline in Skindex-10 total score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	Skindex-10 total score	Baseline	CR845	87	85 (97.7)	37.6 (14.5)	0	38.0	60	
			Placebo	85	83 (97.6)	35.2 (14.4)	3	36.0	60	
		Week 4	CR845	87	73 (83.9)	25.3 (17.6)	0	22.0	60	
			Placebo	85	74 (87.1)	26.8 (15.9)	0	24.0	60	
		Week 8	CR845	87	67 (77.0)	23.1 (18.1)	0	21.0	60	
			Placebo	85	78 (91.8)	24.2 (16.8)	0	21.5	59	
		Week 10	CR845	87	72 (82.8)	20.3 (17.3)	0	19.0	58	
			Placebo	85	75 (88.2)	23.1 (16.9)	0	21.0	60	
		Week 12	CR845	87	70 (80.5)	20.4 (16.3)	0	20.0	59	
			Placebo	85	74 (87.1)	22.0 (16.6)	0	17.5	60	
	Change from baseline in Skindex-10 total score	Week 4	CR845	87	72 (82.8)	-12.9 (13.7)	-51	-13.0	22	-0.35 [-0.68, -0.02]
			Placebo	85	73 (85.9)	-7.7 (15.6)	-49	-7.0	39	
		Week 8	CR845	87	66 (75.9)	-15.2 (16.7)	-51	-15.5	19	-0.27 [-0.60, 0.06]
			Placebo	85	76 (89.4)	-11.0 (14.3)	-51	-9.0	28	
		Week 10	CR845	87	72 (82.8)	-17.7 (16.4)	-55	-15.5	18	-0.43 [-0.76, -0.10]
			Placebo	85	73 (85.9)	-11.4 (12.6)	-51	-10.0	19	
		Week 12	CR845	87	70 (80.5)	-18.1 (15.5)	-58	-18.5	18	-0.34 [-0.67, -0.01]
			Placebo	85	73 (85.9)	-12.9 (15.0)	-57	-12.0	41	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2STC_ISHG: Change from baseline in Skindex-10 total score by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
USA	Skindex-10 total score	Baseline	CR845	146	140 (95.9)	36.4 (14.4)	0	38.5	60	
			Placebo	133	131 (98.5)	35.1 (14.3)	3	35.0	60	
		Week 4	CR845	146	129 (88.4)	26.7 (15.2)	0	22.0	60	
			Placebo	133	117 (88.0)	27.8 (15.2)	2	26.0	60	
		Week 8	CR845	146	125 (85.6)	24.7 (16.9)	0	24.0	60	
			Placebo	133	122 (91.7)	23.2 (14.7)	0	23.0	59	
		Week 10	CR845	146	127 (87.0)	22.8 (16.9)	0	20.0	60	
			Placebo	133	119 (89.5)	22.2 (14.5)	0	19.0	59	
		Week 12	CR845	146	126 (86.3)	21.7 (16.3)	0	20.5	60	
			Placebo	133	124 (93.2)	20.7 (14.9)	0	18.0	60	
	Change from baseline in Skindex-10 total score	Week 4	CR845	146	125 (85.6)	-9.6 (15.3)	-47	-9.0	40	-0.20 [-0.45, 0.05]
			Placebo	133	116 (87.2)	-6.3 (17.0)	-55	-4.0	52	
		Week 8	CR845	146	121 (82.9)	-11.6 (16.2)	-48	-13.0	43	-0.02 [-0.27, 0.24]
			Placebo	133	121 (91.0)	-11.3 (16.0)	-57	-10.0	44	
		Week 10	CR845	146	124 (84.9)	-13.4 (15.3)	-50	-12.5	31	-0.06 [-0.31, 0.20]
			Placebo	133	117 (88.0)	-12.5 (16.8)	-57	-9.0	41	
		Week 12	CR845	146	123 (84.2)	-14.6 (15.4)	-56	-16.0	39	-0.00 [-0.25, 0.25]
			Placebo	133	122 (91.7)	-14.5 (17.7)	-59	-12.5	41	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2STC_ISHG: Change from baseline in Skindex-10 total score by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Asia	Skindex-10 total score	Baseline	CR845	8	8 (100.0)	37.6 (9.6)	28	35.5	56	
			Placebo	12	12 (100.0)	35.2 (14.8)	10	40.0	55	
		Week 4	CR845	8	8 (100.0)	18.5 (12.8)	0	14.5	40	
			Placebo	12	12 (100.0)	22.9 (15.7)	3	18.5	57	
		Week 8	CR845	8	7 (87.5)	16.7 (7.9)	5	15.0	30	
			Placebo	12	12 (100.0)	16.7 (10.0)	2	16.0	33	
		Week 10	CR845	8	7 (87.5)	10.6 (10.9)	0	10.0	31	
			Placebo	12	11 (91.7)	15.6 (11.9)	0	16.0	35	
		Week 12	CR845	8	7 (87.5)	14.1 (10.4)	1	10.0	33	
			Placebo	12	11 (91.7)	14.4 (13.3)	0	12.0	43	
	Change from baseline in Skindex-10 total score	Week 4	CR845	8	8 (100.0)	-19.1 (10.8)	-31	-19.5	0	-0.59 [-1.50, 0.33]
			Placebo	12	12 (100.0)	-12.3 (12.2)	-35	-12.0	7	
		Week 8	CR845	8	7 (87.5)	-22.0 (8.8)	-33	-23.0	-10	-0.27 [-1.20, 0.67]
			Placebo	12	12 (100.0)	-18.5 (14.9)	-44	-18.5	4	
		Week 10	CR845	8	7 (87.5)	-28.1 (9.8)	-40	-29.0	-13	-0.68 [-1.66, 0.29]
			Placebo	12	11 (91.7)	-17.7 (17.8)	-43	-19.0	15	
		Week 12	CR845	8	7 (87.5)	-24.6 (9.5)	-37	-25.0	-7	-0.42 [-1.38, 0.54]
			Placebo	12	11 (91.7)	-19.0 (15.2)	-44	-13.0	-2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2STC_ISHG: Change from baseline in Skindex-10 total score by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Eastern Europe	Skindex-10 total score	Baseline	CR845	54	54 (100.0)	30.5 (16.5)	0	28.0	60	
			Placebo	60	60 (100.0)	28.4 (14.1)	0	28.5	60	
		Week 4	CR845	54	52 (96.3)	19.3 (16.5)	0	13.5	58	
			Placebo	60	57 (95.0)	19.6 (14.3)	0	18.0	57	
		Week 8	CR845	54	48 (88.9)	14.1 (16.2)	0	8.5	60	
			Placebo	60	58 (96.7)	17.9 (15.1)	0	15.5	59	
		Week 10	CR845	54	47 (87.0)	11.9 (13.7)	0	7.0	57	
			Placebo	60	58 (96.7)	19.1 (15.4)	0	18.5	60	
		Week 12	CR845	54	47 (87.0)	13.6 (15.0)	0	9.0	59	
			Placebo	60	55 (91.7)	18.3 (14.9)	0	15.0	60	
	Change from baseline in Skindex-10 total score	Week 4	CR845	54	52 (96.3)	-11.7 (13.9)	-51	-11.0	23	-0.26 [-0.63, 0.12]
			Placebo	60	57 (95.0)	-8.1 (13.8)	-41	-7.0	23	
		Week 8	CR845	54	48 (88.9)	-16.4 (15.4)	-53	-13.0	11	-0.42 [-0.80, -0.03]
			Placebo	60	58 (96.7)	-10.2 (14.5)	-46	-8.5	28	
		Week 10	CR845	54	47 (87.0)	-17.3 (14.6)	-53	-17.0	8	-0.60 [-0.99, -0.20]
			Placebo	60	58 (96.7)	-9.1 (13.0)	-41	-9.0	32	
		Week 12	CR845	54	47 (87.0)	-16.2 (17.2)	-58	-15.0	27	-0.41 [-0.80, -0.01]
			Placebo	60	55 (91.7)	-10.0 (13.6)	-45	-9.0	26	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2STC_ISHG: Change from baseline in Skindex-10 total score by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Western Europe/European origin	Skindex-10 total score	Baseline	CR845	29	29 (100.0)	39.7 (14.7)	8	44.0	60	
			Placebo	31	27 (87.1)	42.9 (13.0)	18	41.0	60	
		Week 4	CR845	29	22 (75.9)	25.0 (19.9)	0	27.0	60	
			Placebo	31	29 (93.5)	29.0 (17.6)	3	24.0	60	
		Week 8	CR845	29	22 (75.9)	25.5 (17.6)	0	28.0	60	
			Placebo	31	25 (80.6)	29.7 (18.3)	0	29.0	60	
		Week 10	CR845	29	22 (75.9)	19.5 (17.2)	0	18.0	60	
			Placebo	31	23 (74.2)	31.4 (19.2)	0	35.0	60	
		Week 12	CR845	29	22 (75.9)	22.1 (20.2)	0	16.0	60	
			Placebo	31	24 (77.4)	29.0 (18.4)	0	32.5	56	
	Change from baseline in Skindex-10 total score	Week 4	CR845	29	22 (75.9)	-15.0 (18.9)	-56	-10.0	12	-0.04 [-0.61, 0.53]
			Placebo	31	26 (83.9)	-14.3 (14.4)	-49	-10.0	8	
		Week 8	CR845	29	22 (75.9)	-16.1 (17.7)	-51	-14.0	12	0.00 [-0.59, 0.59]
			Placebo	31	22 (71.0)	-16.1 (12.3)	-37	-18.0	10	
		Week 10	CR845	29	22 (75.9)	-21.0 (17.8)	-56	-15.0	4	-0.56 [-1.18, 0.06]
			Placebo	31	20 (64.5)	-12.0 (13.9)	-31	-13.5	19	
		Week 12	CR845	29	22 (75.9)	-18.5 (18.7)	-56	-15.0	9	-0.30 [-0.90, 0.29]
			Placebo	31	22 (71.0)	-13.5 (14.1)	-36	-13.0	12	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2STC_ISHH: Change from baseline in Skindex-10 total score by dialysis method
ITT

H: Dialysis method	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Hemodialysis (HD)	Skindex-10 total score	Baseline	CR845	222	216 (97.3)	35.9 (15.0)	0	38.0	60	
			Placebo	199	194 (97.5)	34.2 (14.6)	0	35.0	60	
		Week 4	CR845	222	198 (89.2)	24.8 (16.3)	0	22.0	60	
			Placebo	199	179 (89.9)	26.1 (15.8)	0	24.0	60	
		Week 8	CR845	222	189 (85.1)	22.3 (17.2)	0	20.0	60	
			Placebo	199	183 (92.0)	22.6 (15.2)	0	20.0	60	
		Week 10	CR845	222	191 (86.0)	20.2 (16.8)	0	17.0	60	
			Placebo	199	179 (89.9)	21.9 (15.2)	0	19.0	60	
		Week 12	CR845	222	189 (85.1)	19.9 (16.7)	0	17.0	60	
			Placebo	199	181 (91.0)	20.1 (15.1)	0	17.0	60	
	Change from baseline in Skindex-10 total score	Week 4	CR845	222	194 (87.4)	-11.0 (15.1)	-51	-11.0	40	-0.23 [-0.43, -0.02]
			Placebo	199	176 (88.4)	-7.4 (16.4)	-55	-6.0	52	
		Week 8	CR845	222	185 (83.3)	-13.7 (16.2)	-53	-13.0	43	-0.14 [-0.34, 0.07]
			Placebo	199	180 (90.5)	-11.5 (15.5)	-57	-10.0	44	
		Week 10	CR845	222	188 (84.7)	-15.3 (15.6)	-55	-14.0	31	-0.21 [-0.41, 0.00]
			Placebo	199	175 (87.9)	-12.1 (15.9)	-57	-10.0	41	
		Week 12	CR845	222	186 (83.8)	-15.7 (16.2)	-58	-16.0	39	-0.10 [-0.31, 0.11]
			Placebo	199	178 (89.4)	-14.1 (16.7)	-59	-11.5	41	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2STC_ISHH: Change from baseline in Skindex-10 total score by dialysis method
ITT

H: Dialysis method	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Hemodiafiltration (HDF)	Skindex-10 total score	Baseline	CR845	15	15 (100.0)	29.4 (14.7)	8	25.0	56	
			Placebo	37	36 (97.3)	34.4 (15.1)	5	36.0	58	
		Week 4	CR845	15	13 (86.7)	18.7 (14.7)	0	15.0	41	
			Placebo	37	36 (97.3)	22.7 (14.7)	0	22.0	53	
		Week 8	CR845	15	13 (86.7)	17.9 (16.2)	3	13.0	51	
			Placebo	37	34 (91.9)	20.0 (16.4)	0	16.0	56	
		Week 10	CR845	15	12 (80.0)	8.9 (9.5)	0	6.0	33	
			Placebo	37	32 (86.5)	22.3 (17.7)	0	21.5	60	
		Week 12	CR845	15	13 (86.7)	14.7 (15.2)	0	9.0	45	
			Placebo	37	33 (89.2)	23.8 (17.6)	0	23.0	60	
	Change from baseline in Skindex-10 total score	Week 4	CR845	15	13 (86.7)	-12.1 (18.8)	-56	-10.0	23	-0.01 [-0.64, 0.63]
			Placebo	37	35 (94.6)	-12.0 (11.6)	-38	-10.0	9	
		Week 8	CR845	15	13 (86.7)	-12.8 (15.0)	-50	-9.0	5	0.08 [-0.56, 0.72]
			Placebo	37	33 (89.2)	-14.0 (14.4)	-46	-11.0	10	
		Week 10	CR845	15	12 (80.0)	-20.2 (15.3)	-56	-17.5	-2	-0.72 [-1.40, -0.03]
			Placebo	37	31 (83.8)	-9.7 (14.4)	-41	-9.0	19	
		Week 12	CR845	15	13 (86.7)	-16.1 (15.4)	-56	-14.0	4	-0.43 [-1.08, 0.22]
			Placebo	37	32 (86.5)	-9.9 (13.7)	-45	-9.5	13	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SDC_ISHA: Change from baseline in Skindex-10 disease score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
< 65 years	Skindex-10 disease score	Baseline	CR845	147	144 (98.0)	13.0 (4.2)	0	14.0	18	
			Placebo	153	150 (98.0)	12.4 (3.8)	3	12.5	18	
		Week 4	CR845	147	135 (91.8)	9.1 (5.0)	0	9.0	18	
			Placebo	153	140 (91.5)	10.1 (4.7)	0	10.0	18	
		Week 8	CR845	147	132 (89.8)	8.2 (5.3)	0	7.5	18	
			Placebo	153	143 (93.5)	8.3 (4.6)	0	8.0	18	
		Week 10	CR845	147	131 (89.1)	7.4 (5.2)	0	7.0	18	
			Placebo	153	138 (90.2)	8.3 (4.6)	0	8.0	18	
		Week 12	CR845	147	130 (88.4)	7.5 (5.4)	0	7.0	18	
			Placebo	153	140 (91.5)	7.8 (4.8)	0	7.0	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	147	133 (90.5)	-3.9 (4.7)	-16	-4.0	9	-0.37 [-0.61, -0.13]
			Placebo	153	138 (90.2)	-2.1 (4.9)	-17	-2.0	12	
		Week 8	CR845	147	130 (88.4)	-4.8 (5.0)	-16	-5.0	9	-0.18 [-0.41, 0.06]
			Placebo	153	141 (92.2)	-4.0 (4.6)	-16	-4.0	7	
		Week 10	CR845	147	129 (87.8)	-5.7 (4.9)	-17	-6.0	9	-0.33 [-0.58, -0.09]
			Placebo	153	136 (88.9)	-4.1 (4.6)	-15	-4.0	8	
		Week 12	CR845	147	128 (87.1)	-5.6 (5.4)	-18	-5.5	9	-0.21 [-0.46, 0.03]
			Placebo	153	139 (90.8)	-4.5 (5.1)	-18	-4.0	12	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SDC_ISHA: Change from baseline in Skindex-10 disease score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 65 years	Skindex-10 disease score	Baseline	CR845	90	89 (98.9)	12.6 (4.2)	1	13.0	18	
			Placebo	83	83 (100.0)	12.5 (4.2)	0	13.0	18	
		Week 4	CR845	90	77 (85.6)	8.9 (5.5)	0	9.0	18	
			Placebo	83	77 (92.8)	9.2 (5.2)	0	9.0	18	
		Week 8	CR845	90	77 (85.6)	8.4 (5.5)	0	8.0	18	
			Placebo	83	75 (90.4)	8.8 (5.0)	0	8.0	18	
		Week 10	CR845	90	74 (82.2)	7.1 (5.2)	0	6.0	18	
			Placebo	83	75 (90.4)	8.5 (4.8)	0	9.0	18	
		Week 12	CR845	90	73 (81.1)	7.2 (5.1)	0	8.0	18	
			Placebo	83	75 (90.4)	8.4 (4.9)	0	9.0	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	90	77 (85.6)	-3.8 (5.4)	-17	-3.0	7	-0.14 [-0.46, 0.17]
			Placebo	83	77 (92.8)	-3.1 (4.8)	-16	-3.0	6	
		Week 8	CR845	90	77 (85.6)	-4.2 (5.7)	-17	-5.0	11	-0.11 [-0.43, 0.20]
			Placebo	83	75 (90.4)	-3.6 (4.8)	-15	-3.0	9	
		Week 10	CR845	90	74 (82.2)	-5.3 (5.3)	-17	-5.0	8	-0.30 [-0.63, 0.02]
			Placebo	83	75 (90.4)	-3.7 (4.8)	-15	-3.0	8	
		Week 12	CR845	90	73 (81.1)	-5.2 (5.6)	-18	-6.0	7	-0.23 [-0.56, 0.09]
			Placebo	83	75 (90.4)	-4.0 (4.9)	-16	-4.0	7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SDC_ISHB: Change from baseline in Skindex-10 disease score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Male	Skindex-10 disease score	Baseline	CR845	137	135 (98.5)	12.5 (4.2)	0	13.0	18	
			Placebo	139	137 (98.6)	12.1 (4.1)	0	12.0	18	
		Week 4	CR845	137	124 (90.5)	9.3 (5.1)	0	9.0	18	
			Placebo	139	128 (92.1)	9.1 (5.0)	0	9.0	18	
		Week 8	CR845	137	122 (89.1)	9.0 (5.2)	0	8.0	18	
			Placebo	139	130 (93.5)	8.0 (4.5)	0	8.0	18	
		Week 10	CR845	137	118 (86.1)	8.1 (5.1)	0	8.0	18	
			Placebo	139	124 (89.2)	7.8 (4.4)	0	7.5	18	
		Week 12	CR845	137	116 (84.7)	8.1 (5.2)	0	8.0	18	
			Placebo	139	125 (89.9)	7.8 (4.4)	0	7.0	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	137	123 (89.8)	-3.2 (4.5)	-15	-3.0	7	-0.07 [-0.32, 0.17]
			Placebo	139	126 (90.6)	-2.8 (5.3)	-17	-2.0	12	
		Week 8	CR845	137	121 (88.3)	-3.5 (4.8)	-14	-4.0	11	0.11 [-0.13, 0.36]
			Placebo	139	129 (92.8)	-4.0 (4.5)	-16	-3.0	6	
		Week 10	CR845	137	117 (85.4)	-4.3 (4.4)	-15	-4.0	8	-0.06 [-0.31, 0.20]
			Placebo	139	123 (88.5)	-4.1 (4.6)	-15	-3.0	8	
		Week 12	CR845	137	115 (83.9)	-4.4 (4.8)	-15	-4.0	7	-0.05 [-0.30, 0.20]
			Placebo	139	124 (89.2)	-4.1 (4.9)	-16	-4.0	12	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SDC_ISHB: Change from baseline in Skindex-10 disease score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Female	Skindex-10 disease score	Baseline	CR845	100	98 (98.0)	13.4 (4.1)	1	14.0	18	
			Placebo	97	96 (99.0)	12.8 (3.7)	3	13.0	18	
		Week 4	CR845	100	88 (88.0)	8.6 (5.4)	0	9.0	18	
			Placebo	97	89 (91.8)	10.8 (4.6)	1	11.0	18	
		Week 8	CR845	100	87 (87.0)	7.3 (5.5)	0	7.0	18	
			Placebo	97	88 (90.7)	9.2 (5.0)	0	8.5	18	
		Week 10	CR845	100	87 (87.0)	6.2 (5.0)	0	6.0	18	
			Placebo	97	89 (91.8)	9.1 (4.9)	0	9.0	18	
		Week 12	CR845	100	87 (87.0)	6.5 (5.2)	0	6.0	18	
			Placebo	97	90 (92.8)	8.3 (5.2)	0	9.0	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	100	87 (87.0)	-4.9 (5.5)	-17	-5.0	9	-0.59 [-0.89, -0.28]
			Placebo	97	89 (91.8)	-2.0 (4.3)	-13	-2.0	7	
		Week 8	CR845	100	86 (86.0)	-6.1 (5.5)	-17	-6.0	9	-0.49 [-0.79, -0.18]
			Placebo	97	87 (89.7)	-3.5 (5.0)	-15	-3.0	9	
		Week 10	CR845	100	86 (86.0)	-7.1 (5.5)	-17	-8.0	9	-0.66 [-0.97, -0.36]
			Placebo	97	88 (90.7)	-3.8 (4.8)	-15	-3.0	5	
		Week 12	CR845	100	86 (86.0)	-7.0 (6.0)	-18	-7.0	9	-0.43 [-0.73, -0.13]
			Placebo	97	90 (92.8)	-4.6 (5.2)	-18	-3.0	5	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SDC_ISHC: Change from baseline in Skindex-10 disease score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Black/African American	Skindex-10 disease score	Baseline	CR845	53	50 (94.3)	13.3 (4.1)	2	14.0	18	
			Placebo	38	37 (97.4)	13.1 (4.0)	4	14.0	18	
		Week 4	CR845	53	46 (86.8)	10.8 (4.7)	0	10.5	18	
			Placebo	38	33 (86.8)	10.3 (4.5)	2	9.0	18	
		Week 8	CR845	53	47 (88.7)	9.7 (5.3)	0	9.0	18	
			Placebo	38	36 (94.7)	9.6 (4.7)	0	9.0	18	
		Week 10	CR845	53	44 (83.0)	8.4 (5.2)	0	8.0	18	
			Placebo	38	34 (89.5)	9.4 (5.1)	0	9.0	18	
		Week 12	CR845	53	43 (81.1)	7.9 (5.6)	0	6.0	18	
			Placebo	38	36 (94.7)	8.4 (5.0)	0	8.0	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	53	44 (83.0)	-2.8 (4.7)	-12	-3.0	9	-0.09 [-0.55, 0.36]
			Placebo	38	32 (84.2)	-2.4 (4.6)	-13	-2.0	7	
		Week 8	CR845	53	45 (84.9)	-4.0 (4.7)	-14	-5.0	6	-0.08 [-0.52, 0.37]
			Placebo	38	35 (92.1)	-3.7 (4.1)	-14	-3.0	5	
		Week 10	CR845	53	42 (79.2)	-5.3 (4.7)	-15	-6.0	4	-0.29 [-0.74, 0.17]
			Placebo	38	33 (86.8)	-3.9 (4.8)	-14	-4.0	5	
		Week 12	CR845	53	41 (77.4)	-5.7 (5.2)	-18	-6.0	6	-0.13 [-0.58, 0.32]
			Placebo	38	35 (92.1)	-5.0 (5.1)	-16	-5.0	5	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SDC_ISHC: Change from baseline in Skindex-10 disease score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
White	Skindex-10 disease score	Baseline	CR845	164	163 (99.4)	12.8 (4.2)	0	13.0	18	
			Placebo	169	169 (100.0)	12.3 (4.0)	0	13.0	18	
		Week 4	CR845	164	149 (90.9)	8.5 (5.3)	0	9.0	18	
			Placebo	169	158 (93.5)	9.8 (5.1)	0	9.0	18	
		Week 8	CR845	164	145 (88.4)	7.9 (5.5)	0	7.0	18	
			Placebo	169	157 (92.9)	8.3 (4.8)	0	8.0	18	
		Week 10	CR845	164	145 (88.4)	7.0 (5.2)	0	6.0	18	
			Placebo	169	155 (91.7)	8.2 (4.5)	0	8.0	18	
		Week 12	CR845	164	144 (87.8)	7.2 (5.2)	0	7.0	18	
			Placebo	169	156 (92.3)	8.2 (4.8)	0	8.0	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	164	149 (90.9)	-4.3 (5.1)	-17	-4.0	9	-0.36 [-0.58, -0.13]
			Placebo	169	158 (93.5)	-2.4 (5.1)	-17	-2.0	12	
		Week 8	CR845	164	145 (88.4)	-4.8 (5.5)	-17	-5.0	11	-0.17 [-0.40, 0.06]
			Placebo	169	157 (92.9)	-3.9 (4.9)	-16	-3.0	9	
		Week 10	CR845	164	145 (88.4)	-5.6 (5.1)	-17	-6.0	9	-0.34 [-0.57, -0.11]
			Placebo	169	155 (91.7)	-3.9 (4.7)	-15	-3.0	8	
		Week 12	CR845	164	144 (87.8)	-5.5 (5.5)	-18	-5.0	9	-0.28 [-0.51, -0.05]
			Placebo	169	156 (92.3)	-4.0 (5.1)	-18	-3.0	12	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SDC_ISHC: Change from baseline in Skindex-10 disease score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Other	Skindex-10 disease score	Baseline	CR845	20	20 (100.0)	12.4 (3.9)	5	12.0	18	
			Placebo	29	27 (93.1)	12.0 (3.6)	6	11.0	18	
		Week 4	CR845	20	17 (85.0)	8.9 (5.0)	0	9.0	18	
			Placebo	29	26 (89.7)	9.1 (4.3)	1	9.0	18	
		Week 8	CR845	20	17 (85.0)	8.1 (3.6)	2	7.0	13	
			Placebo	29	25 (86.2)	8.4 (4.2)	2	8.0	18	
		Week 10	CR845	20	16 (80.0)	6.5 (4.6)	0	5.5	14	
			Placebo	29	24 (82.8)	8.0 (4.7)	0	8.5	18	
		Week 12	CR845	20	16 (80.0)	7.8 (5.0)	0	8.0	18	
			Placebo	29	23 (79.3)	6.6 (4.4)	0	5.0	15	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	20	17 (85.0)	-3.3 (4.7)	-11	-3.0	5	-0.12 [-0.73, 0.50]
			Placebo	29	25 (86.2)	-2.8 (4.0)	-13	-3.0	4	
		Week 8	CR845	20	17 (85.0)	-4.5 (5.0)	-12	-4.0	7	-0.16 [-0.79, 0.46]
			Placebo	29	24 (82.8)	-3.7 (4.4)	-11	-4.0	7	
		Week 10	CR845	20	16 (80.0)	-5.8 (5.8)	-15	-5.0	8	-0.30 [-0.94, 0.34]
			Placebo	29	23 (79.3)	-4.3 (4.4)	-15	-4.0	3	
		Week 12	CR845	20	16 (80.0)	-4.8 (6.5)	-15	-5.0	7	0.09 [-0.55, 0.72]
			Placebo	29	23 (79.3)	-5.3 (4.1)	-16	-5.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SDC_ISHD: Change from baseline in Skindex-10 disease score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 4 to < 7	Skindex-10 disease score	Baseline	CR845	102	101 (99.0)	11.0 (4.2)	0	11.0	18	
			Placebo	113	112 (99.1)	10.8 (3.9)	0	10.0	18	
		Week 4	CR845	102	95 (93.1)	7.0 (4.4)	0	8.0	18	
			Placebo	113	106 (93.8)	8.3 (4.5)	0	8.0	18	
		Week 8	CR845	102	95 (93.1)	6.6 (4.6)	0	6.0	18	
			Placebo	113	105 (92.9)	7.6 (4.3)	0	7.0	18	
		Week 10	CR845	102	92 (90.2)	5.7 (4.3)	0	5.5	18	
			Placebo	113	101 (89.4)	7.2 (4.4)	0	7.0	18	
		Week 12	CR845	102	91 (89.2)	5.8 (4.5)	0	5.0	18	
			Placebo	113	102 (90.3)	7.0 (4.4)	0	6.5	16	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	102	94 (92.2)	-3.9 (4.9)	-15	-4.0	9	-0.32 [-0.60, -0.04]
			Placebo	113	105 (92.9)	-2.3 (5.2)	-16	-2.0	12	
		Week 8	CR845	102	94 (92.2)	-4.3 (5.4)	-15	-5.5	9	-0.23 [-0.51, 0.05]
			Placebo	113	105 (92.9)	-3.2 (4.3)	-14	-3.0	9	
		Week 10	CR845	102	91 (89.2)	-5.1 (4.8)	-15	-6.0	9	-0.33 [-0.61, -0.04]
			Placebo	113	101 (89.4)	-3.5 (4.6)	-14	-3.0	8	
		Week 12	CR845	102	90 (88.2)	-5.1 (5.4)	-16	-6.0	9	-0.26 [-0.55, 0.02]
			Placebo	113	102 (90.3)	-3.7 (4.8)	-16	-3.0	12	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SDC_ISHD: Change from baseline in Skindex-10 disease score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 7	Skindex-10 disease score	Baseline	CR845	135	132 (97.8)	14.3 (3.5)	0	15.0	18	
			Placebo	123	121 (98.4)	13.9 (3.4)	5	15.0	18	
		Week 4	CR845	135	117 (86.7)	10.7 (5.2)	0	11.0	18	
			Placebo	123	111 (90.2)	11.1 (4.9)	0	11.0	18	
		Week 8	CR845	135	114 (84.4)	9.7 (5.5)	0	10.0	18	
			Placebo	123	113 (91.9)	9.4 (4.9)	0	9.0	18	
		Week 10	CR845	135	113 (83.7)	8.6 (5.4)	0	9.0	18	
			Placebo	123	112 (91.1)	9.4 (4.7)	0	9.0	18	
		Week 12	CR845	135	112 (83.0)	8.7 (5.5)	0	9.0	18	
			Placebo	123	113 (91.9)	8.9 (4.9)	0	9.0	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	135	116 (85.9)	-3.8 (5.1)	-17	-3.0	9	-0.25 [-0.51, 0.01]
			Placebo	123	110 (89.4)	-2.6 (4.6)	-17	-2.0	7	
		Week 8	CR845	135	113 (83.7)	-4.8 (5.1)	-17	-4.0	11	-0.07 [-0.33, 0.19]
			Placebo	123	111 (90.2)	-4.5 (4.9)	-16	-4.0	7	
		Week 10	CR845	135	112 (83.0)	-5.9 (5.2)	-17	-6.0	3	-0.31 [-0.58, -0.05]
			Placebo	123	110 (89.4)	-4.3 (4.7)	-15	-4.0	5	
		Week 12	CR845	135	111 (82.2)	-5.8 (5.5)	-18	-4.0	5	-0.18 [-0.44, 0.09]
			Placebo	123	112 (91.1)	-4.9 (5.1)	-18	-5.0	5	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SDC_ISHE: Change from baseline in Skindex-10 disease score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	Skindex-10 disease score	Baseline	CR845	195	191 (97.9)	12.8 (4.2)	0	13.0	18	
			Placebo	199	197 (99.0)	12.1 (3.9)	0	12.0	18	
		Week 4	CR845	195	175 (89.7)	9.1 (5.1)	0	9.0	18	
			Placebo	199	186 (93.5)	9.6 (4.8)	0	9.0	18	
		Week 8	CR845	195	174 (89.2)	8.3 (5.2)	0	8.0	18	
			Placebo	199	182 (91.5)	8.2 (4.6)	0	8.0	18	
		Week 10	CR845	195	170 (87.2)	7.4 (5.1)	0	6.5	18	
			Placebo	199	178 (89.4)	8.1 (4.6)	0	8.0	18	
		Week 12	CR845	195	168 (86.2)	7.4 (5.4)	0	7.0	18	
			Placebo	199	180 (90.5)	7.8 (4.7)	0	7.0	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	195	173 (88.7)	-3.8 (4.9)	-17	-3.0	9	-0.30 [-0.51, -0.09]
			Placebo	199	185 (93.0)	-2.3 (4.8)	-17	-2.0	12	
		Week 8	CR845	195	172 (88.2)	-4.5 (4.9)	-15	-5.0	9	-0.17 [-0.38, 0.04]
			Placebo	199	181 (91.0)	-3.7 (4.8)	-16	-3.0	9	
		Week 10	CR845	195	168 (86.2)	-5.4 (4.9)	-17	-6.0	9	-0.31 [-0.52, -0.10]
			Placebo	199	177 (88.9)	-3.9 (4.8)	-15	-3.0	8	
		Week 12	CR845	195	166 (85.1)	-5.4 (5.3)	-18	-6.0	9	-0.24 [-0.45, -0.03]
			Placebo	199	180 (90.5)	-4.2 (5.1)	-18	-3.5	12	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SDC_ISHE: Change from baseline in Skindex-10 disease score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	Skindex-10 disease score	Baseline	CR845	42	42 (100.0)	13.2 (3.8)	2	13.5	18	
			Placebo	37	36 (97.3)	14.3 (3.6)	7	15.0	18	
		Week 4	CR845	42	37 (88.1)	8.5 (5.5)	0	9.0	18	
			Placebo	37	31 (83.8)	10.5 (5.5)	0	10.0	18	
		Week 8	CR845	42	35 (83.3)	8.3 (6.1)	0	9.0	18	
			Placebo	37	36 (97.3)	9.8 (5.1)	0	9.0	18	
		Week 10	CR845	42	35 (83.3)	7.0 (5.6)	0	6.0	18	
			Placebo	37	35 (94.6)	10.0 (4.5)	0	10.0	18	
		Week 12	CR845	42	35 (83.3)	7.5 (4.9)	0	8.0	18	
			Placebo	37	35 (94.6)	9.0 (5.3)	0	10.0	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	42	37 (88.1)	-4.5 (5.3)	-16	-4.0	7	-0.18 [-0.66, 0.31]
			Placebo	37	30 (81.1)	-3.6 (5.5)	-16	-2.0	7	
		Week 8	CR845	42	35 (83.3)	-4.8 (6.8)	-17	-5.0	11	-0.07 [-0.53, 0.40]
			Placebo	37	35 (94.6)	-4.5 (4.1)	-15	-3.0	3	
		Week 10	CR845	42	35 (83.3)	-6.1 (5.9)	-16	-6.0	4	-0.38 [-0.86, 0.10]
			Placebo	37	34 (91.9)	-4.3 (3.7)	-14	-3.5	1	
		Week 12	CR845	42	35 (83.3)	-5.8 (6.4)	-18	-5.0	6	-0.11 [-0.58, 0.37]
			Placebo	37	34 (91.9)	-5.2 (4.6)	-16	-4.5	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SDC_ISHF: Change from baseline in Skindex-10 disease score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	Skindex-10 disease score	Baseline	CR845	150	147 (98.0)	12.6 (4.4)	0	13.0	18	
			Placebo	151	149 (98.7)	12.3 (4.1)	0	13.0	18	
		Week 4	CR845	150	139 (92.7)	9.2 (5.2)	0	9.0	18	
			Placebo	151	143 (94.7)	9.8 (4.8)	0	9.0	18	
		Week 8	CR845	150	137 (91.3)	8.2 (5.3)	0	7.0	18	
			Placebo	151	140 (92.7)	8.3 (4.5)	0	8.0	18	
		Week 10	CR845	150	133 (88.7)	7.3 (5.1)	0	6.0	18	
			Placebo	151	137 (90.7)	8.3 (4.5)	0	8.0	18	
		Week 12	CR845	150	132 (88.0)	7.4 (5.4)	0	7.0	18	
			Placebo	151	140 (92.7)	8.0 (4.5)	0	8.0	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	150	137 (91.3)	-3.5 (5.3)	-17	-3.0	9	-0.18 [-0.42, 0.05]
			Placebo	151	141 (93.4)	-2.5 (5.0)	-17	-2.0	12	
		Week 8	CR845	150	135 (90.0)	-4.3 (5.3)	-17	-5.0	11	-0.08 [-0.32, 0.16]
			Placebo	151	139 (92.1)	-3.9 (4.7)	-16	-3.0	9	
		Week 10	CR845	150	131 (87.3)	-5.1 (4.9)	-17	-6.0	9	-0.22 [-0.46, 0.03]
			Placebo	151	136 (90.1)	-4.1 (4.9)	-15	-3.0	8	
		Week 12	CR845	150	130 (86.7)	-5.1 (5.7)	-18	-5.0	9	-0.14 [-0.38, 0.10]
			Placebo	151	139 (92.1)	-4.3 (5.0)	-17	-3.0	7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SDC_ISHF: Change from baseline in Skindex-10 disease score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	Skindex-10 disease score	Baseline	CR845	87	86 (98.9)	13.4 (3.8)	0	14.0	18	
			Placebo	85	84 (98.8)	12.5 (3.8)	3	13.0	18	
		Week 4	CR845	87	73 (83.9)	8.7 (5.2)	0	9.0	18	
			Placebo	85	74 (87.1)	9.8 (5.0)	0	9.0	18	
		Week 8	CR845	87	72 (82.8)	8.5 (5.5)	0	8.0	18	
			Placebo	85	78 (91.8)	8.8 (5.1)	0	9.0	18	
		Week 10	CR845	87	72 (82.8)	7.3 (5.3)	0	6.5	18	
			Placebo	85	76 (89.4)	8.6 (4.9)	0	8.0	18	
		Week 12	CR845	87	71 (81.6)	7.5 (5.0)	0	7.0	18	
			Placebo	85	75 (88.2)	8.0 (5.3)	0	9.0	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	87	73 (83.9)	-4.7 (4.3)	-16	-4.0	5	-0.50 [-0.83, -0.18]
			Placebo	85	74 (87.1)	-2.4 (4.7)	-15	-2.0	10	
		Week 8	CR845	87	72 (82.8)	-5.0 (5.2)	-16	-5.0	6	-0.28 [-0.60, 0.04]
			Placebo	85	77 (90.6)	-3.6 (4.6)	-15	-3.0	6	
		Week 10	CR845	87	72 (82.8)	-6.3 (5.4)	-17	-6.0	5	-0.52 [-0.85, -0.20]
			Placebo	85	75 (88.2)	-3.7 (4.2)	-15	-4.0	5	
		Week 12	CR845	87	71 (81.6)	-6.2 (4.9)	-18	-6.0	3	-0.37 [-0.70, -0.05]
			Placebo	85	75 (88.2)	-4.4 (5.0)	-18	-4.0	12	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SDC_ISHG: Change from baseline in Skindex-10 disease score by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
USA	Skindex-10 disease score	Baseline	CR845	146	142 (97.3)	13.3 (4.0)	0	14.0	18	
			Placebo	133	133 (100.0)	12.5 (3.9)	3	12.0	18	
		Week 4	CR845	146	130 (89.0)	10.1 (4.7)	0	9.5	18	
			Placebo	133	119 (89.5)	10.7 (4.8)	0	11.0	18	
		Week 8	CR845	146	130 (89.0)	9.3 (5.2)	0	9.0	18	
			Placebo	133	123 (92.5)	8.8 (4.5)	0	9.0	18	
		Week 10	CR845	146	128 (87.7)	8.2 (5.1)	0	8.0	18	
			Placebo	133	120 (90.2)	8.4 (4.4)	0	8.0	18	
		Week 12	CR845	146	127 (87.0)	8.0 (5.1)	0	8.0	18	
			Placebo	133	124 (93.2)	8.0 (4.5)	0	7.5	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	146	128 (87.7)	-3.2 (4.7)	-15	-3.0	9	-0.31 [-0.56, -0.06]
			Placebo	133	119 (89.5)	-1.7 (5.1)	-17	-1.0	12	
		Week 8	CR845	146	128 (87.7)	-4.0 (5.1)	-17	-4.0	11	-0.07 [-0.31, 0.18]
			Placebo	133	123 (92.5)	-3.6 (4.7)	-16	-3.0	9	
		Week 10	CR845	146	126 (86.3)	-5.0 (5.0)	-17	-5.0	9	-0.19 [-0.44, 0.06]
			Placebo	133	120 (90.2)	-4.0 (4.7)	-15	-3.0	8	
		Week 12	CR845	146	125 (85.6)	-5.3 (5.3)	-18	-5.0	9	-0.15 [-0.40, 0.09]
			Placebo	133	124 (93.2)	-4.5 (5.2)	-18	-4.0	12	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SDC_ISHG: Change from baseline in Skindex-10 disease score by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Asia	Skindex-10 disease score	Baseline	CR845	8	8 (100.0)	12.5 (2.9)	9	12.0	17	
			Placebo	12	12 (100.0)	12.7 (3.4)	8	12.0	18	
		Week 4	CR845	8	8 (100.0)	6.4 (4.3)	0	6.0	13	
			Placebo	12	12 (100.0)	8.8 (4.8)	1	9.5	18	
		Week 8	CR845	8	7 (87.5)	5.9 (2.2)	2	6.0	9	
			Placebo	12	12 (100.0)	7.7 (3.4)	2	8.0	12	
		Week 10	CR845	8	7 (87.5)	4.7 (3.6)	0	5.0	10	
			Placebo	12	11 (91.7)	6.5 (4.2)	0	7.0	11	
		Week 12	CR845	8	7 (87.5)	5.9 (3.4)	1	8.0	9	
			Placebo	12	11 (91.7)	5.5 (4.4)	0	5.0	15	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	8	8 (100.0)	-6.1 (4.1)	-11	-6.0	0	-0.54 [-1.45, 0.37]
			Placebo	12	12 (100.0)	-3.8 (4.3)	-13	-4.5	4	
		Week 8	CR845	8	7 (87.5)	-6.7 (3.5)	-12	-7.0	-3	-0.42 [-1.37, 0.52]
			Placebo	12	12 (100.0)	-5.0 (4.3)	-11	-5.5	2	
		Week 10	CR845	8	7 (87.5)	-7.9 (3.3)	-12	-8.0	-4	-0.42 [-1.38, 0.54]
			Placebo	12	11 (91.7)	-5.9 (5.3)	-15	-5.0	1	
		Week 12	CR845	8	7 (87.5)	-6.7 (4.6)	-14	-7.0	-1	0.02 [-0.93, 0.97]
			Placebo	12	11 (91.7)	-6.8 (4.7)	-16	-7.0	-1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SDC_ISHG: Change from baseline in Skindex-10 disease score by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Eastern Europe	Skindex-10 disease score	Baseline	CR845	54	54 (100.0)	11.6 (4.5)	0	12.0	18	
			Placebo	60	60 (100.0)	11.2 (4.2)	0	11.0	18	
		Week 4	CR845	54	52 (96.3)	6.8 (4.8)	0	6.0	17	
			Placebo	60	57 (95.0)	7.8 (4.6)	0	8.0	18	
		Week 8	CR845	54	49 (90.7)	5.9 (5.2)	0	5.0	18	
			Placebo	60	58 (96.7)	7.3 (4.9)	0	6.0	18	
		Week 10	CR845	54	48 (88.9)	5.0 (4.5)	0	4.0	17	
			Placebo	60	58 (96.7)	7.8 (4.6)	0	7.0	18	
		Week 12	CR845	54	47 (87.0)	5.8 (5.4)	0	4.0	18	
			Placebo	60	56 (93.3)	7.7 (5.0)	0	8.0	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	54	52 (96.3)	-5.0 (4.6)	-15	-4.5	5	-0.41 [-0.79, -0.03]
			Placebo	60	57 (95.0)	-3.1 (4.4)	-13	-3.0	5	
		Week 8	CR845	54	49 (90.7)	-5.7 (5.3)	-15	-6.0	6	-0.36 [-0.75, 0.02]
			Placebo	60	58 (96.7)	-3.8 (4.9)	-15	-3.0	6	
		Week 10	CR845	54	48 (88.9)	-6.5 (4.6)	-16	-7.0	3	-0.72 [-1.12, -0.33]
			Placebo	60	58 (96.7)	-3.2 (4.3)	-15	-3.0	8	
		Week 12	CR845	54	47 (87.0)	-5.7 (5.9)	-18	-6.0	9	-0.39 [-0.78, 0.00]
			Placebo	60	56 (93.3)	-3.6 (4.8)	-15	-3.0	7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SDC_ISHG: Change from baseline in Skindex-10 disease score by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Western Europe/European origin	Skindex-10 disease score	Baseline	CR845	29	29 (100.0)	13.3 (4.1)	5	14.0	18	
			Placebo	31	28 (90.3)	14.3 (3.1)	8	14.0	18	
		Week 4	CR845	29	22 (75.9)	8.8 (7.0)	0	9.5	18	
			Placebo	31	29 (93.5)	10.1 (5.1)	2	9.0	18	
		Week 8	CR845	29	23 (79.3)	8.5 (5.6)	0	8.0	18	
			Placebo	31	25 (80.6)	10.4 (5.1)	0	10.0	18	
		Week 10	CR845	29	22 (75.9)	7.6 (5.7)	0	6.5	18	
			Placebo	31	24 (77.4)	10.2 (5.5)	0	10.0	18	
		Week 12	CR845	29	22 (75.9)	8.1 (6.1)	0	8.5	18	
			Placebo	31	24 (77.4)	10.1 (5.3)	0	11.5	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	29	22 (75.9)	-4.5 (7.0)	-17	-3.0	5	-0.08 [-0.64, 0.48]
			Placebo	31	27 (87.1)	-4.1 (4.5)	-15	-4.0	3	
		Week 8	CR845	29	23 (79.3)	-5.0 (5.9)	-16	-6.0	7	-0.13 [-0.71, 0.44]
			Placebo	31	23 (74.2)	-4.3 (4.4)	-15	-4.0	5	
		Week 10	CR845	29	22 (75.9)	-5.9 (6.3)	-17	-5.5	8	-0.27 [-0.87, 0.32]
			Placebo	31	22 (71.0)	-4.3 (5.0)	-15	-4.5	5	
		Week 12	CR845	29	22 (75.9)	-5.6 (6.2)	-17	-5.0	7	-0.31 [-0.90, 0.28]
			Placebo	31	23 (74.2)	-3.9 (4.4)	-15	-4.0	5	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SDC_ISHH: Change from baseline in Skindex-10 disease score by dialysis method
ITT

H: Dialysis method	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Hemodialysis (HD)	Skindex-10 disease score	Baseline	CR845	222	218 (98.2)	13.0 (4.2)	0	13.5	18	
			Placebo	199	197 (99.0)	12.3 (4.1)	0	12.0	18	
		Week 4	CR845	222	199 (89.6)	9.1 (5.2)	0	9.0	18	
			Placebo	199	181 (91.0)	9.9 (5.0)	0	9.0	18	
		Week 8	CR845	222	196 (88.3)	8.3 (5.4)	0	8.0	18	
			Placebo	199	184 (92.5)	8.5 (4.7)	0	8.0	18	
		Week 10	CR845	222	193 (86.9)	7.4 (5.2)	0	7.0	18	
			Placebo	199	181 (91.0)	8.2 (4.5)	0	8.0	18	
		Week 12	CR845	222	190 (85.6)	7.4 (5.3)	0	7.5	18	
			Placebo	199	182 (91.5)	7.8 (4.7)	0	7.0	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	222	197 (88.7)	-3.9 (4.9)	-16	-4.0	9	-0.34 [-0.54, -0.14]
			Placebo	199	180 (90.5)	-2.2 (5.0)	-17	-1.5	12	
		Week 8	CR845	222	194 (87.4)	-4.6 (5.2)	-17	-5.0	11	-0.19 [-0.39, 0.01]
			Placebo	199	183 (92.0)	-3.7 (4.6)	-16	-3.0	9	
		Week 10	CR845	222	191 (86.0)	-5.5 (5.1)	-17	-6.0	9	-0.30 [-0.50, -0.09]
			Placebo	199	180 (90.5)	-4.0 (4.7)	-15	-3.5	8	
		Week 12	CR845	222	188 (84.7)	-5.5 (5.5)	-18	-6.0	9	-0.19 [-0.40, 0.01]
			Placebo	199	182 (91.5)	-4.5 (5.1)	-18	-4.0	12	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SDC_ISHH: Change from baseline in Skindex-10 disease score by dialysis method
ITT

H: Dialysis method	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Hemodiafiltration (HDF)	Skindex-10 disease score	Baseline	CR845	15	15 (100.0)	11.6 (3.8)	7	11.0	18	
			Placebo	37	36 (97.3)	13.0 (3.5)	5	14.0	18	
		Week 4	CR845	15	13 (86.7)	7.7 (4.7)	0	9.0	15	
			Placebo	37	36 (97.3)	9.0 (4.4)	0	9.0	18	
		Week 8	CR845	15	13 (86.7)	8.0 (5.5)	1	7.0	18	
			Placebo	37	34 (91.9)	8.3 (4.9)	0	6.5	18	
		Week 10	CR845	15	12 (80.0)	5.1 (3.8)	0	4.5	11	
			Placebo	37	32 (86.5)	9.0 (5.2)	0	10.0	18	
		Week 12	CR845	15	13 (86.7)	6.9 (5.5)	0	5.0	18	
			Placebo	37	33 (89.2)	9.5 (5.1)	0	10.0	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	15	13 (86.7)	-4.2 (5.8)	-17	-3.0	5	-0.04 [-0.68, 0.59]
			Placebo	37	35 (94.6)	-4.0 (4.2)	-13	-3.0	5	
		Week 8	CR845	15	13 (86.7)	-3.9 (5.6)	-15	-4.0	6	0.15 [-0.50, 0.79]
			Placebo	37	33 (89.2)	-4.7 (4.9)	-14	-4.0	5	
		Week 10	CR845	15	12 (80.0)	-6.5 (5.2)	-17	-8.0	3	-0.61 [-1.29, 0.07]
			Placebo	37	31 (83.8)	-3.6 (4.7)	-15	-3.0	5	
		Week 12	CR845	15	13 (86.7)	-5.0 (5.4)	-17	-5.0	4	-0.32 [-0.97, 0.32]
			Placebo	37	32 (86.5)	-3.4 (4.7)	-15	-3.0	5	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SMC_ISHA: Change from baseline in Skindex-10 mood/emotional distress score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
< 65 years	Skindex-10 mood/emotional distress score	Baseline	CR845	147	143 (97.3)	11.7 (4.9)	0	12.0	18	
			Placebo	153	150 (98.0)	11.0 (4.7)	0	11.0	18	
		Week 4	CR845	147	134 (91.2)	7.7 (5.3)	0	7.0	18	
			Placebo	153	143 (93.5)	8.5 (5.1)	0	9.0	18	
		Week 8	CR845	147	128 (87.1)	7.1 (5.6)	0	6.5	18	
			Placebo	153	142 (92.8)	6.8 (5.1)	0	6.0	18	
		Week 10	CR845	147	131 (89.1)	6.5 (5.6)	0	6.0	18	
			Placebo	153	140 (91.5)	6.9 (5.0)	0	6.0	18	
		Week 12	CR845	147	131 (89.1)	6.4 (5.6)	0	6.0	18	
			Placebo	153	141 (92.2)	6.1 (5.1)	0	5.0	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	147	131 (89.1)	-3.9 (4.7)	-17	-3.0	9	-0.28 [-0.52, -0.04]
			Placebo	153	140 (91.5)	-2.4 (5.4)	-17	-2.0	17	
		Week 8	CR845	147	125 (85.0)	-4.5 (5.3)	-16	-4.0	11	-0.07 [-0.31, 0.17]
			Placebo	153	140 (91.5)	-4.2 (5.1)	-17	-4.0	12	
		Week 10	CR845	147	128 (87.1)	-5.1 (5.4)	-18	-5.0	11	-0.20 [-0.44, 0.04]
			Placebo	153	138 (90.2)	-4.1 (5.3)	-18	-3.0	13	
		Week 12	CR845	147	128 (87.1)	-5.4 (5.8)	-18	-6.0	13	-0.10 [-0.34, 0.14]
			Placebo	153	139 (90.8)	-4.8 (5.5)	-18	-4.0	11	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SMC_ISHA: Change from baseline in Skindex-10 mood/emotional distress score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 65 years	Skindex-10 mood/emotional distress score	Baseline	CR845	90	89 (98.9)	11.0 (5.2)	0	12.0	18	
			Placebo	83	83 (100.0)	10.9 (5.2)	0	12.0	18	
		Week 4	CR845	90	78 (86.7)	7.6 (5.6)	0	8.0	18	
			Placebo	83	79 (95.2)	8.1 (5.8)	0	8.0	18	
		Week 8	CR845	90	77 (85.6)	6.7 (5.6)	0	6.0	18	
			Placebo	83	77 (92.8)	7.1 (5.4)	0	7.0	18	
		Week 10	CR845	90	73 (81.1)	5.6 (5.4)	0	4.0	18	
			Placebo	83	74 (89.2)	7.1 (5.4)	0	8.0	18	
		Week 12	CR845	90	74 (82.2)	5.6 (5.2)	0	4.0	18	
			Placebo	83	76 (91.6)	7.0 (5.7)	0	6.0	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	90	77 (85.6)	-3.6 (6.0)	-18	-4.0	14	-0.17 [-0.48, 0.15]
			Placebo	83	79 (95.2)	-2.7 (5.2)	-15	-2.0	10	
		Week 8	CR845	90	76 (84.4)	-4.3 (5.6)	-18	-3.0	9	-0.11 [-0.43, 0.21]
			Placebo	83	77 (92.8)	-3.7 (5.5)	-15	-4.0	15	
		Week 10	CR845	90	72 (80.0)	-5.3 (5.4)	-18	-4.5	5	-0.34 [-0.67, -0.02]
			Placebo	83	74 (89.2)	-3.4 (5.3)	-18	-3.0	11	
		Week 12	CR845	90	73 (81.1)	-5.3 (5.4)	-18	-5.0	6	-0.25 [-0.58, 0.07]
			Placebo	83	76 (91.6)	-3.9 (5.7)	-17	-3.0	8	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SMC_ISHB: Change from baseline in Skindex-10 mood/emotional distress score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Male	Skindex-10 mood/emotional distress score	Baseline	CR845	137	134 (97.8)	11.3 (5.0)	0	12.0	18	
			Placebo	139	136 (97.8)	10.5 (5.0)	0	11.0	18	
		Week 4	CR845	137	124 (90.5)	7.9 (5.2)	0	7.0	18	
			Placebo	139	130 (93.5)	7.9 (5.2)	0	8.0	18	
		Week 8	CR845	137	121 (88.3)	7.6 (5.8)	0	8.0	18	
			Placebo	139	131 (94.2)	6.3 (4.9)	0	5.0	18	
		Week 10	CR845	137	117 (85.4)	6.9 (5.6)	0	6.0	18	
			Placebo	139	124 (89.2)	6.2 (4.9)	0	6.0	18	
		Week 12	CR845	137	118 (86.1)	6.6 (5.6)	0	6.0	18	
			Placebo	139	126 (90.6)	5.7 (4.7)	0	5.0	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	137	122 (89.1)	-3.3 (4.7)	-15	-3.0	14	-0.15 [-0.40, 0.09]
			Placebo	139	127 (91.4)	-2.5 (5.8)	-17	-2.0	17	
		Week 8	CR845	137	119 (86.9)	-3.6 (4.9)	-15	-3.0	8	0.11 [-0.14, 0.36]
			Placebo	139	129 (92.8)	-4.2 (5.2)	-17	-4.0	12	
		Week 10	CR845	137	115 (83.9)	-4.3 (4.4)	-17	-4.0	6	-0.05 [-0.31, 0.20]
			Placebo	139	122 (87.8)	-4.0 (5.6)	-18	-3.0	13	
		Week 12	CR845	137	116 (84.7)	-4.7 (4.8)	-16	-4.0	6	-0.00 [-0.26, 0.25]
			Placebo	139	124 (89.2)	-4.6 (5.6)	-18	-4.0	11	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SMC_ISHB: Change from baseline in Skindex-10 mood/emotional distress score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Female	Skindex-10 mood/emotional distress score	Baseline	CR845	100	98 (98.0)	11.6 (5.0)	0	12.5	18	
			Placebo	97	97 (100.0)	11.6 (4.6)	0	12.0	18	
		Week 4	CR845	100	88 (88.0)	7.3 (5.7)	0	7.0	18	
			Placebo	97	92 (94.8)	9.0 (5.5)	0	9.0	18	
		Week 8	CR845	100	84 (84.0)	5.9 (5.2)	0	5.5	18	
			Placebo	97	88 (90.7)	7.8 (5.5)	0	8.0	18	
		Week 10	CR845	100	87 (87.0)	5.3 (5.3)	0	3.0	18	
			Placebo	97	90 (92.8)	8.1 (5.3)	0	8.0	18	
		Week 12	CR845	100	87 (87.0)	5.5 (5.3)	0	4.0	18	
			Placebo	97	91 (93.8)	7.4 (6.0)	0	7.0	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	100	86 (86.0)	-4.4 (5.8)	-18	-4.0	10	-0.36 [-0.66, -0.06]
			Placebo	97	92 (94.8)	-2.6 (4.7)	-14	-2.0	10	
		Week 8	CR845	100	82 (82.0)	-5.6 (6.0)	-18	-6.0	11	-0.33 [-0.63, -0.03]
			Placebo	97	88 (90.7)	-3.8 (5.3)	-17	-4.0	15	
		Week 10	CR845	100	85 (85.0)	-6.3 (6.3)	-18	-6.0	11	-0.49 [-0.80, -0.19]
			Placebo	97	90 (92.8)	-3.6 (4.8)	-17	-3.0	8	
		Week 12	CR845	100	85 (85.0)	-6.3 (6.5)	-18	-6.0	13	-0.33 [-0.63, -0.03]
			Placebo	97	91 (93.8)	-4.3 (5.5)	-18	-4.0	8	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SMC_ISHC: Change from baseline in Skindex-10 mood/emotional distress score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Black/African American	Skindex-10 mood/emotional distress score	Baseline	CR845	53	51 (96.2)	11.3 (4.6)	0	12.0	18	
			Placebo	38	37 (97.4)	12.5 (4.9)	3	13.0	18	
		Week 4	CR845	53	45 (84.9)	8.9 (5.0)	0	8.0	18	
			Placebo	38	34 (89.5)	9.8 (5.5)	0	9.0	18	
		Week 8	CR845	53	46 (86.8)	8.2 (6.0)	0	9.0	18	
			Placebo	38	36 (94.7)	8.2 (5.4)	0	9.0	18	
		Week 10	CR845	53	44 (83.0)	8.1 (5.7)	0	8.0	18	
			Placebo	38	35 (92.1)	7.9 (5.6)	0	8.0	18	
		Week 12	CR845	53	45 (84.9)	7.2 (5.7)	0	8.0	18	
			Placebo	38	37 (97.4)	6.6 (6.2)	0	4.0	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	53	43 (81.1)	-2.6 (4.7)	-10	-3.0	10	0.00 [-0.45, 0.46]
			Placebo	38	33 (86.8)	-2.6 (4.6)	-14	-3.0	10	
		Week 8	CR845	53	44 (83.0)	-3.3 (5.5)	-15	-3.0	9	0.30 [-0.15, 0.75]
			Placebo	38	35 (92.1)	-4.8 (4.1)	-17	-4.0	4	
		Week 10	CR845	53	42 (79.2)	-3.4 (4.7)	-13	-3.0	6	0.36 [-0.10, 0.81]
			Placebo	38	34 (89.5)	-5.1 (5.2)	-18	-4.5	4	
		Week 12	CR845	53	43 (81.1)	-4.3 (5.1)	-14	-4.0	4	0.41 [-0.03, 0.86]
			Placebo	38	36 (94.7)	-6.4 (5.1)	-18	-6.0	4	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SMC_ISHC: Change from baseline in Skindex-10 mood/emotional distress score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
White	Skindex-10 mood/emotional distress score	Baseline	CR845	164	161 (98.2)	11.3 (5.1)	0	12.0	18	
			Placebo	169	168 (99.4)	10.6 (4.8)	0	11.0	18	
		Week 4	CR845	164	150 (91.5)	7.2 (5.4)	0	7.0	18	
			Placebo	169	162 (95.9)	8.2 (5.4)	0	8.0	18	
		Week 8	CR845	164	142 (86.6)	6.3 (5.5)	0	6.0	18	
			Placebo	169	158 (93.5)	6.8 (5.2)	0	6.0	18	
		Week 10	CR845	164	144 (87.8)	5.6 (5.3)	0	4.0	18	
			Placebo	169	155 (91.7)	6.7 (5.0)	0	6.0	18	
		Week 12	CR845	164	144 (87.8)	5.7 (5.3)	0	4.5	18	
			Placebo	169	157 (92.9)	6.5 (5.2)	0	6.0	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	164	148 (90.2)	-4.1 (5.4)	-18	-4.0	14	-0.30 [-0.53, -0.08]
			Placebo	169	161 (95.3)	-2.4 (5.6)	-17	-2.0	17	
		Week 8	CR845	164	140 (85.4)	-4.7 (5.5)	-18	-4.0	11	-0.19 [-0.41, 0.04]
			Placebo	169	157 (92.9)	-3.7 (5.4)	-17	-3.0	15	
		Week 10	CR845	164	142 (86.6)	-5.5 (5.4)	-18	-5.0	11	-0.36 [-0.59, -0.13]
			Placebo	169	154 (91.1)	-3.6 (5.3)	-18	-3.0	13	
		Week 12	CR845	164	142 (86.6)	-5.6 (5.8)	-18	-6.0	13	-0.28 [-0.51, -0.05]
			Placebo	169	156 (92.3)	-4.0 (5.5)	-18	-3.0	11	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SMC_ISHC: Change from baseline in Skindex-10 mood/emotional distress score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Other	Skindex-10 mood/emotional distress score	Baseline	CR845	20	20 (100.0)	12.9 (4.9)	5	14.5	18	
			Placebo	29	28 (96.6)	11.1 (5.0)	0	12.0	18	
		Week 4	CR845	20	17 (85.0)	8.8 (5.8)	0	9.0	18	
			Placebo	29	26 (89.7)	7.5 (4.7)	0	7.5	18	
		Week 8	CR845	20	17 (85.0)	8.4 (5.0)	0	9.0	18	
			Placebo	29	25 (86.2)	6.0 (4.7)	0	5.0	18	
		Week 10	CR845	20	16 (80.0)	6.2 (6.3)	0	4.5	18	
			Placebo	29	24 (82.8)	7.2 (5.1)	0	8.0	18	
		Week 12	CR845	20	16 (80.0)	7.4 (6.2)	0	6.5	18	
			Placebo	29	23 (79.3)	5.9 (5.1)	0	4.0	15	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	20	17 (85.0)	-4.0 (4.1)	-13	-4.0	2	-0.23 [-0.85, 0.39]
			Placebo	29	25 (86.2)	-3.0 (4.8)	-15	-3.0	6	
		Week 8	CR845	20	17 (85.0)	-5.1 (4.8)	-12	-6.0	5	-0.07 [-0.68, 0.55]
			Placebo	29	25 (86.2)	-4.8 (5.7)	-15	-4.0	3	
		Week 10	CR845	20	16 (80.0)	-7.0 (5.9)	-18	-6.5	0	-0.58 [-1.22, 0.07]
			Placebo	29	24 (82.8)	-3.7 (5.6)	-17	-3.5	7	
		Week 12	CR845	20	16 (80.0)	-5.9 (5.8)	-18	-6.5	2	-0.20 [-0.84, 0.44]
			Placebo	29	23 (79.3)	-4.7 (6.0)	-17	-4.0	7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SMC_ISHD: Change from baseline in Skindex-10 mood/emotional distress score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 4 to < 7	Skindex-10 mood/emotional distress score	Baseline	CR845	102	101 (99.0)	10.0 (5.1)	0	11.0	18	
			Placebo	113	111 (98.2)	9.2 (5.0)	0	9.0	18	
		Week 4	CR845	102	95 (93.1)	5.6 (4.3)	0	5.0	18	
			Placebo	113	109 (96.5)	6.7 (4.7)	0	6.0	18	
		Week 8	CR845	102	94 (92.2)	5.4 (4.6)	0	4.0	18	
			Placebo	113	105 (92.9)	6.0 (5.0)	0	5.0	18	
		Week 10	CR845	102	91 (89.2)	4.4 (4.3)	0	3.0	18	
			Placebo	113	101 (89.4)	5.5 (4.7)	0	5.0	18	
		Week 12	CR845	102	91 (89.2)	4.3 (4.4)	0	3.0	18	
			Placebo	113	102 (90.3)	5.5 (4.8)	0	5.0	17	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	102	94 (92.2)	-4.2 (4.9)	-17	-4.0	9	-0.32 [-0.60, -0.04]
			Placebo	113	107 (94.7)	-2.5 (5.8)	-14	-3.0	17	
		Week 8	CR845	102	93 (91.2)	-4.4 (5.5)	-15	-4.0	11	-0.22 [-0.50, 0.06]
			Placebo	113	104 (92.0)	-3.2 (5.4)	-17	-2.0	15	
		Week 10	CR845	102	90 (88.2)	-5.4 (5.2)	-18	-5.0	11	-0.33 [-0.62, -0.05]
			Placebo	113	100 (88.5)	-3.6 (5.5)	-18	-3.0	13	
		Week 12	CR845	102	90 (88.2)	-5.6 (5.8)	-18	-6.0	13	-0.35 [-0.64, -0.06]
			Placebo	113	101 (89.4)	-3.7 (5.5)	-18	-3.0	11	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SMC_ISHD: Change from baseline in Skindex-10 mood/emotional distress score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 7	Skindex-10 mood/emotional distress score	Baseline	CR845	135	131 (97.0)	12.6 (4.6)	0	13.0	18	
			Placebo	123	122 (99.2)	12.6 (4.1)	0	12.0	18	
		Week 4	CR845	135	117 (86.7)	9.3 (5.7)	0	9.0	18	
			Placebo	123	113 (91.9)	10.0 (5.4)	0	10.0	18	
		Week 8	CR845	135	111 (82.2)	8.2 (6.0)	0	8.0	18	
			Placebo	123	114 (92.7)	7.8 (5.2)	0	7.0	18	
		Week 10	CR845	135	113 (83.7)	7.7 (5.9)	0	7.0	18	
			Placebo	123	113 (91.9)	8.3 (5.2)	0	8.0	18	
		Week 12	CR845	135	114 (84.4)	7.6 (5.8)	0	8.0	18	
			Placebo	123	115 (93.5)	7.3 (5.6)	0	6.0	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	135	114 (84.4)	-3.4 (5.4)	-18	-3.0	14	-0.17 [-0.43, 0.09]
			Placebo	123	112 (91.1)	-2.5 (4.9)	-17	-1.0	10	
		Week 8	CR845	135	108 (80.0)	-4.5 (5.4)	-18	-4.0	9	0.05 [-0.21, 0.31]
			Placebo	123	113 (91.9)	-4.8 (5.0)	-17	-5.0	7	
		Week 10	CR845	135	110 (81.5)	-5.0 (5.5)	-18	-4.0	6	-0.18 [-0.44, 0.09]
			Placebo	123	112 (91.1)	-4.1 (5.1)	-18	-3.0	8	
		Week 12	CR845	135	111 (82.2)	-5.1 (5.5)	-18	-4.0	6	0.02 [-0.24, 0.29]
			Placebo	123	114 (92.7)	-5.3 (5.5)	-18	-5.0	7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SMC_ISHE: Change from baseline in Skindex-10 mood/emotional distress score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	Skindex-10 mood/emotional distress score	Baseline	CR845	195	190 (97.4)	11.6 (5.0)	0	12.0	18	
			Placebo	199	197 (99.0)	10.6 (4.8)	0	11.0	18	
		Week 4	CR845	195	175 (89.7)	7.8 (5.3)	0	7.0	18	
			Placebo	199	189 (95.0)	8.2 (5.3)	0	8.0	18	
		Week 8	CR845	195	170 (87.2)	7.0 (5.6)	0	6.0	18	
			Placebo	199	184 (92.5)	6.7 (5.1)	0	6.0	18	
		Week 10	CR845	195	170 (87.2)	6.4 (5.6)	0	6.0	18	
			Placebo	199	178 (89.4)	6.7 (5.0)	0	6.0	18	
		Week 12	CR845	195	170 (87.2)	6.2 (5.6)	0	5.0	18	
			Placebo	199	182 (91.5)	6.2 (5.1)	0	5.0	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	195	171 (87.7)	-3.8 (4.9)	-18	-4.0	9	-0.29 [-0.50, -0.08]
			Placebo	199	187 (94.0)	-2.3 (5.4)	-17	-2.0	17	
		Week 8	CR845	195	166 (85.1)	-4.5 (5.1)	-18	-4.0	9	-0.11 [-0.33, 0.10]
			Placebo	199	183 (92.0)	-3.9 (5.3)	-17	-4.0	15	
		Week 10	CR845	195	166 (85.1)	-5.1 (5.1)	-18	-5.0	9	-0.26 [-0.48, -0.05]
			Placebo	199	177 (88.9)	-3.8 (5.4)	-18	-3.0	13	
		Week 12	CR845	195	166 (85.1)	-5.4 (5.5)	-18	-6.0	9	-0.19 [-0.40, 0.02]
			Placebo	199	181 (91.0)	-4.4 (5.6)	-18	-4.0	11	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SMC_ISHE: Change from baseline in Skindex-10 mood/emotional distress score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	Skindex-10 mood/emotional distress score	Baseline	CR845	42	42 (100.0)	10.9 (5.0)	0	12.0	18	
			Placebo	37	36 (97.3)	12.8 (4.7)	0	13.0	18	
		Week 4	CR845	42	37 (88.1)	7.2 (5.8)	0	8.0	18	
			Placebo	37	33 (89.2)	9.0 (5.6)	0	9.0	18	
		Week 8	CR845	42	35 (83.3)	6.5 (5.7)	0	6.0	18	
			Placebo	37	35 (94.6)	8.3 (5.6)	0	8.0	18	
		Week 10	CR845	42	34 (81.0)	5.3 (5.4)	0	4.5	18	
			Placebo	37	36 (97.3)	8.4 (5.5)	0	9.0	18	
		Week 12	CR845	42	35 (83.3)	5.8 (5.2)	0	6.0	18	
			Placebo	37	35 (94.6)	7.4 (6.3)	0	8.0	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	42	37 (88.1)	-3.7 (6.4)	-17	-3.0	14	0.03 [-0.44, 0.51]
			Placebo	37	32 (86.5)	-3.9 (4.9)	-14	-3.0	5	
		Week 8	CR845	42	35 (83.3)	-4.2 (6.9)	-16	-3.0	11	0.06 [-0.41, 0.54]
			Placebo	37	34 (91.9)	-4.6 (4.9)	-17	-4.5	4	
		Week 10	CR845	42	34 (81.0)	-5.4 (6.7)	-18	-4.5	11	-0.18 [-0.65, 0.29]
			Placebo	37	35 (94.6)	-4.3 (4.8)	-18	-3.0	2	
		Week 12	CR845	42	35 (83.3)	-5.1 (6.4)	-18	-5.0	13	0.03 [-0.44, 0.50]
			Placebo	37	34 (91.9)	-5.3 (5.6)	-18	-3.0	4	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SMC_ISHF: Change from baseline in Skindex-10 mood/emotional distress score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	Skindex-10 mood/emotional distress score	Baseline	CR845	150	146 (97.3)	11.1 (5.0)	0	12.0	18	
			Placebo	151	148 (98.0)	10.6 (4.9)	0	11.0	18	
		Week 4	CR845	150	139 (92.7)	7.5 (5.2)	0	7.0	18	
			Placebo	151	144 (95.4)	8.0 (5.4)	0	8.0	18	
		Week 8	CR845	150	137 (91.3)	6.7 (5.5)	0	6.0	18	
			Placebo	151	140 (92.7)	6.5 (5.0)	0	6.0	18	
		Week 10	CR845	150	131 (87.3)	6.0 (5.5)	0	5.0	18	
			Placebo	151	138 (91.4)	6.8 (5.1)	0	6.0	18	
		Week 12	CR845	150	134 (89.3)	5.8 (5.4)	0	4.5	18	
			Placebo	151	141 (93.4)	6.1 (5.3)	0	5.0	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	150	136 (90.7)	-3.7 (5.6)	-18	-4.0	14	-0.21 [-0.45, 0.02]
			Placebo	151	141 (93.4)	-2.5 (5.3)	-17	-2.0	17	
		Week 8	CR845	150	134 (89.3)	-4.4 (5.6)	-18	-3.5	11	-0.05 [-0.29, 0.19]
			Placebo	151	138 (91.4)	-4.1 (5.4)	-17	-4.0	15	
		Week 10	CR845	150	128 (85.3)	-4.9 (5.5)	-18	-4.0	11	-0.21 [-0.45, 0.04]
			Placebo	151	136 (90.1)	-3.8 (5.6)	-18	-3.0	13	
		Week 12	CR845	150	131 (87.3)	-5.2 (5.8)	-18	-5.0	13	-0.11 [-0.35, 0.13]
			Placebo	151	139 (92.1)	-4.6 (5.8)	-18	-4.0	11	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SMC_ISHF: Change from baseline in Skindex-10 mood/emotional distress score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	Skindex-10 mood/emotional distress score	Baseline	CR845	87	86 (98.9)	12.0 (4.9)	0	13.0	18	
			Placebo	85	85 (100.0)	11.6 (4.8)	0	12.0	18	
		Week 4	CR845	87	73 (83.9)	8.1 (5.8)	0	8.0	18	
			Placebo	85	78 (91.8)	8.9 (5.2)	0	8.5	18	
		Week 8	CR845	87	68 (78.2)	7.3 (5.9)	0	7.5	18	
			Placebo	85	79 (92.9)	7.7 (5.4)	0	7.0	18	
		Week 10	CR845	87	73 (83.9)	6.5 (5.7)	0	7.0	18	
			Placebo	85	76 (89.4)	7.3 (5.3)	0	7.0	18	
		Week 12	CR845	87	71 (81.6)	6.7 (5.6)	0	6.0	18	
			Placebo	85	76 (89.4)	7.1 (5.4)	0	6.5	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	87	72 (82.8)	-3.9 (4.3)	-16	-4.0	5	-0.29 [-0.61, 0.03]
			Placebo	85	78 (91.8)	-2.5 (5.5)	-14	-2.5	14	
		Week 8	CR845	87	67 (77.0)	-4.6 (5.2)	-16	-4.0	6	-0.14 [-0.47, 0.18]
			Placebo	85	79 (92.9)	-3.8 (5.0)	-17	-3.0	10	
		Week 10	CR845	87	72 (82.8)	-5.6 (5.0)	-18	-5.5	5	-0.34 [-0.66, -0.01]
			Placebo	85	76 (89.4)	-4.0 (4.6)	-18	-3.5	4	
		Week 12	CR845	87	70 (80.5)	-5.6 (5.4)	-18	-6.0	4	-0.23 [-0.55, 0.10]
			Placebo	85	76 (89.4)	-4.4 (5.2)	-17	-4.0	10	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SMC_ISHG: Change from baseline in Skindex-10 mood/emotional distress score by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
USA	Skindex-10 mood/emotional distress score	Baseline	CR845	146	141 (96.6)	11.7 (4.7)	0	12.0	18	
			Placebo	133	132 (99.2)	11.2 (4.5)	0	12.0	18	
		Week 4	CR845	146	130 (89.0)	8.4 (5.2)	0	8.0	18	
			Placebo	133	121 (91.0)	9.3 (5.1)	0	9.0	18	
		Week 8	CR845	146	126 (86.3)	7.7 (5.5)	0	8.0	18	
			Placebo	133	123 (92.5)	7.2 (5.0)	0	7.0	18	
		Week 10	CR845	146	128 (87.7)	7.4 (5.5)	0	7.0	18	
			Placebo	133	121 (91.0)	7.1 (4.7)	0	7.0	18	
		Week 12	CR845	146	129 (88.4)	7.0 (5.4)	0	7.0	18	
			Placebo	133	125 (94.0)	6.4 (5.1)	0	5.0	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	146	126 (86.3)	-3.4 (5.3)	-17	-3.0	14	-0.29 [-0.54, -0.04]
			Placebo	133	120 (90.2)	-1.8 (5.7)	-17	-1.0	17	
		Week 8	CR845	146	122 (83.6)	-3.9 (5.5)	-15	-3.5	11	0.02 [-0.23, 0.27]
			Placebo	133	122 (91.7)	-4.0 (5.5)	-17	-4.0	15	
		Week 10	CR845	146	124 (84.9)	-4.4 (5.3)	-18	-4.0	11	-0.05 [-0.30, 0.21]
			Placebo	133	120 (90.2)	-4.1 (5.6)	-18	-3.0	13	
		Week 12	CR845	146	125 (85.6)	-4.8 (5.5)	-18	-5.0	13	-0.00 [-0.25, 0.25]
			Placebo	133	124 (93.2)	-4.8 (5.9)	-18	-4.0	11	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SMC_ISHG: Change from baseline in Skindex-10 mood/emotional distress score by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Asia	Skindex-10 mood/emotional distress score	Baseline	CR845	8	8 (100.0)	11.8 (4.1)	6	11.0	18	
			Placebo	12	12 (100.0)	11.3 (5.5)	0	13.0	18	
		Week 4	CR845	8	8 (100.0)	5.5 (4.5)	0	5.0	12	
			Placebo	12	12 (100.0)	7.2 (5.4)	1	5.0	18	
		Week 8	CR845	8	7 (87.5)	6.0 (2.7)	2	6.0	9	
			Placebo	12	12 (100.0)	4.8 (4.1)	0	5.0	13	
		Week 10	CR845	8	7 (87.5)	3.4 (4.1)	0	2.0	9	
			Placebo	12	11 (91.7)	4.8 (4.0)	0	4.0	10	
		Week 12	CR845	8	7 (87.5)	4.1 (3.3)	0	3.0	9	
			Placebo	12	11 (91.7)	4.5 (4.2)	0	4.0	13	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	8	8 (100.0)	-6.3 (3.8)	-13	-6.5	0	-0.46 [-1.36, 0.45]
			Placebo	12	12 (100.0)	-4.2 (5.0)	-15	-5.0	2	
		Week 8	CR845	8	7 (87.5)	-6.6 (3.8)	-12	-7.0	-1	-0.01 [-0.95, 0.92]
			Placebo	12	12 (100.0)	-6.5 (5.6)	-15	-8.0	2	
		Week 10	CR845	8	7 (87.5)	-9.1 (5.1)	-16	-9.0	-1	-0.52 [-1.48, 0.44]
			Placebo	12	11 (91.7)	-6.0 (6.6)	-17	-7.0	4	
		Week 12	CR845	8	7 (87.5)	-8.4 (4.1)	-13	-9.0	-1	-0.44 [-1.40, 0.52]
			Placebo	12	11 (91.7)	-6.3 (5.4)	-17	-4.0	0	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SMC_ISHG: Change from baseline in Skindex-10 mood/emotional distress score by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Eastern Europe	Skindex-10 mood/emotional distress score	Baseline	CR845	54	54 (100.0)	9.3 (5.5)	0	10.5	18	
			Placebo	60	60 (100.0)	8.7 (5.0)	0	10.0	18	
		Week 4	CR845	54	52 (96.3)	6.0 (5.3)	0	4.5	18	
			Placebo	60	59 (98.3)	5.9 (4.9)	0	5.0	18	
		Week 8	CR845	54	49 (90.7)	4.2 (5.2)	0	3.0	18	
			Placebo	60	58 (96.7)	5.5 (5.0)	0	5.0	17	
		Week 10	CR845	54	47 (87.0)	3.3 (4.3)	0	2.0	18	
			Placebo	60	58 (96.7)	5.8 (5.3)	0	5.5	18	
		Week 12	CR845	54	47 (87.0)	3.6 (4.5)	0	2.0	18	
			Placebo	60	56 (93.3)	5.2 (4.7)	0	4.0	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	54	52 (96.3)	-3.4 (4.7)	-15	-3.5	7	-0.15 [-0.52, 0.22]
			Placebo	60	59 (98.3)	-2.7 (4.8)	-13	-2.0	10	
		Week 8	CR845	54	49 (90.7)	-5.1 (5.2)	-18	-5.0	4	-0.38 [-0.77, 0.00]
			Placebo	60	58 (96.7)	-3.1 (4.8)	-15	-2.5	10	
		Week 10	CR845	54	47 (87.0)	-5.6 (4.9)	-18	-5.0	3	-0.59 [-0.98, -0.19]
			Placebo	60	58 (96.7)	-2.8 (4.6)	-13	-2.0	11	
		Week 12	CR845	54	47 (87.0)	-5.5 (5.7)	-17	-6.0	8	-0.36 [-0.76, 0.03]
			Placebo	60	56 (93.3)	-3.6 (5.0)	-16	-3.0	8	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SMC_ISHG: Change from baseline in Skindex-10 mood/emotional distress score by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Western Europe/European origin	Skindex-10 mood/emotional distress score	Baseline	CR845	29	29 (100.0)	13.7 (4.4)	3	15.0	18	
			Placebo	31	29 (93.5)	14.3 (3.4)	6	15.0	18	
		Week 4	CR845	29	22 (75.9)	8.2 (6.5)	0	9.0	18	
			Placebo	31	30 (96.8)	9.8 (5.8)	0	9.5	18	
		Week 8	CR845	29	23 (79.3)	8.5 (5.9)	0	9.0	18	
			Placebo	31	26 (83.9)	9.7 (5.8)	0	11.0	18	
		Week 10	CR845	29	22 (75.9)	6.4 (5.9)	0	5.5	18	
			Placebo	31	24 (77.4)	10.4 (6.1)	0	12.0	18	
		Week 12	CR845	29	22 (75.9)	6.9 (6.9)	0	5.5	18	
			Placebo	31	25 (80.6)	10.2 (6.6)	0	12.0	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	29	22 (75.9)	-5.6 (5.8)	-18	-4.5	2	-0.27 [-0.83, 0.29]
			Placebo	31	28 (90.3)	-4.2 (4.5)	-13	-3.0	4	
		Week 8	CR845	29	23 (79.3)	-5.5 (5.6)	-16	-4.0	5	-0.11 [-0.68, 0.45]
			Placebo	31	25 (80.6)	-5.0 (4.3)	-12	-6.0	6	
		Week 10	CR845	29	22 (75.9)	-7.4 (5.6)	-18	-6.0	0	-0.69 [-1.29, -0.09]
			Placebo	31	23 (74.2)	-3.9 (4.7)	-11	-4.0	6	
		Week 12	CR845	29	22 (75.9)	-7.0 (6.3)	-18	-6.0	2	-0.48 [-1.07, 0.10]
			Placebo	31	24 (77.4)	-4.3 (5.0)	-12	-4.5	5	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SMC_ISHH: Change from baseline in Skindex-10 mood/emotional distress score by dialysis method
ITT

H: Dialysis method	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Hemodialysis (HD)	Skindex-10 mood/emotional distress score	Baseline	CR845	222	217 (97.7)	11.5 (5.0)	0	12.0	18	
			Placebo	199	197 (99.0)	10.9 (4.9)	0	11.0	18	
		Week 4	CR845	222	199 (89.6)	7.8 (5.4)	0	7.0	18	
			Placebo	199	185 (93.0)	8.6 (5.4)	0	9.0	18	
		Week 8	CR845	222	192 (86.5)	7.0 (5.6)	0	7.0	18	
			Placebo	199	184 (92.5)	7.0 (5.1)	0	6.5	18	
		Week 10	CR845	222	192 (86.5)	6.4 (5.6)	0	6.0	18	
			Placebo	199	182 (91.5)	7.0 (4.9)	0	6.0	18	
		Week 12	CR845	222	192 (86.5)	6.3 (5.5)	0	6.0	18	
			Placebo	199	183 (92.0)	6.2 (5.1)	0	5.0	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	222	195 (87.8)	-3.7 (5.1)	-17	-4.0	14	-0.29 [-0.50, -0.09]
			Placebo	199	183 (92.0)	-2.1 (5.5)	-17	-2.0	17	
		Week 8	CR845	222	188 (84.7)	-4.4 (5.4)	-18	-4.0	11	-0.10 [-0.31, 0.10]
			Placebo	199	183 (92.0)	-3.8 (5.2)	-17	-3.0	15	
		Week 10	CR845	222	188 (84.7)	-5.0 (5.3)	-18	-4.5	11	-0.21 [-0.41, -0.00]
			Placebo	199	181 (91.0)	-3.9 (5.3)	-18	-3.0	13	
		Week 12	CR845	222	188 (84.7)	-5.2 (5.6)	-18	-5.0	13	-0.11 [-0.31, 0.09]
			Placebo	199	182 (91.5)	-4.6 (5.6)	-18	-4.0	11	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SMC_ISHH: Change from baseline in Skindex-10 mood/emotional distress score by dialysis method
ITT

H: Dialysis method	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Hemodiafiltration (HDF)	Skindex-10 mood/emotional distress score	Baseline	CR845	15	15 (100.0)	10.6 (5.1)	0	12.0	18	
			Placebo	37	36 (97.3)	11.4 (5.0)	0	12.0	18	
		Week 4	CR845	15	13 (86.7)	5.8 (5.0)	0	5.0	13	
			Placebo	37	37 (100.0)	7.0 (5.2)	0	7.0	18	
		Week 8	CR845	15	13 (86.7)	5.5 (5.0)	0	4.0	15	
			Placebo	37	35 (94.6)	6.4 (5.7)	0	5.0	18	
		Week 10	CR845	15	12 (80.0)	2.4 (3.1)	0	1.5	10	
			Placebo	37	32 (86.5)	7.2 (6.3)	0	7.5	18	
		Week 12	CR845	15	13 (86.7)	3.5 (3.6)	0	3.0	12	
			Placebo	37	34 (91.9)	7.5 (6.3)	0	7.5	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	15	13 (86.7)	-5.0 (6.3)	-18	-4.0	6	-0.11 [-0.75, 0.52]
			Placebo	37	36 (97.3)	-4.5 (3.9)	-13	-6.0	4	
		Week 8	CR845	15	13 (86.7)	-5.3 (5.5)	-16	-6.0	2	-0.07 [-0.71, 0.57]
			Placebo	37	34 (91.9)	-4.9 (5.3)	-15	-5.5	7	
		Week 10	CR845	15	12 (80.0)	-7.8 (5.4)	-18	-8.0	0	-0.83 [-1.53, -0.14]
			Placebo	37	31 (83.8)	-3.5 (5.2)	-13	-3.0	8	
		Week 12	CR845	15	13 (86.7)	-7.4 (5.3)	-18	-7.0	1	-0.65 [-1.30, 0.01]
			Placebo	37	33 (89.2)	-4.0 (5.2)	-16	-4.0	7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SSC_ISHA: Change from baseline in Skindex-10 social functioning score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
< 65 years	Skindex-10 social functioning score	Baseline	CR845	147	144 (98.0)	11.5 (7.8)	0	12.0	24	
			Placebo	153	151 (98.7)	11.3 (7.9)	0	11.0	24	
		Week 4	CR845	147	135 (91.8)	8.3 (7.3)	0	8.0	24	
			Placebo	153	142 (92.8)	8.1 (7.4)	0	6.0	24	
		Week 8	CR845	147	131 (89.1)	7.0 (7.1)	0	5.0	24	
			Placebo	153	143 (93.5)	6.8 (7.0)	0	5.0	24	
		Week 10	CR845	147	132 (89.8)	6.6 (7.1)	0	4.0	24	
			Placebo	153	140 (91.5)	7.2 (7.2)	0	5.0	24	
		Week 12	CR845	147	130 (88.4)	6.5 (7.2)	0	4.0	24	
			Placebo	153	140 (91.5)	6.5 (7.0)	0	4.0	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	147	133 (90.5)	-3.2 (7.1)	-24	-3.0	19	0.00 [-0.23, 0.24]
			Placebo	153	141 (92.2)	-3.2 (7.8)	-24	-2.0	23	
		Week 8	CR845	147	129 (87.8)	-4.5 (7.8)	-23	-4.0	16	-0.03 [-0.27, 0.21]
			Placebo	153	142 (92.8)	-4.2 (7.4)	-24	-3.0	22	
		Week 10	CR845	147	130 (88.4)	-4.9 (7.7)	-24	-4.0	20	-0.12 [-0.36, 0.12]
			Placebo	153	139 (90.8)	-3.9 (7.8)	-24	-2.0	22	
		Week 12	CR845	147	128 (87.1)	-5.0 (7.9)	-23	-4.0	20	-0.04 [-0.28, 0.20]
			Placebo	153	140 (91.5)	-4.7 (8.2)	-24	-3.0	24	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SSC_ISHA: Change from baseline in Skindex-10 social functioning score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 65 years	Skindex-10 social functioning score	Baseline	CR845	90	90 (100.0)	10.7 (8.0)	0	10.0	24	
			Placebo	83	81 (97.6)	10.2 (7.3)	0	10.0	24	
		Week 4	CR845	90	78 (86.7)	7.4 (7.1)	0	5.0	24	
			Placebo	83	80 (96.4)	6.6 (6.9)	0	4.5	24	
		Week 8	CR845	90	76 (84.4)	6.3 (7.2)	0	4.0	24	
			Placebo	83	77 (92.8)	6.6 (6.9)	0	5.0	24	
		Week 10	CR845	90	74 (82.2)	5.7 (7.1)	0	2.0	24	
			Placebo	83	74 (89.2)	6.0 (6.7)	0	4.5	24	
		Week 12	CR845	90	74 (82.2)	5.9 (7.1)	0	2.5	24	
			Placebo	83	76 (91.6)	5.9 (6.6)	0	5.0	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	90	78 (86.7)	-3.4 (7.5)	-23	-3.0	19	0.02 [-0.29, 0.33]
			Placebo	83	79 (95.2)	-3.6 (7.1)	-24	-2.0	13	
		Week 8	CR845	90	76 (84.4)	-4.5 (6.9)	-23	-4.0	24	-0.13 [-0.44, 0.19]
			Placebo	83	76 (91.6)	-3.6 (6.9)	-21	-2.5	20	
		Week 10	CR845	90	74 (82.2)	-4.9 (6.6)	-23	-4.0	13	-0.14 [-0.46, 0.18]
			Placebo	83	72 (86.7)	-3.9 (6.9)	-24	-3.0	13	
		Week 12	CR845	90	74 (82.2)	-4.6 (6.4)	-22	-4.0	12	-0.04 [-0.36, 0.28]
			Placebo	83	74 (89.2)	-4.3 (7.0)	-24	-3.0	11	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SSC_ISHB: Change from baseline in Skindex-10 social functioning score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Male	Skindex-10 social functioning score	Baseline	CR845	137	135 (98.5)	11.1 (7.7)	0	11.0	24	
			Placebo	139	137 (98.6)	10.6 (7.5)	0	10.0	24	
		Week 4	CR845	137	125 (91.2)	8.3 (7.1)	0	8.0	24	
			Placebo	139	130 (93.5)	6.6 (6.7)	0	4.0	24	
		Week 8	CR845	137	123 (89.8)	7.4 (7.3)	0	6.0	24	
			Placebo	139	131 (94.2)	6.1 (6.3)	0	4.0	24	
		Week 10	CR845	137	118 (86.1)	6.8 (7.4)	0	5.0	24	
			Placebo	139	125 (89.9)	5.9 (6.4)	0	4.0	24	
		Week 12	CR845	137	118 (86.1)	7.0 (7.1)	0	4.0	24	
			Placebo	139	126 (90.6)	5.7 (6.4)	0	4.0	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	137	124 (90.5)	-2.9 (6.3)	-24	-3.0	19	0.16 [-0.09, 0.41]
			Placebo	139	128 (92.1)	-4.1 (8.2)	-24	-2.0	23	
		Week 8	CR845	137	122 (89.1)	-3.8 (7.0)	-23	-4.0	24	0.10 [-0.15, 0.35]
			Placebo	139	130 (93.5)	-4.5 (7.4)	-24	-2.5	22	
		Week 10	CR845	137	117 (85.4)	-4.2 (6.4)	-24	-4.0	20	0.03 [-0.22, 0.28]
			Placebo	139	124 (89.2)	-4.4 (8.3)	-24	-3.0	22	
		Week 12	CR845	137	117 (85.4)	-4.2 (6.3)	-23	-4.0	16	0.09 [-0.16, 0.34]
			Placebo	139	125 (89.9)	-4.8 (8.3)	-24	-4.0	24	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SSC_ISHB: Change from baseline in Skindex-10 social functioning score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Female	Skindex-10 social functioning score	Baseline	CR845	100	99 (99.0)	11.4 (8.3)	0	12.0	24	
			Placebo	97	95 (97.9)	11.4 (8.0)	0	12.0	24	
		Week 4	CR845	100	88 (88.0)	7.4 (7.4)	0	4.0	24	
			Placebo	97	92 (94.8)	8.8 (7.8)	0	8.0	24	
		Week 8	CR845	100	84 (84.0)	5.8 (6.8)	0	4.0	24	
			Placebo	97	89 (91.8)	7.7 (7.7)	0	6.0	24	
		Week 10	CR845	100	88 (88.0)	5.5 (6.7)	0	2.0	24	
			Placebo	97	89 (91.8)	7.9 (7.6)	0	7.0	24	
		Week 12	CR845	100	86 (86.0)	5.3 (7.1)	0	1.0	24	
			Placebo	97	90 (92.8)	7.2 (7.4)	0	5.0	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	100	87 (87.0)	-3.8 (8.4)	-23	-4.0	13	-0.20 [-0.49, 0.09]
			Placebo	97	92 (94.8)	-2.3 (6.3)	-22	-2.0	12	
		Week 8	CR845	100	83 (83.0)	-5.5 (8.1)	-23	-5.0	15	-0.29 [-0.59, 0.01]
			Placebo	97	88 (90.7)	-3.3 (7.0)	-24	-3.0	20	
		Week 10	CR845	100	87 (87.0)	-5.8 (8.3)	-23	-4.0	17	-0.34 [-0.64, -0.04]
			Placebo	97	87 (89.7)	-3.3 (6.1)	-24	-2.0	10	
		Week 12	CR845	100	85 (85.0)	-5.7 (8.7)	-23	-5.0	20	-0.20 [-0.50, 0.09]
			Placebo	97	89 (91.8)	-4.1 (7.0)	-24	-2.0	7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SSC_ISHC: Change from baseline in Skindex-10 social functioning score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Black/African American	Skindex-10 social functioning score	Baseline	CR845	53	51 (96.2)	10.9 (7.5)	0	9.0	24	
			Placebo	38	38 (100.0)	11.9 (8.9)	0	12.5	24	
		Week 4	CR845	53	46 (86.8)	8.7 (7.2)	0	7.5	24	
			Placebo	38	35 (92.1)	6.5 (7.9)	0	3.0	24	
		Week 8	CR845	53	47 (88.7)	6.6 (7.3)	0	4.0	24	
			Placebo	38	37 (97.4)	7.9 (7.5)	0	6.0	24	
		Week 10	CR845	53	44 (83.0)	7.0 (7.8)	0	4.0	24	
			Placebo	38	36 (94.7)	7.9 (8.0)	0	6.0	24	
		Week 12	CR845	53	45 (84.9)	6.6 (7.4)	0	4.0	24	
			Placebo	38	37 (97.4)	6.1 (7.9)	0	1.0	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	53	44 (83.0)	-2.4 (6.7)	-24	-2.0	13	0.37 [-0.08, 0.81]
			Placebo	38	35 (92.1)	-5.0 (7.5)	-24	-3.0	6	
		Week 8	CR845	53	45 (84.9)	-4.4 (6.9)	-23	-3.0	12	-0.03 [-0.47, 0.40]
			Placebo	38	37 (97.4)	-4.2 (7.1)	-24	-4.0	10	
		Week 10	CR845	53	42 (79.2)	-3.8 (6.0)	-22	-3.0	9	0.10 [-0.34, 0.55]
			Placebo	38	36 (94.7)	-4.4 (7.1)	-24	-3.0	10	
		Week 12	CR845	53	43 (81.1)	-4.4 (6.5)	-20	-4.0	12	0.23 [-0.21, 0.67]
			Placebo	38	37 (97.4)	-6.0 (7.8)	-24	-5.0	5	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SSC_ISHC: Change from baseline in Skindex-10 social functioning score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
White	Skindex-10 social functioning score	Baseline	CR845	164	163 (99.4)	11.1 (8.1)	0	11.0	24	
			Placebo	169	168 (99.4)	10.5 (7.4)	0	10.0	24	
		Week 4	CR845	164	150 (91.5)	7.4 (7.2)	0	5.5	24	
			Placebo	169	161 (95.3)	7.9 (7.4)	0	5.0	24	
		Week 8	CR845	164	143 (87.2)	6.6 (7.2)	0	4.0	24	
			Placebo	169	158 (93.5)	6.6 (7.0)	0	4.5	24	
		Week 10	CR845	164	146 (89.0)	6.0 (6.8)	0	4.0	24	
			Placebo	169	154 (91.1)	6.6 (6.8)	0	5.0	24	
		Week 12	CR845	164	143 (87.2)	6.0 (6.9)	0	4.0	24	
			Placebo	169	156 (92.3)	6.4 (6.7)	0	4.5	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	164	150 (91.5)	-3.6 (7.4)	-23	-3.0	19	-0.10 [-0.33, 0.12]
			Placebo	169	160 (94.7)	-2.8 (7.5)	-22	-2.0	23	
		Week 8	CR845	164	143 (87.2)	-4.4 (7.6)	-23	-4.0	24	-0.10 [-0.32, 0.13]
			Placebo	169	157 (92.9)	-3.7 (7.3)	-24	-2.0	22	
		Week 10	CR845	164	146 (89.0)	-4.9 (7.3)	-24	-4.0	17	-0.17 [-0.40, 0.06]
			Placebo	169	153 (90.5)	-3.6 (7.6)	-24	-2.0	22	
		Week 12	CR845	164	143 (87.2)	-4.9 (7.6)	-23	-4.0	20	-0.11 [-0.34, 0.12]
			Placebo	169	155 (91.7)	-4.1 (7.8)	-24	-3.0	24	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SSC_ISHC: Change from baseline in Skindex-10 social functioning score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Other	Skindex-10 social functioning score	Baseline	CR845	20	20 (100.0)	13.5 (7.4)	1	13.0	24	
			Placebo	29	26 (89.7)	11.8 (7.7)	0	13.0	24	
		Week 4	CR845	20	17 (85.0)	10.4 (7.1)	0	11.0	24	
			Placebo	29	26 (89.7)	6.9 (5.3)	0	6.5	21	
		Week 8	CR845	20	17 (85.0)	8.7 (6.3)	0	8.0	20	
			Placebo	29	25 (86.2)	5.9 (5.7)	0	5.0	23	
		Week 10	CR845	20	16 (80.0)	6.4 (8.1)	0	2.0	21	
			Placebo	29	24 (82.8)	6.3 (6.8)	0	6.0	24	
		Week 12	CR845	20	16 (80.0)	8.3 (8.2)	0	3.5	22	
			Placebo	29	23 (79.3)	5.6 (6.2)	0	4.0	19	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	20	17 (85.0)	-2.8 (7.5)	-12	-3.0	19	0.23 [-0.39, 0.85]
			Placebo	29	25 (86.2)	-4.5 (7.1)	-18	-2.0	4	
		Week 8	CR845	20	17 (85.0)	-5.2 (8.1)	-19	-7.0	16	0.08 [-0.54, 0.71]
			Placebo	29	24 (82.8)	-5.9 (7.3)	-21	-3.5	4	
		Week 10	CR845	20	16 (80.0)	-7.3 (9.4)	-22	-8.5	20	-0.24 [-0.89, 0.41]
			Placebo	29	22 (75.9)	-5.2 (8.0)	-24	-7.5	11	
		Week 12	CR845	20	16 (80.0)	-5.1 (8.2)	-22	-4.5	16	0.04 [-0.60, 0.69]
			Placebo	29	22 (75.9)	-5.5 (7.5)	-24	-3.5	5	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SSC_ISHD: Change from baseline in Skindex-10 social functioning score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 4 to < 7	Skindex-10 social functioning score	Baseline	CR845	102	101 (99.0)	9.5 (7.2)	0	9.0	24	
			Placebo	113	112 (99.1)	9.1 (7.5)	0	9.5	24	
		Week 4	CR845	102	95 (93.1)	5.6 (5.6)	0	4.0	21	
			Placebo	113	109 (96.5)	6.0 (6.2)	0	4.0	24	
		Week 8	CR845	102	94 (92.2)	4.5 (5.1)	0	4.0	24	
			Placebo	113	105 (92.9)	5.5 (6.4)	0	4.0	24	
		Week 10	CR845	102	92 (90.2)	4.3 (5.3)	0	2.5	24	
			Placebo	113	101 (89.4)	5.1 (6.4)	0	2.0	24	
		Week 12	CR845	102	91 (89.2)	4.2 (5.5)	0	2.0	24	
			Placebo	113	102 (90.3)	5.3 (6.1)	0	3.0	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	102	94 (92.2)	-3.6 (6.2)	-20	-3.5	12	-0.10 [-0.37, 0.18]
			Placebo	113	108 (95.6)	-2.9 (7.9)	-24	-1.0	23	
		Week 8	CR845	102	93 (91.2)	-5.0 (6.8)	-22	-4.0	12	-0.24 [-0.52, 0.04]
			Placebo	113	105 (92.9)	-3.3 (7.4)	-24	-2.0	22	
		Week 10	CR845	102	91 (89.2)	-5.1 (6.8)	-24	-5.0	17	-0.19 [-0.48, 0.09]
			Placebo	113	101 (89.4)	-3.7 (8.0)	-24	-2.0	22	
		Week 12	CR845	102	90 (88.2)	-5.4 (7.0)	-23	-5.0	20	-0.24 [-0.52, 0.04]
			Placebo	113	102 (90.3)	-3.6 (7.7)	-24	-2.5	24	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SSC_ISHD: Change from baseline in Skindex-10 social functioning score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 7	Skindex-10 social functioning score	Baseline	CR845	135	133 (98.5)	12.6 (8.2)	0	14.0	24	
			Placebo	123	120 (97.6)	12.6 (7.4)	0	13.5	24	
		Week 4	CR845	135	118 (87.4)	9.8 (7.8)	0	9.0	24	
			Placebo	123	113 (91.9)	9.0 (7.9)	0	7.0	24	
		Week 8	CR845	135	113 (83.7)	8.7 (8.0)	0	8.0	24	
			Placebo	123	115 (93.5)	7.9 (7.3)	0	6.0	24	
		Week 10	CR845	135	114 (84.4)	7.9 (8.0)	0	6.0	24	
			Placebo	123	113 (91.9)	8.2 (7.2)	0	7.0	24	
		Week 12	CR845	135	113 (83.7)	8.0 (7.8)	0	7.0	24	
			Placebo	123	114 (92.7)	7.1 (7.4)	0	5.0	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	135	117 (86.7)	-3.0 (8.0)	-24	-2.0	19	0.10 [-0.16, 0.36]
			Placebo	123	112 (91.1)	-3.7 (7.1)	-24	-2.0	10	
		Week 8	CR845	135	112 (83.0)	-4.0 (8.0)	-23	-4.0	24	0.08 [-0.18, 0.34]
			Placebo	123	113 (91.9)	-4.7 (7.0)	-24	-4.0	10	
		Week 10	CR845	135	113 (83.7)	-4.7 (7.7)	-23	-3.0	20	-0.06 [-0.33, 0.20]
			Placebo	123	110 (89.4)	-4.2 (7.0)	-24	-3.0	14	
		Week 12	CR845	135	112 (83.0)	-4.4 (7.7)	-23	-3.0	16	0.13 [-0.13, 0.39]
			Placebo	123	112 (91.1)	-5.4 (7.7)	-24	-4.0	8	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SSC_ISHE: Change from baseline in Skindex-10 social functioning score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	Skindex-10 social functioning score	Baseline	CR845	195	192 (98.5)	11.4 (8.0)	0	11.5	24	
			Placebo	199	195 (98.0)	10.4 (7.5)	0	10.0	24	
		Week 4	CR845	195	176 (90.3)	8.1 (7.1)	0	8.0	24	
			Placebo	199	188 (94.5)	7.6 (7.4)	0	5.0	24	
		Week 8	CR845	195	172 (88.2)	6.9 (7.2)	0	4.0	24	
			Placebo	199	184 (92.5)	6.5 (6.9)	0	4.5	24	
		Week 10	CR845	195	171 (87.7)	6.4 (7.1)	0	4.0	24	
			Placebo	199	179 (89.9)	6.5 (6.9)	0	5.0	24	
		Week 12	CR845	195	169 (86.7)	6.4 (7.2)	0	4.0	24	
			Placebo	199	181 (91.0)	6.2 (6.7)	0	4.0	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	195	174 (89.2)	-3.2 (7.0)	-24	-3.0	19	-0.06 [-0.27, 0.15]
			Placebo	199	186 (93.5)	-2.8 (7.2)	-24	-1.5	23	
		Week 8	CR845	195	170 (87.2)	-4.6 (7.1)	-23	-4.0	16	-0.13 [-0.34, 0.08]
			Placebo	199	182 (91.5)	-3.6 (7.0)	-24	-3.0	22	
		Week 10	CR845	195	169 (86.7)	-4.9 (7.0)	-24	-4.0	20	-0.17 [-0.38, 0.05]
			Placebo	199	176 (88.4)	-3.7 (7.4)	-24	-3.0	22	
		Week 12	CR845	195	167 (85.6)	-4.9 (6.9)	-23	-4.0	16	-0.10 [-0.31, 0.11]
			Placebo	199	179 (89.9)	-4.1 (7.5)	-24	-3.0	24	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SSC_ISHE: Change from baseline in Skindex-10 social functioning score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	Skindex-10 social functioning score	Baseline	CR845	42	42 (100.0)	10.6 (7.6)	0	9.0	24	
			Placebo	37	37 (100.0)	13.7 (7.9)	0	15.0	24	
		Week 4	CR845	42	37 (88.1)	7.0 (7.5)	0	4.0	24	
			Placebo	37	34 (91.9)	7.1 (6.7)	0	7.0	24	
		Week 8	CR845	42	35 (83.3)	6.3 (7.2)	0	4.0	24	
			Placebo	37	36 (97.3)	7.9 (7.3)	0	6.5	24	
		Week 10	CR845	42	35 (83.3)	5.6 (7.0)	0	3.0	24	
			Placebo	37	35 (94.6)	8.3 (7.7)	0	7.0	24	
		Week 12	CR845	42	35 (83.3)	5.9 (7.0)	0	2.0	24	
			Placebo	37	35 (94.6)	6.9 (7.7)	0	5.0	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	42	37 (88.1)	-3.5 (8.3)	-20	-2.0	19	0.34 [-0.13, 0.81]
			Placebo	37	34 (91.9)	-6.3 (8.5)	-24	-4.5	6	
		Week 8	CR845	42	35 (83.3)	-4.1 (9.1)	-21	-5.0	24	0.20 [-0.26, 0.67]
			Placebo	37	36 (97.3)	-5.9 (8.2)	-24	-4.0	10	
		Week 10	CR845	42	35 (83.3)	-4.9 (8.8)	-22	-5.0	17	0.05 [-0.42, 0.52]
			Placebo	37	35 (94.6)	-5.3 (8.1)	-24	-2.0	7	
		Week 12	CR845	42	35 (83.3)	-4.7 (9.7)	-23	-5.0	20	0.21 [-0.26, 0.68]
			Placebo	37	35 (94.6)	-6.6 (8.6)	-24	-4.0	5	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SSC_ISHF: Change from baseline in Skindex-10 social functioning score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	Skindex-10 social functioning score	Baseline	CR845	150	147 (98.0)	10.5 (8.0)	0	10.0	24	
			Placebo	151	149 (98.7)	10.8 (7.7)	0	10.0	24	
		Week 4	CR845	150	140 (93.3)	7.7 (7.0)	0	6.0	24	
			Placebo	151	144 (95.4)	7.1 (7.2)	0	5.0	24	
		Week 8	CR845	150	137 (91.3)	6.6 (7.0)	0	4.0	24	
			Placebo	151	141 (93.4)	6.2 (6.7)	0	5.0	24	
		Week 10	CR845	150	133 (88.7)	6.0 (7.0)	0	4.0	24	
			Placebo	151	139 (92.1)	6.5 (6.6)	0	5.0	24	
		Week 12	CR845	150	134 (89.3)	6.2 (7.3)	0	3.0	24	
			Placebo	151	141 (93.4)	6.0 (6.7)	0	4.0	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	150	138 (92.0)	-2.7 (7.4)	-23	-2.0	19	0.11 [-0.12, 0.35]
			Placebo	151	143 (94.7)	-3.6 (7.7)	-24	-2.0	23	
		Week 8	CR845	150	135 (90.0)	-3.8 (7.1)	-23	-3.0	24	0.07 [-0.17, 0.30]
			Placebo	151	141 (93.4)	-4.3 (7.6)	-24	-4.0	22	
		Week 10	CR845	150	131 (87.3)	-4.4 (7.0)	-24	-4.0	17	-0.05 [-0.29, 0.19]
			Placebo	151	138 (91.4)	-4.0 (8.2)	-24	-3.0	22	
		Week 12	CR845	150	132 (88.0)	-4.1 (7.3)	-23	-3.0	20	0.08 [-0.15, 0.32]
			Placebo	151	140 (92.7)	-4.7 (8.2)	-24	-3.0	24	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SSC_ISHF: Change from baseline in Skindex-10 social functioning score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	Skindex-10 social functioning score	Baseline	CR845	87	87 (100.0)	12.5 (7.7)	0	12.0	24	
			Placebo	85	83 (97.6)	11.2 (7.6)	0	12.0	24	
		Week 4	CR845	87	73 (83.9)	8.5 (7.6)	0	6.0	24	
			Placebo	85	78 (91.8)	8.3 (7.4)	0	7.5	24	
		Week 8	CR845	87	70 (80.5)	7.2 (7.6)	0	5.0	24	
			Placebo	85	79 (92.9)	7.7 (7.4)	0	6.0	24	
		Week 10	CR845	87	73 (83.9)	6.8 (7.3)	0	5.0	24	
			Placebo	85	75 (88.2)	7.2 (7.7)	0	5.0	24	
		Week 12	CR845	87	70 (80.5)	6.5 (6.8)	0	4.0	24	
			Placebo	85	75 (88.2)	6.8 (7.2)	0	3.0	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	87	73 (83.9)	-4.3 (6.7)	-24	-4.0	19	-0.21 [-0.53, 0.11]
			Placebo	85	77 (90.6)	-2.8 (7.2)	-21	-2.0	15	
		Week 8	CR845	87	70 (80.5)	-5.8 (8.0)	-23	-5.5	16	-0.31 [-0.64, 0.01]
			Placebo	85	77 (90.6)	-3.5 (6.5)	-20	-2.0	12	
		Week 10	CR845	87	73 (83.9)	-5.8 (7.8)	-22	-6.0	20	-0.27 [-0.60, 0.05]
			Placebo	85	73 (85.9)	-3.9 (6.0)	-22	-2.0	10	
		Week 12	CR845	87	70 (80.5)	-6.2 (7.3)	-23	-5.0	16	-0.29 [-0.62, 0.04]
			Placebo	85	74 (87.1)	-4.2 (6.8)	-24	-3.0	19	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SSC_ISHG: Change from baseline in Skindex-10 social functioning score by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
USA	Skindex-10 social functioning score	Baseline	CR845	146	143 (97.9)	11.5 (7.8)	0	11.0	24	
			Placebo	133	132 (99.2)	11.3 (7.8)	0	10.5	24	
		Week 4	CR845	146	131 (89.7)	8.6 (7.1)	0	8.0	24	
			Placebo	133	121 (91.0)	8.0 (7.4)	0	6.0	24	
		Week 8	CR845	146	130 (89.0)	7.5 (7.2)	0	6.0	24	
			Placebo	133	124 (93.2)	7.1 (6.7)	0	5.5	24	
		Week 10	CR845	146	129 (88.4)	7.5 (7.4)	0	6.0	24	
			Placebo	133	122 (91.7)	6.9 (6.7)	0	5.0	24	
		Week 12	CR845	146	128 (87.7)	7.0 (7.2)	0	5.0	24	
			Placebo	133	125 (94.0)	6.2 (6.7)	0	4.0	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	146	129 (88.4)	-2.8 (7.4)	-24	-3.0	19	0.04 [-0.20, 0.29]
			Placebo	133	121 (91.0)	-3.1 (8.1)	-24	-2.0	23	
		Week 8	CR845	146	128 (87.7)	-3.8 (7.7)	-23	-3.5	24	0.01 [-0.24, 0.26]
			Placebo	133	124 (93.2)	-3.8 (7.7)	-24	-2.5	22	
		Week 10	CR845	146	127 (87.0)	-3.9 (7.2)	-24	-3.0	20	0.04 [-0.21, 0.29]
			Placebo	133	121 (91.0)	-4.2 (8.3)	-24	-3.0	22	
		Week 12	CR845	146	126 (86.3)	-4.3 (7.3)	-23	-4.0	20	0.10 [-0.15, 0.35]
			Placebo	133	124 (93.2)	-5.1 (8.6)	-24	-4.0	24	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SSC_ISHG: Change from baseline in Skindex-10 social functioning score by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Asia	Skindex-10 social functioning score	Baseline	CR845	8	8 (100.0)	13.4 (4.9)	8	12.0	24	
			Placebo	12	12 (100.0)	11.2 (7.7)	0	13.5	22	
		Week 4	CR845	8	8 (100.0)	6.6 (5.6)	0	4.5	16	
			Placebo	12	12 (100.0)	6.9 (6.3)	0	5.0	21	
		Week 8	CR845	8	7 (87.5)	4.9 (4.3)	0	4.0	12	
			Placebo	12	12 (100.0)	4.2 (4.1)	0	4.0	12	
		Week 10	CR845	8	7 (87.5)	2.4 (4.6)	0	0.0	12	
			Placebo	12	11 (91.7)	4.4 (5.0)	0	2.0	15	
		Week 12	CR845	8	7 (87.5)	4.1 (5.5)	0	3.0	16	
			Placebo	12	11 (91.7)	4.3 (5.5)	0	3.0	15	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	8	8 (100.0)	-6.8 (3.9)	-12	-7.5	0	-0.46 [-1.37, 0.45]
			Placebo	12	12 (100.0)	-4.3 (6.2)	-16	-5.0	4	
		Week 8	CR845	8	7 (87.5)	-8.7 (3.6)	-15	-8.0	-4	-0.28 [-1.22, 0.65]
			Placebo	12	12 (100.0)	-7.0 (7.0)	-18	-7.5	4	
		Week 10	CR845	8	7 (87.5)	-11.1 (2.6)	-16	-11.0	-8	-0.84 [-1.83, 0.15]
			Placebo	12	11 (91.7)	-5.8 (7.7)	-16	-9.0	11	
		Week 12	CR845	8	7 (87.5)	-9.4 (2.6)	-12	-10.0	-5	-0.67 [-1.65, 0.31]
			Placebo	12	11 (91.7)	-5.9 (6.3)	-16	-4.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SSC_ISHG: Change from baseline in Skindex-10 social functioning score by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Eastern Europe	Skindex-10 social functioning score	Baseline	CR845	54	54 (100.0)	9.5 (8.2)	0	8.5	24	
			Placebo	60	60 (100.0)	8.5 (6.8)	0	8.0	24	
		Week 4	CR845	54	52 (96.3)	6.5 (7.4)	0	3.0	24	
			Placebo	60	59 (98.3)	6.1 (6.5)	0	4.0	24	
		Week 8	CR845	54	48 (88.9)	4.2 (6.7)	0	0.5	24	
			Placebo	60	58 (96.7)	5.2 (6.7)	0	2.0	24	
		Week 10	CR845	54	48 (88.9)	3.8 (5.8)	0	0.0	24	
			Placebo	60	58 (96.7)	5.4 (6.7)	0	3.0	24	
		Week 12	CR845	54	47 (87.0)	4.2 (6.3)	0	0.0	24	
			Placebo	60	55 (91.7)	5.5 (6.6)	0	3.0	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	54	52 (96.3)	-3.2 (7.0)	-23	-1.0	12	-0.11 [-0.49, 0.26]
			Placebo	60	59 (98.3)	-2.5 (6.5)	-20	-1.0	13	
		Week 8	CR845	54	48 (88.9)	-5.4 (6.9)	-23	-3.5	4	-0.32 [-0.70, 0.07]
			Placebo	60	58 (96.7)	-3.3 (6.6)	-22	-1.5	12	
		Week 10	CR845	54	48 (88.9)	-5.3 (7.2)	-23	-4.5	13	-0.35 [-0.73, 0.04]
			Placebo	60	58 (96.7)	-3.0 (6.3)	-21	-1.0	13	
		Week 12	CR845	54	47 (87.0)	-5.0 (7.7)	-23	-3.0	11	-0.30 [-0.69, 0.10]
			Placebo	60	55 (91.7)	-3.0 (6.3)	-21	-2.0	11	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SSC_ISHG: Change from baseline in Skindex-10 social functioning score by region
ITT

G: Region	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Western Europe/European origin	Skindex-10 social functioning score	Baseline	CR845	29	29 (100.0)	12.7 (8.4)	0	15.0	24	
			Placebo	31	28 (90.3)	14.4 (7.5)	0	15.0	24	
		Week 4	CR845	29	22 (75.9)	8.0 (8.0)	0	6.5	24	
			Placebo	31	30 (96.8)	8.9 (8.3)	0	6.5	24	
		Week 8	CR845	29	22 (75.9)	8.5 (7.3)	0	7.5	24	
			Placebo	31	26 (83.9)	9.6 (8.5)	0	6.5	24	
		Week 10	CR845	29	22 (75.9)	5.5 (7.2)	0	2.0	24	
			Placebo	31	23 (74.2)	10.5 (9.0)	0	10.0	24	
		Week 12	CR845	29	22 (75.9)	7.1 (8.3)	0	3.5	24	
			Placebo	31	25 (80.6)	9.4 (8.2)	0	9.0	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	29	22 (75.9)	-4.9 (7.6)	-21	-4.0	6	0.11 [-0.45, 0.67]
			Placebo	31	28 (90.3)	-5.6 (7.0)	-21	-4.0	7	
		Week 8	CR845	29	22 (75.9)	-5.4 (8.1)	-19	-4.0	9	0.00 [-0.58, 0.58]
			Placebo	31	24 (77.4)	-5.4 (6.2)	-15	-6.0	8	
		Week 10	CR845	29	22 (75.9)	-7.7 (7.4)	-22	-6.0	4	-0.51 [-1.11, 0.10]
			Placebo	31	21 (67.7)	-4.3 (5.9)	-15	-4.0	10	
		Week 12	CR845	29	22 (75.9)	-5.9 (8.1)	-22	-4.0	9	-0.17 [-0.75, 0.41]
			Placebo	31	24 (77.4)	-4.6 (7.0)	-16	-5.0	7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SSC_ISHH: Change from baseline in Skindex-10 social functioning score by dialysis method
ITT

H: Dialysis method	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Hemodialysis (HD)	Skindex-10 social functioning score	Baseline	CR845	222	219 (98.6)	11.5 (7.8)	0	11.0	24	
			Placebo	199	195 (98.0)	11.0 (7.6)	0	11.0	24	
		Week 4	CR845	222	200 (90.1)	8.1 (7.2)	0	7.0	24	
			Placebo	199	185 (93.0)	7.7 (7.3)	0	6.0	24	
		Week 8	CR845	222	194 (87.4)	6.9 (7.1)	0	5.0	24	
			Placebo	199	185 (93.0)	7.0 (6.9)	0	5.0	24	
		Week 10	CR845	222	194 (87.4)	6.6 (7.2)	0	4.0	24	
			Placebo	199	182 (91.5)	6.9 (7.0)	0	5.0	24	
		Week 12	CR845	222	191 (86.0)	6.4 (7.1)	0	4.0	24	
			Placebo	199	182 (91.5)	6.1 (6.6)	0	4.0	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	222	198 (89.2)	-3.3 (7.2)	-24	-3.0	19	0.00 [-0.20, 0.20]
			Placebo	199	183 (92.0)	-3.3 (7.8)	-24	-2.0	23	
		Week 8	CR845	222	192 (86.5)	-4.5 (7.6)	-23	-4.0	24	-0.07 [-0.27, 0.13]
			Placebo	199	183 (92.0)	-4.0 (7.4)	-24	-3.0	22	
		Week 10	CR845	222	192 (86.5)	-4.8 (7.3)	-24	-4.0	20	-0.09 [-0.29, 0.12]
			Placebo	199	179 (89.9)	-4.2 (7.6)	-24	-3.0	22	
		Week 12	CR845	222	189 (85.1)	-4.9 (7.4)	-23	-4.0	20	0.01 [-0.20, 0.21]
			Placebo	199	180 (90.5)	-5.0 (7.9)	-24	-3.0	24	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2SSC_ISHH: Change from baseline in Skindex-10 social functioning score by dialysis method
ITT

H: Dialysis method	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Hemodiafiltration (HDF)	Skindex-10 social functioning score	Baseline	CR845	15	15 (100.0)	7.2 (7.9)	0	5.0	21	
			Placebo	37	37 (100.0)	10.2 (8.0)	0	10.0	24	
		Week 4	CR845	15	13 (86.7)	5.2 (7.0)	0	0.0	17	
			Placebo	37	37 (100.0)	6.7 (7.0)	0	4.0	24	
		Week 8	CR845	15	13 (86.7)	4.4 (7.4)	0	1.0	20	
			Placebo	37	35 (94.6)	5.5 (7.4)	0	3.0	23	
		Week 10	CR845	15	12 (80.0)	1.4 (3.5)	0	0.0	12	
			Placebo	37	32 (86.5)	6.0 (7.3)	0	3.0	24	
		Week 12	CR845	15	13 (86.7)	4.3 (7.1)	0	0.0	21	
			Placebo	37	34 (91.9)	7.4 (8.0)	0	4.5	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	15	13 (86.7)	-2.8 (7.9)	-21	-1.0	12	0.10 [-0.53, 0.73]
			Placebo	37	37 (100.0)	-3.5 (6.2)	-18	-1.0	7	
		Week 8	CR845	15	13 (86.7)	-3.6 (6.1)	-19	-1.0	3	0.05 [-0.59, 0.69]
			Placebo	37	35 (94.6)	-3.9 (6.8)	-21	-3.0	8	
		Week 10	CR845	15	12 (80.0)	-5.8 (7.3)	-21	-5.0	4	-0.46 [-1.13, 0.21]
			Placebo	37	32 (86.5)	-2.7 (6.7)	-21	-1.0	10	
		Week 12	CR845	15	13 (86.7)	-3.7 (7.1)	-21	-1.0	5	-0.21 [-0.85, 0.43]
			Placebo	37	34 (91.9)	-2.3 (6.3)	-21	-1.0	7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin, created on: 17FEB2022

Table BT2STC_ISCA: Change from baseline in Skindex-10 total score - MMRM results by age
ITT

Change from baseline in Skindex-10 total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
A: Age									0.982
< 65 years	Week 4	CR845	147	131 (89.1)	-11.5 (1.4)	(-14.3, -8.7)	-2.5 (1.7)	(-5.8, 0.8)	0.141
		Placebo	153	136 (88.9)	-9.0 (1.4)	(-11.8, -6.2)			
>= 65 years	Week 4	CR845	90	76 (84.4)	-9.7 (1.8)	(-13.2, -6.2)	-0.6 (2.3)	(-5.2, 3.9)	0.788
		Placebo	83	75 (90.4)	-9.0 (1.8)	(-12.6, -5.5)			
< 65 years	Week 8	CR845	147	125 (85.0)	-14.2 (1.5)	(-17.1, -11.3)	-0.3 (1.7)	(-3.6, 3.1)	0.878
		Placebo	153	139 (90.8)	-13.9 (1.4)	(-16.8, -11.1)			
>= 65 years	Week 8	CR845	90	73 (81.1)	-12.0 (1.8)	(-15.5, -8.6)	-1.6 (2.3)	(-6.1, 2.9)	0.487
		Placebo	83	74 (89.2)	-10.5 (1.8)	(-13.9, -7.0)			
< 65 years	Week 10	CR845	147	128 (87.1)	-16.1 (1.5)	(-19.0, -13.2)	-2.2 (1.7)	(-5.7, 1.2)	0.201
		Placebo	153	135 (88.2)	-13.8 (1.5)	(-16.7, -11.0)			
>= 65 years	Week 10	CR845	90	72 (80.0)	-15.1 (1.7)	(-18.4, -11.7)	-4.0 (2.2)	(-8.4, 0.3)	0.067
		Placebo	83	71 (85.5)	-11.0 (1.7)	(-14.4, -7.6)			
< 65 years	Week 12	CR845	147	127 (86.4)	-16.4 (1.5)	(-19.4, -13.4)	-1.5 (1.8)	(-5.1, 2.1)	0.413
		Placebo	153	137 (89.5)	-14.9 (1.5)	(-17.9, -12.0)			
>= 65 years	Week 12	CR845	90	72 (80.0)	-14.3 (1.7)	(-17.7, -11.0)	-2.3 (2.2)	(-6.6, 2.0)	0.286
		Placebo	83	73 (88.0)	-12.0 (1.7)	(-15.3, -8.6)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table BT2STC_ISCB: Change from baseline in Skindex-10 total score - MMRM results by sex
ITT

Change from baseline in Skindex-10 total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
B: Sex									<0.001 i
Male	Week 4	CR845	137	121 (88.3)	-8.2 (1.4)	(-11.0, -5.3)	1.0 (1.7)	(-2.5, 4.4)	0.579
		Placebo	139	122 (87.8)	-9.1 (1.4)	(-12.0, -6.3)			
Female	Week 4	CR845	100	86 (86.0)	-13.8 (1.7)	(-17.1, -10.5)	-5.7 (2.1)	(-9.9, -1.5)	0.009 *
		Placebo	97	89 (91.8)	-8.1 (1.7)	(-11.5, -4.7)			
Male	Week 8	CR845	137	118 (86.1)	-9.7 (1.4)	(-12.5, -6.9)	2.9 (1.7)	(-0.4, 6.2)	0.085
		Placebo	139	127 (91.4)	-12.6 (1.4)	(-15.4, -9.9)			
Female	Week 8	CR845	100	80 (80.0)	-17.7 (1.7)	(-21.1, -14.3)	-5.7 (2.2)	(-10.1, -1.3)	0.011 *
		Placebo	97	86 (88.7)	-11.9 (1.8)	(-15.4, -8.5)			
Male	Week 10	CR845	137	115 (83.9)	-11.8 (1.4)	(-14.6, -9.0)	0.8 (1.7)	(-2.6, 4.2)	0.634
		Placebo	139	120 (86.3)	-12.6 (1.4)	(-15.4, -9.9)			
Female	Week 10	CR845	100	85 (85.0)	-20.3 (1.7)	(-23.6, -16.9)	-8.0 (2.2)	(-12.3, -3.7)	<0.001 *
		Placebo	97	86 (88.7)	-12.3 (1.7)	(-15.7, -8.8)			
Male	Week 12	CR845	137	114 (83.2)	-12.1 (1.4)	(-14.9, -9.3)	1.4 (1.7)	(-2.0, 4.7)	0.425
		Placebo	139	122 (87.8)	-13.5 (1.4)	(-16.2, -10.7)			
Female	Week 12	CR845	100	85 (85.0)	-19.8 (1.8)	(-23.3, -16.2)	-6.1 (2.3)	(-10.7, -1.5)	0.010 *
		Placebo	97	88 (90.7)	-13.7 (1.8)	(-17.3, -10.1)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table BT2STC_ISCC: Change from baseline in Skindex-10 total score - MMRM results by race
ITT

Change from baseline in Skindex-10 total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
C: Race									0.111
Black/African American	Week 4	CR845	53	43 (81.1)	-8.2 (1.9)	(-12.1, -4.4)	2.8 (2.8)	(-2.7, 8.4)	0.317
		Placebo	38	31 (81.6)	-11.0 (2.2)	(-15.4, -6.7)			
White	Week 4	CR845	164	147 (89.6)	-11.4 (1.4)	(-14.2, -8.6)	-3.6 (1.7)	(-6.8, -0.3)	0.033 *
		Placebo	169	155 (91.7)	-7.8 (1.4)	(-10.6, -5.1)			
Other	Week 4	CR845	20	17 (85.0)	-8.2 (4.0)	(-16.4, -0.1)	2.1 (4.2)	(-6.4, 10.6)	0.620
		Placebo	29	25 (86.2)	-10.3 (3.5)	(-17.5, -3.2)			
Black/African American	Week 8	CR845	53	44 (83.0)	-12.4 (2.1)	(-16.5, -8.3)	1.1 (3.0)	(-4.8, 7.0)	0.716
		Placebo	38	34 (89.5)	-13.5 (2.3)	(-18.1, -8.9)			
White	Week 8	CR845	164	137 (83.5)	-13.3 (1.4)	(-16.1, -10.5)	-1.8 (1.7)	(-5.1, 1.5)	0.284
		Placebo	169	155 (91.7)	-11.5 (1.4)	(-14.3, -8.8)			
Other	Week 8	CR845	20	17 (85.0)	-11.9 (3.8)	(-19.7, -4.2)	3.5 (3.9)	(-4.5, 11.5)	0.378
		Placebo	29	24 (82.8)	-15.5 (3.4)	(-22.3, -8.6)			
Black/African American	Week 10	CR845	53	42 (79.2)	-12.7 (2.1)	(-16.8, -8.6)	2.5 (3.0)	(-3.4, 8.5)	0.400
		Placebo	38	32 (84.2)	-15.2 (2.3)	(-19.8, -10.6)			
White	Week 10	CR845	164	142 (86.6)	-15.9 (1.4)	(-18.7, -13.2)	-4.5 (1.6)	(-7.6, -1.3)	0.006 *
		Placebo	169	152 (89.9)	-11.5 (1.4)	(-14.1, -8.8)			
Other	Week 10	CR845	20	16 (80.0)	-16.8 (4.5)	(-25.8, -7.7)	-1.9 (5.0)	(-11.9, 8.2)	0.712
		Placebo	29	22 (75.9)	-14.9 (3.9)	(-22.8, -7.0)			
Black/African American	Week 12	CR845	53	41 (77.4)	-14.8 (2.1)	(-19.1, -10.6)	3.2 (3.1)	(-2.9, 9.3)	0.303
		Placebo	38	35 (92.1)	-18.0 (2.3)	(-22.7, -13.3)			
White	Week 12	CR845	164	142 (86.6)	-15.7 (1.4)	(-18.5, -12.9)	-3.7 (1.7)	(-7.0, -0.4)	0.027 *
		Placebo	169	153 (90.5)	-12.0 (1.4)	(-14.8, -9.3)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table BT2STC_ISCC: Change from baseline in Skindex-10 total score - MMRM results by race
ITT

Change from baseline in Skindex-10 total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Other	Week 12	CR845	20	16 (80.0)	-12.5 (4.6)	(-21.7, -3.3)	4.4 (5.1)	(-6.1, 14.8)	0.402
		Placebo	29	22 (75.9)	-16.9 (4.0)	(-25.0, -8.8)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table BT2STC_ISCD: Change from baseline in Skindex-10 total score - MMRM results by baseline WI-NRS
ITT

Change from baseline in Skindex-10 total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
D: Baseline worst itching NRS score (WI-NRS)									0.169
>= 4 to < 7	Week 4	CR845	102	94 (92.2)	-12.4 (1.6)	(-15.5, -9.4)	-3.4 (1.8)	(-6.9, 0.1)	0.056
		Placebo	113	104 (92.0)	-9.0 (1.5)	(-12.0, -6.1)			
>= 7	Week 4	CR845	135	113 (83.7)	-9.8 (1.5)	(-12.7, -6.8)	-0.8 (1.9)	(-4.6, 3.0)	0.676
		Placebo	123	107 (87.0)	-9.0 (1.6)	(-12.0, -5.9)			
>= 4 to < 7	Week 8	CR845	102	92 (90.2)	-14.1 (1.6)	(-17.2, -10.9)	-3.0 (1.9)	(-6.6, 0.7)	0.109
		Placebo	113	104 (92.0)	-11.1 (1.5)	(-14.1, -8.0)			
>= 7	Week 8	CR845	135	106 (78.5)	-13.1 (1.5)	(-16.1, -10.1)	1.0 (2.0)	(-2.9, 4.9)	0.608
		Placebo	123	109 (88.6)	-14.1 (1.5)	(-17.2, -11.1)			
>= 4 to < 7	Week 10	CR845	102	90 (88.2)	-15.9 (1.6)	(-19.1, -12.7)	-3.7 (1.9)	(-7.4, -0.0)	0.048 *
		Placebo	113	100 (88.5)	-12.2 (1.5)	(-15.3, -9.2)			
>= 7	Week 10	CR845	135	110 (81.5)	-15.8 (1.5)	(-18.8, -12.9)	-2.6 (1.9)	(-6.4, 1.3)	0.188
		Placebo	123	106 (86.2)	-13.3 (1.5)	(-16.3, -10.2)			
>= 4 to < 7	Week 12	CR845	102	90 (88.2)	-16.0 (1.6)	(-19.2, -12.8)	-3.8 (1.9)	(-7.5, -0.1)	0.044 *
		Placebo	113	101 (89.4)	-12.2 (1.6)	(-15.3, -9.1)			
>= 7	Week 12	CR845	135	109 (80.7)	-15.6 (1.5)	(-18.7, -12.6)	-0.3 (2.0)	(-4.3, 3.7)	0.894
		Placebo	123	109 (88.6)	-15.4 (1.6)	(-18.5, -12.2)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table BT2STC_ISCE: Change from baseline in Skindex-10 total score - MMRM results by specific medical condition
ITT

Change from baseline in Skindex-10 total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
E: Presence of specific medical conditions									0.988
No	Week 4	CR845	195	170 (87.2)	-9.7 (1.1)	(-11.8, -7.7)	-1.9 (1.4)	(-4.8, 0.9)	0.182
		Placebo	199	182 (91.5)	-7.8 (1.0)	(-9.8, -5.8)			
Yes	Week 4	CR845	42	37 (88.1)	-13.6 (2.6)	(-18.8, -8.4)	-1.8 (3.9)	(-9.6, 6.0)	0.649
		Placebo	37	29 (78.4)	-11.8 (2.9)	(-17.5, -6.2)			
No	Week 8	CR845	195	165 (84.6)	-12.6 (1.1)	(-14.7, -10.5)	-0.8 (1.5)	(-3.7, 2.1)	0.583
		Placebo	199	179 (89.9)	-11.8 (1.0)	(-13.8, -9.7)			
Yes	Week 8	CR845	42	33 (78.6)	-14.6 (2.7)	(-19.9, -9.3)	-1.1 (3.9)	(-8.8, 6.6)	0.781
		Placebo	37	34 (91.9)	-13.5 (2.7)	(-19.0, -8.1)			
No	Week 10	CR845	195	166 (85.1)	-14.6 (1.1)	(-16.7, -12.5)	-2.5 (1.5)	(-5.4, 0.4)	0.085
		Placebo	199	173 (86.9)	-12.0 (1.0)	(-14.1, -10.0)			
Yes	Week 10	CR845	42	34 (81.0)	-18.6 (2.6)	(-23.8, -13.5)	-5.7 (3.7)	(-13.1, 1.7)	0.129
		Placebo	37	33 (89.2)	-12.9 (2.6)	(-18.2, -7.7)			
No	Week 12	CR845	195	164 (84.1)	-14.8 (1.1)	(-17.0, -12.7)	-1.9 (1.5)	(-4.9, 1.0)	0.198
		Placebo	199	176 (88.4)	-12.9 (1.1)	(-15.0, -10.8)			
Yes	Week 12	CR845	42	35 (83.3)	-17.3 (2.7)	(-22.7, -11.8)	-2.2 (3.9)	(-10.0, 5.7)	0.584
		Placebo	37	34 (91.9)	-15.1 (2.8)	(-20.7, -9.5)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor previous use of anti-itch medication is also included in the model.
Source Data: askin, created on: 17FEB2022

Table BT2STC_ISCF: Change from baseline in Skindex-10 total score - MMRM results by use of concomitant itch medication
ITT

Change from baseline in Skindex-10 total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
F: Use of concomitant itch medication									0.365
No	Week 4	CR845	150	135 (90.0)	-9.4 (1.4)	(-12.1, -6.6)	-0.9 (1.7)	(-4.3, 2.4)	0.580
		Placebo	151	138 (91.4)	-8.4 (1.4)	(-11.2, -5.6)			
Yes	Week 4	CR845	87	72 (82.8)	-12.9 (1.7)	(-16.4, -9.5)	-3.7 (2.3)	(-8.2, 0.8)	0.107
		Placebo	85	73 (85.9)	-9.2 (1.8)	(-12.7, -5.8)			
No	Week 8	CR845	150	132 (88.0)	-12.0 (1.4)	(-14.7, -9.3)	0.0 (1.7)	(-3.3, 3.3)	0.989
		Placebo	151	137 (90.7)	-12.0 (1.4)	(-14.8, -9.3)			
Yes	Week 8	CR845	87	66 (75.9)	-15.3 (1.8)	(-18.9, -11.6)	-2.3 (2.4)	(-7.0, 2.4)	0.336
		Placebo	85	76 (89.4)	-13.0 (1.8)	(-16.5, -9.4)			
No	Week 10	CR845	150	128 (85.3)	-14.3 (1.4)	(-17.1, -11.5)	-2.6 (1.7)	(-5.9, 0.8)	0.133
		Placebo	151	133 (88.1)	-11.7 (1.4)	(-14.5, -8.9)			
Yes	Week 10	CR845	87	72 (82.8)	-17.7 (1.8)	(-21.2, -14.2)	-3.8 (2.3)	(-8.3, 0.7)	0.099
		Placebo	85	73 (85.9)	-13.9 (1.7)	(-17.4, -10.5)			
No	Week 12	CR845	150	129 (86.0)	-14.0 (1.5)	(-16.9, -11.2)	-1.0 (1.8)	(-4.4, 2.5)	0.588
		Placebo	151	137 (90.7)	-13.1 (1.4)	(-15.9, -10.2)			
Yes	Week 12	CR845	87	70 (80.5)	-18.0 (1.8)	(-21.6, -14.5)	-3.6 (2.3)	(-8.2, 1.0)	0.123
		Placebo	85	73 (85.9)	-14.4 (1.8)	(-17.9, -11.0)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor presence of medical condition is also included in the model.
Source Data: askin, created on: 17FEB2022

Table BT2STC_ISCG: Change from baseline in Skindex-10 total score - MMRM results by region
ITT

Change from baseline in Skindex-10 total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
G: Region									0.393
USA	Week 4	CR845	146	125 (85.6)	-9.6 (1.4)	(-12.3, -6.9)	-1.8 (1.8)	(-5.4, 1.7)	0.310
		Placebo	133	116 (87.2)	-7.8 (1.5)	(-10.7, -4.9)			
Asia	Week 4	CR845	8	8 (100.0)	-18.1 (4.3)	(-27.4, -8.8)	-5.3 (5.6)	(-17.4, 6.7)	0.360
		Placebo	12	12 (100.0)	-12.8 (3.6)	(-20.5, -5.1)			
Eastern Europe	Week 4	CR845	54	52 (96.3)	-10.7 (2.3)	(-15.2, -6.1)	-1.7 (2.4)	(-6.5, 3.1)	0.486
		Placebo	60	57 (95.0)	-9.0 (2.2)	(-13.3, -4.6)			
Western Europe/European origin	Week 4	CR845	29	22 (75.9)	-16.7 (3.5)	(-23.8, -9.6)	-1.5 (4.6)	(-10.8, 7.8)	0.748
		Placebo	31	26 (83.9)	-15.2 (3.4)	(-22.0, -8.5)			
USA	Week 8	CR845	146	121 (82.9)	-11.9 (1.4)	(-14.7, -9.2)	0.8 (1.8)	(-2.8, 4.3)	0.674
		Placebo	133	121 (91.0)	-12.7 (1.5)	(-15.6, -9.8)			
Asia	Week 8	CR845	8	7 (87.5)	-20.5 (3.5)	(-28.1, -12.9)	-1.5 (4.6)	(-11.3, 8.3)	0.746
		Placebo	12	12 (100.0)	-19.0 (2.8)	(-25.0, -13.0)			
Eastern Europe	Week 8	CR845	54	48 (88.9)	-14.8 (2.4)	(-19.7, -10.0)	-4.3 (2.6)	(-9.6, 0.9)	0.105
		Placebo	60	58 (96.7)	-10.5 (2.3)	(-15.0, -6.0)			
Western Europe/European origin	Week 8	CR845	29	22 (75.9)	-17.1 (3.3)	(-23.7, -10.5)	-1.0 (4.4)	(-9.8, 7.8)	0.818
		Placebo	31	22 (71.0)	-16.1 (3.3)	(-22.6, -9.6)			
USA	Week 10	CR845	146	124 (84.9)	-13.6 (1.4)	(-16.3, -10.8)	0.4 (1.8)	(-3.1, 4.0)	0.802
		Placebo	133	117 (88.0)	-14.0 (1.5)	(-16.9, -11.1)			
Asia	Week 10	CR845	8	7 (87.5)	-26.6 (4.6)	(-36.5, -16.7)	-6.4 (5.9)	(-19.1, 6.3)	0.296
		Placebo	12	11 (91.7)	-20.2 (3.7)	(-28.0, -12.3)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table BT2STC_ISCG: Change from baseline in Skindex-10 total score - MMRM results by region
ITT

Change from baseline in Skindex-10 total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Eastern Europe	Week 10	CR845	54	47 (87.0)	-17.3 (2.3)	(-21.9, -12.7)	-7.9 (2.4)	(-12.7, -3.0)	0.002 *
		Placebo	60	58 (96.7)	-9.4 (2.2)	(-13.7, -5.1)			
Western Europe/European origin	Week 10	CR845	29	22 (75.9)	-21.8 (3.4)	(-28.6, -15.0)	-9.1 (4.6)	(-18.4, 0.1)	0.052
		Placebo	31	20 (64.5)	-12.6 (3.4)	(-19.5, -5.8)			
USA	Week 12	CR845	146	123 (84.2)	-14.7 (1.4)	(-17.5, -11.9)	0.7 (1.8)	(-2.9, 4.2)	0.717
		Placebo	133	122 (91.7)	-15.3 (1.5)	(-18.2, -12.4)			
Asia	Week 12	CR845	8	7 (87.5)	-23.2 (4.3)	(-32.3, -14.0)	-2.3 (5.6)	(-14.1, 9.5)	0.687
		Placebo	12	11 (91.7)	-20.9 (3.5)	(-28.3, -13.5)			
Eastern Europe	Week 12	CR845	54	47 (87.0)	-15.9 (2.5)	(-20.8, -11.0)	-5.9 (2.7)	(-11.2, -0.6)	0.029 *
		Placebo	60	55 (91.7)	-10.0 (2.3)	(-14.5, -5.5)			
Western Europe/European origin	Week 12	CR845	29	22 (75.9)	-19.4 (3.5)	(-26.5, -12.3)	-6.1 (4.8)	(-15.7, 3.6)	0.212
		Placebo	31	22 (71.0)	-13.3 (3.5)	(-20.4, -6.2)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table BT2STC_ISCH: Change from baseline in Skindex-10 total score - MMRM results by dialysis method
ITT

Change from baseline in Skindex-10 total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
H: Dialysis method									0.575
Hemodialysis (HD)	Week 4	CR845	222	194 (87.4)	-10.8 (1.1)	(-13.0, -8.5)	-2.3 (1.5)	(-5.1, 0.6)	0.124
		Placebo	199	176 (88.4)	-8.5 (1.2)	(-10.8, -6.2)			
Hemodiafiltration (HDF)	Week 4	CR845	15	13 (86.7)	-11.5 (6.7)	(-24.9, 2.0)	-1.7 (4.2)	(-10.2, 6.8)	0.691
		Placebo	37	35 (94.6)	-9.8 (5.2)	(-20.3, 0.7)			
Hemodialysis (HD)	Week 8	CR845	222	185 (83.3)	-13.4 (1.1)	(-15.7, -11.2)	-1.0 (1.5)	(-3.8, 1.9)	0.505
		Placebo	199	180 (90.5)	-12.5 (1.2)	(-14.8, -10.2)			
Hemodiafiltration (HDF)	Week 8	CR845	15	13 (86.7)	-12.2 (6.8)	(-26.0, 1.5)	-0.2 (4.6)	(-9.4, 9.0)	0.964
		Placebo	37	33 (89.2)	-12.0 (5.3)	(-22.7, -1.4)			
Hemodialysis (HD)	Week 10	CR845	222	188 (84.7)	-15.5 (1.1)	(-17.7, -13.2)	-2.2 (1.4)	(-5.1, 0.6)	0.126
		Placebo	199	175 (87.9)	-13.2 (1.2)	(-15.5, -10.9)			
Hemodiafiltration (HDF)	Week 10	CR845	15	12 (80.0)	-19.1 (6.9)	(-33.0, -5.2)	-10.5 (4.7)	(-20.1, -1.0)	0.032 *
		Placebo	37	31 (83.8)	-8.6 (5.3)	(-19.3, 2.1)			
Hemodialysis (HD)	Week 12	CR845	222	186 (83.8)	-15.6 (1.2)	(-17.9, -13.3)	-1.2 (1.5)	(-4.1, 1.8)	0.441
		Placebo	199	178 (89.4)	-14.5 (1.2)	(-16.8, -12.1)			
Hemodiafiltration (HDF)	Week 12	CR845	15	13 (86.7)	-15.5 (6.9)	(-29.4, -1.6)	-6.8 (4.7)	(-16.3, 2.8)	0.161
		Placebo	37	32 (86.5)	-8.7 (5.3)	(-19.4, 2.0)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table BT2SDC_ISCA: Change from baseline in Skindex-10 disease score - MMRM results by age
ITT

Change from baseline in Skindex-10 disease score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
A: Age									0.852
< 65 years	Week 4	CR845	147	133 (90.5)	-4.0 (0.4)	(-4.8, -3.1)	-1.4 (0.5)	(-2.5, -0.4)	0.008 *
		Placebo	153	138 (90.2)	-2.5 (0.4)	(-3.4, -1.7)			
>= 65 years	Week 4	CR845	90	77 (85.6)	-3.6 (0.6)	(-4.8, -2.4)	-0.5 (0.8)	(-2.1, 1.0)	0.482
		Placebo	83	77 (92.8)	-3.0 (0.6)	(-4.2, -1.8)			
< 65 years	Week 8	CR845	147	130 (88.4)	-4.8 (0.5)	(-5.6, -3.9)	-0.4 (0.5)	(-1.4, 0.7)	0.487
		Placebo	153	141 (92.2)	-4.4 (0.4)	(-5.3, -3.5)			
>= 65 years	Week 8	CR845	90	77 (85.6)	-4.0 (0.6)	(-5.2, -2.9)	-0.5 (0.8)	(-2.0, 1.0)	0.508
		Placebo	83	75 (90.4)	-3.5 (0.6)	(-4.7, -2.4)			
< 65 years	Week 10	CR845	147	129 (87.8)	-5.6 (0.4)	(-6.5, -4.7)	-1.1 (0.5)	(-2.2, -0.1)	0.033 *
		Placebo	153	136 (88.9)	-4.5 (0.4)	(-5.3, -3.6)			
>= 65 years	Week 10	CR845	90	74 (82.2)	-5.3 (0.6)	(-6.4, -4.1)	-1.5 (0.7)	(-3.0, -0.1)	0.041 *
		Placebo	83	75 (90.4)	-3.7 (0.6)	(-4.9, -2.6)			
< 65 years	Week 12	CR845	147	128 (87.1)	-5.6 (0.5)	(-6.6, -4.7)	-0.8 (0.6)	(-2.0, 0.3)	0.152
		Placebo	153	139 (90.8)	-4.8 (0.5)	(-5.7, -3.9)			
>= 65 years	Week 12	CR845	90	73 (81.1)	-5.1 (0.6)	(-6.3, -3.9)	-1.1 (0.8)	(-2.6, 0.4)	0.148
		Placebo	83	75 (90.4)	-4.0 (0.6)	(-5.1, -2.8)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table BT2SDC_ISCB: Change from baseline in Skindex-10 disease score - MMRM results by sex
ITT

Change from baseline in Skindex-10 disease score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
B: Sex									<0.001 i
Male	Week 4	CR845	137	123 (89.8)	-2.8 (0.5)	(-3.7, -1.9)	-0.1 (0.6)	(-1.3, 1.0)	0.811
		Placebo	139	126 (90.6)	-2.7 (0.5)	(-3.6, -1.8)			
Female	Week 4	CR845	100	87 (87.0)	-5.0 (0.5)	(-6.1, -3.9)	-2.5 (0.7)	(-3.8, -1.1)	<0.001 *
		Placebo	97	89 (91.8)	-2.5 (0.5)	(-3.6, -1.4)			
Male	Week 8	CR845	137	121 (88.3)	-3.1 (0.4)	(-4.0, -2.2)	0.8 (0.5)	(-0.2, 1.9)	0.117
		Placebo	139	129 (92.8)	-3.9 (0.4)	(-4.8, -3.1)			
Female	Week 8	CR845	100	86 (86.0)	-6.2 (0.6)	(-7.3, -5.0)	-2.1 (0.7)	(-3.6, -0.7)	0.004 *
		Placebo	97	87 (89.7)	-4.0 (0.6)	(-5.2, -2.9)			
Male	Week 10	CR845	137	117 (85.4)	-4.0 (0.4)	(-4.9, -3.1)	-0.0 (0.5)	(-1.1, 1.0)	0.945
		Placebo	139	123 (88.5)	-4.0 (0.4)	(-4.8, -3.1)			
Female	Week 10	CR845	100	86 (86.0)	-7.3 (0.5)	(-8.4, -6.2)	-3.0 (0.7)	(-4.4, -1.6)	<0.001 *
		Placebo	97	88 (90.7)	-4.3 (0.6)	(-5.4, -3.2)			
Male	Week 12	CR845	137	115 (83.9)	-4.0 (0.5)	(-4.9, -3.1)	-0.0 (0.6)	(-1.1, 1.1)	0.950
		Placebo	139	124 (89.2)	-4.0 (0.5)	(-4.9, -3.1)			
Female	Week 12	CR845	100	86 (86.0)	-7.1 (0.6)	(-8.3, -5.9)	-2.1 (0.8)	(-3.6, -0.6)	0.006 *
		Placebo	97	90 (92.8)	-5.0 (0.6)	(-6.1, -3.8)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table BT2SDC_ISCC: Change from baseline in Skindex-10 disease score - MMRM results by race
ITT

Change from baseline in Skindex-10 disease score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
C: Race									0.407
Black/African American	Week 4	CR845	53	44 (83.0)	-3.2 (0.7)	(-4.5, -1.8)	-0.2 (1.0)	(-2.1, 1.7)	0.841
		Placebo	38	32 (84.2)	-3.0 (0.8)	(-4.5, -1.4)			
White	Week 4	CR845	164	149 (90.9)	-4.0 (0.5)	(-4.9, -3.1)	-1.5 (0.5)	(-2.6, -0.5)	0.005 *
		Placebo	169	158 (93.5)	-2.5 (0.4)	(-3.4, -1.6)			
Other	Week 4	CR845	20	17 (85.0)	-2.9 (1.2)	(-5.3, -0.4)	-0.6 (1.3)	(-3.2, 2.1)	0.671
		Placebo	29	25 (86.2)	-2.3 (1.1)	(-4.5, -0.1)			
Black/African American	Week 8	CR845	53	45 (84.9)	-4.1 (0.7)	(-5.5, -2.8)	0.1 (1.0)	(-1.8, 2.1)	0.911
		Placebo	38	35 (92.1)	-4.2 (0.8)	(-5.7, -2.7)			
White	Week 8	CR845	164	145 (88.4)	-4.5 (0.5)	(-5.4, -3.6)	-0.6 (0.5)	(-1.7, 0.4)	0.239
		Placebo	169	157 (92.9)	-3.9 (0.4)	(-4.8, -3.0)			
Other	Week 8	CR845	20	17 (85.0)	-3.8 (1.1)	(-6.1, -1.5)	-0.4 (1.2)	(-2.7, 2.0)	0.734
		Placebo	29	24 (82.8)	-3.4 (1.0)	(-5.4, -1.4)			
Black/African American	Week 10	CR845	53	42 (79.2)	-5.2 (0.7)	(-6.6, -3.9)	-0.8 (1.0)	(-2.7, 1.2)	0.453
		Placebo	38	33 (86.8)	-4.5 (0.8)	(-6.0, -3.0)			
White	Week 10	CR845	164	145 (88.4)	-5.5 (0.4)	(-6.3, -4.6)	-1.5 (0.5)	(-2.5, -0.5)	0.003 *
		Placebo	169	155 (91.7)	-3.9 (0.4)	(-4.8, -3.1)			
Other	Week 10	CR845	20	16 (80.0)	-5.1 (1.3)	(-7.6, -2.5)	-1.0 (1.4)	(-3.7, 1.8)	0.496
		Placebo	29	23 (79.3)	-4.1 (1.1)	(-6.4, -1.9)			
Black/African American	Week 12	CR845	53	41 (77.4)	-5.7 (0.7)	(-7.2, -4.3)	-0.3 (1.1)	(-2.4, 1.8)	0.789
		Placebo	38	35 (92.1)	-5.5 (0.8)	(-7.1, -3.8)			
White	Week 12	CR845	164	144 (87.8)	-5.4 (0.5)	(-6.3, -4.5)	-1.4 (0.5)	(-2.4, -0.3)	0.012 *
		Placebo	169	156 (92.3)	-4.0 (0.4)	(-4.9, -3.1)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table BT2SDC_ISCC: Change from baseline in Skindex-10 disease score - MMRM results by race
ITT

Change from baseline in Skindex-10 disease score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Other	Week 12	CR845	20	16 (80.0)	-3.8 (1.3)	(-6.5, -1.2)	1.2 (1.5)	(-1.8, 4.2)	0.408
		Placebo	29	23 (79.3)	-5.1 (1.2)	(-7.4, -2.7)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table BT2SDC_ISCD: Change from baseline in Skindex-10 disease score - MMRM results by baseline WI-NRS
ITT

Change from baseline in Skindex-10 disease score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
D: Baseline worst itching NRS score (WI-NRS)									0.394
>= 4 to < 7	Week 4	CR845	102	94 (92.2)	-4.1 (0.5)	(-5.2, -3.1)	-1.5 (0.6)	(-2.7, -0.3)	0.013 *
		Placebo	113	105 (92.9)	-2.6 (0.5)	(-3.6, -1.6)			
>= 7	Week 4	CR845	135	116 (85.9)	-3.7 (0.5)	(-4.6, -2.8)	-0.9 (0.6)	(-2.1, 0.3)	0.138
		Placebo	123	110 (89.4)	-2.8 (0.5)	(-3.8, -1.8)			
>= 4 to < 7	Week 8	CR845	102	94 (92.2)	-4.5 (0.5)	(-5.5, -3.4)	-1.0 (0.6)	(-2.2, 0.2)	0.094
		Placebo	113	105 (92.9)	-3.5 (0.5)	(-4.4, -2.5)			
>= 7	Week 8	CR845	135	113 (83.7)	-4.7 (0.5)	(-5.6, -3.7)	-0.0 (0.6)	(-1.3, 1.2)	0.983
		Placebo	123	111 (90.2)	-4.6 (0.5)	(-5.6, -3.7)			
>= 4 to < 7	Week 10	CR845	102	91 (89.2)	-5.2 (0.5)	(-6.2, -4.2)	-1.4 (0.6)	(-2.6, -0.3)	0.014 *
		Placebo	113	101 (89.4)	-3.8 (0.5)	(-4.7, -2.8)			
>= 7	Week 10	CR845	135	112 (83.0)	-5.9 (0.5)	(-6.8, -4.9)	-1.3 (0.6)	(-2.5, -0.0)	0.047 *
		Placebo	123	110 (89.4)	-4.6 (0.5)	(-5.6, -3.6)			
>= 4 to < 7	Week 12	CR845	102	90 (88.2)	-5.2 (0.5)	(-6.2, -4.1)	-1.2 (0.6)	(-2.4, 0.0)	0.059
		Placebo	113	102 (90.3)	-4.0 (0.5)	(-5.0, -3.0)			
>= 7	Week 12	CR845	135	111 (82.2)	-5.8 (0.5)	(-6.8, -4.8)	-0.8 (0.7)	(-2.1, 0.5)	0.226
		Placebo	123	112 (91.1)	-5.0 (0.5)	(-6.0, -4.0)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table BT2SDC_ISCE: Change from baseline in Skindex-10 disease score - MMRM results by specific medical condition
ITT

Change from baseline in Skindex-10 disease score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
E: Presence of specific medical conditions									0.493
No	Week 4	CR845	195	173 (88.7)	-3.5 (0.3)	(-4.2, -2.8)	-1.0 (0.5)	(-2.0, -0.1)	0.030 *
		Placebo	199	185 (93.0)	-2.4 (0.3)	(-3.1, -1.8)			
Yes	Week 4	CR845	42	37 (88.1)	-5.0 (0.8)	(-6.7, -3.4)	-1.5 (1.3)	(-4.0, 1.0)	0.245
		Placebo	37	30 (81.1)	-3.6 (0.9)	(-5.4, -1.8)			
No	Week 8	CR845	195	172 (88.2)	-4.3 (0.3)	(-5.0, -3.6)	-0.4 (0.5)	(-1.3, 0.6)	0.431
		Placebo	199	181 (91.0)	-3.9 (0.3)	(-4.6, -3.3)			
Yes	Week 8	CR845	42	35 (83.3)	-4.9 (0.9)	(-6.7, -3.2)	-0.7 (1.3)	(-3.2, 1.8)	0.589
		Placebo	37	35 (94.6)	-4.2 (0.9)	(-6.0, -2.4)			
No	Week 10	CR845	195	168 (86.2)	-5.1 (0.3)	(-5.8, -4.5)	-1.0 (0.5)	(-2.0, -0.1)	0.026 *
		Placebo	199	177 (88.9)	-4.1 (0.3)	(-4.7, -3.4)			
Yes	Week 10	CR845	42	35 (83.3)	-6.6 (0.8)	(-8.2, -5.1)	-2.5 (1.1)	(-4.8, -0.3)	0.027 *
		Placebo	37	34 (91.9)	-4.1 (0.8)	(-5.7, -2.5)			
No	Week 12	CR845	195	166 (85.1)	-5.2 (0.4)	(-5.9, -4.4)	-0.9 (0.5)	(-1.8, 0.1)	0.082
		Placebo	199	180 (90.5)	-4.3 (0.4)	(-5.0, -3.6)			
Yes	Week 12	CR845	42	35 (83.3)	-6.2 (0.9)	(-7.9, -4.5)	-1.3 (1.2)	(-3.7, 1.1)	0.290
		Placebo	37	34 (91.9)	-4.9 (0.9)	(-6.6, -3.1)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor previous use of anti-itch medication is also included in the model.
Source Data: askin, created on: 17FEB2022

Table BT2SDC_ISCF: Change from baseline in Skindex-10 disease score - MMRM results by use of concomitant itch medication
ITT

Change from baseline in Skindex-10 disease score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
F: Use of concomitant itch medication									0.403
No	Week 4	CR845	150	137 (91.3)	-3.2 (0.5)	(-4.1, -2.3)	-0.8 (0.6)	(-1.9, 0.3)	0.150
		Placebo	151	141 (93.4)	-2.4 (0.5)	(-3.3, -1.5)			
Yes	Week 4	CR845	87	73 (83.9)	-4.8 (0.6)	(-5.9, -3.7)	-1.8 (0.7)	(-3.2, -0.4)	0.013 *
		Placebo	85	74 (87.1)	-2.9 (0.6)	(-4.0, -1.8)			
No	Week 8	CR845	150	135 (90.0)	-4.1 (0.4)	(-5.0, -3.2)	-0.3 (0.5)	(-1.4, 0.8)	0.571
		Placebo	151	139 (92.1)	-3.8 (0.4)	(-4.7, -2.9)			
Yes	Week 8	CR845	87	72 (82.8)	-5.0 (0.6)	(-6.1, -3.8)	-0.8 (0.8)	(-2.3, 0.8)	0.323
		Placebo	85	77 (90.6)	-4.2 (0.6)	(-5.4, -3.1)			
No	Week 10	CR845	150	131 (87.3)	-5.0 (0.4)	(-5.8, -4.1)	-1.1 (0.5)	(-2.1, -0.0)	0.044 *
		Placebo	151	136 (90.1)	-3.9 (0.4)	(-4.8, -3.0)			
Yes	Week 10	CR845	87	72 (82.8)	-6.2 (0.6)	(-7.3, -5.0)	-1.8 (0.7)	(-3.3, -0.3)	0.017 *
		Placebo	85	75 (88.2)	-4.4 (0.6)	(-5.5, -3.3)			
No	Week 12	CR845	150	130 (86.7)	-4.9 (0.5)	(-5.8, -4.0)	-0.8 (0.6)	(-1.9, 0.3)	0.167
		Placebo	151	139 (92.1)	-4.1 (0.5)	(-5.0, -3.2)			
Yes	Week 12	CR845	87	71 (81.6)	-6.2 (0.6)	(-7.3, -5.0)	-1.3 (0.8)	(-2.9, 0.2)	0.094
		Placebo	85	75 (88.2)	-4.9 (0.6)	(-6.0, -3.7)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor presence of medical condition is also included in the model.
Source Data: askin, created on: 17FEB2022

Table BT2SDC_ISCG: Change from baseline in Skindex-10 disease score - MMRM results by region
ITT

Change from baseline in Skindex-10 disease score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
G: Region									0.334
USA	Week 4	CR845	146	128 (87.7)	-3.2 (0.4)	(-4.0, -2.3)	-1.0 (0.6)	(-2.1, 0.1)	0.064
		Placebo	133	119 (89.5)	-2.2 (0.5)	(-3.1, -1.2)			
Asia	Week 4	CR845	8	8 (100.0)	-6.1 (1.5)	(-9.4, -2.9)	-2.4 (2.0)	(-6.6, 1.9)	0.257
		Placebo	12	12 (100.0)	-3.8 (1.3)	(-6.5, -1.0)			
Eastern Europe	Week 4	CR845	54	52 (96.3)	-4.7 (0.7)	(-6.1, -3.2)	-1.4 (0.8)	(-3.0, 0.1)	0.072
		Placebo	60	57 (95.0)	-3.2 (0.7)	(-4.6, -1.8)			
Western Europe/European origin	Week 4	CR845	29	22 (75.9)	-5.1 (1.2)	(-7.6, -2.6)	-1.0 (1.6)	(-4.3, 2.3)	0.556
		Placebo	31	27 (87.1)	-4.1 (1.2)	(-6.5, -1.8)			
USA	Week 8	CR845	146	128 (87.7)	-3.9 (0.4)	(-4.8, -3.1)	0.2 (0.6)	(-0.9, 1.3)	0.674
		Placebo	133	123 (92.5)	-4.2 (0.5)	(-5.1, -3.3)			
Asia	Week 8	CR845	8	7 (87.5)	-6.7 (1.2)	(-9.2, -4.2)	-1.7 (1.5)	(-5.0, 1.5)	0.276
		Placebo	12	12 (100.0)	-4.9 (1.0)	(-7.0, -2.9)			
Eastern Europe	Week 8	CR845	54	49 (90.7)	-5.3 (0.8)	(-7.0, -3.7)	-1.6 (0.9)	(-3.4, 0.2)	0.078
		Placebo	60	58 (96.7)	-3.7 (0.8)	(-5.2, -2.2)			
Western Europe/European origin	Week 8	CR845	29	23 (79.3)	-5.4 (1.1)	(-7.6, -3.2)	-1.2 (1.5)	(-4.2, 1.7)	0.402
		Placebo	31	23 (74.2)	-4.2 (1.1)	(-6.3, -2.0)			
USA	Week 10	CR845	146	126 (86.3)	-5.0 (0.4)	(-5.8, -4.1)	-0.4 (0.6)	(-1.5, 0.7)	0.451
		Placebo	133	120 (90.2)	-4.6 (0.5)	(-5.5, -3.7)			
Asia	Week 10	CR845	8	7 (87.5)	-7.8 (1.6)	(-11.1, -4.5)	-1.4 (2.0)	(-5.7, 2.8)	0.485
		Placebo	12	11 (91.7)	-6.4 (1.2)	(-9.0, -3.8)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table BT2SDC_ISCG: Change from baseline in Skindex-10 disease score - MMRM results by region
ITT

Change from baseline in Skindex-10 disease score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Eastern Europe	Week 10	CR845	54	48 (88.9)	-6.3 (0.7)	(-7.7, -4.8)	-3.1 (0.8)	(-4.6, -1.5)	<0.001 *
		Placebo	60	58 (96.7)	-3.2 (0.7)	(-4.5, -1.8)			
Western Europe/European origin	Week 10	CR845	29	22 (75.9)	-6.1 (1.2)	(-8.5, -3.8)	-2.1 (1.6)	(-5.2, 1.0)	0.184
		Placebo	31	22 (71.0)	-4.0 (1.1)	(-6.3, -1.7)			
USA	Week 12	CR845	146	125 (85.6)	-5.3 (0.4)	(-6.2, -4.4)	-0.3 (0.6)	(-1.5, 0.8)	0.551
		Placebo	133	124 (93.2)	-4.9 (0.5)	(-5.9, -4.0)			
Asia	Week 12	CR845	8	7 (87.5)	-6.7 (1.6)	(-10.0, -3.4)	0.5 (2.0)	(-3.7, 4.8)	0.796
		Placebo	12	11 (91.7)	-7.2 (1.3)	(-9.9, -4.6)			
Eastern Europe	Week 12	CR845	54	47 (87.0)	-5.6 (0.8)	(-7.3, -3.9)	-2.2 (1.0)	(-4.1, -0.3)	0.023 *
		Placebo	60	56 (93.3)	-3.4 (0.8)	(-4.9, -1.9)			
Western Europe/European origin	Week 12	CR845	29	22 (75.9)	-5.8 (1.2)	(-8.1, -3.4)	-2.0 (1.5)	(-5.1, 1.1)	0.200
		Placebo	31	23 (74.2)	-3.7 (1.1)	(-6.0, -1.5)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table BT2SDC_ISCH: Change from baseline in Skindex-10 disease score - MMRM results by dialysis method
ITT

Change from baseline in Skindex-10 disease score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
H: Dialysis method									0.675
Hemodialysis (HD)	Week 4	CR845	222	197 (88.7)	-3.8 (0.4)	(-4.5, -3.1)	-1.3 (0.5)	(-2.2, -0.4)	0.007 *
		Placebo	199	180 (90.5)	-2.5 (0.4)	(-3.2, -1.8)			
Hemodiafiltration (HDF)	Week 4	CR845	15	13 (86.7)	-3.8 (2.3)	(-8.4, 0.8)	-0.7 (1.5)	(-3.6, 2.3)	0.660
		Placebo	37	35 (94.6)	-3.2 (1.8)	(-6.7, 0.4)			
Hemodialysis (HD)	Week 8	CR845	222	194 (87.4)	-4.5 (0.4)	(-5.2, -3.8)	-0.5 (0.5)	(-1.4, 0.4)	0.280
		Placebo	199	183 (92.0)	-4.0 (0.4)	(-4.7, -3.3)			
Hemodiafiltration (HDF)	Week 8	CR845	15	13 (86.7)	-3.5 (2.3)	(-8.2, 1.2)	0.3 (1.6)	(-3.0, 3.6)	0.866
		Placebo	37	33 (89.2)	-3.8 (1.8)	(-7.4, -0.1)			
Hemodialysis (HD)	Week 10	CR845	222	191 (86.0)	-5.4 (0.4)	(-6.1, -4.7)	-1.1 (0.5)	(-2.0, -0.2)	0.019 *
		Placebo	199	180 (90.5)	-4.3 (0.4)	(-5.1, -3.6)			
Hemodiafiltration (HDF)	Week 10	CR845	15	12 (80.0)	-6.0 (2.3)	(-10.6, -1.3)	-3.3 (1.6)	(-6.5, -0.1)	0.045 *
		Placebo	37	31 (83.8)	-2.7 (1.8)	(-6.3, 0.9)			
Hemodialysis (HD)	Week 12	CR845	222	188 (84.7)	-5.4 (0.4)	(-6.2, -4.7)	-0.7 (0.5)	(-1.7, 0.2)	0.128
		Placebo	199	182 (91.5)	-4.7 (0.4)	(-5.4, -3.9)			
Hemodiafiltration (HDF)	Week 12	CR845	15	13 (86.7)	-4.6 (2.4)	(-9.3, 0.2)	-1.8 (1.6)	(-5.2, 1.5)	0.267
		Placebo	37	32 (86.5)	-2.7 (1.8)	(-6.4, 0.9)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table BT2SMC_ISCA: Change from baseline in Skindex-10 mood/emotional distress score - MMRM results by age
ITT

Change from baseline in Skindex-10 mood/emotional distress score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
A: Age									0.731
< 65 years	Week 4	CR845	147	131 (89.1)	-4.0 (0.5)	(-4.9, -3.1)	-1.2 (0.6)	(-2.3, -0.1)	0.030 *
		Placebo	153	140 (91.5)	-2.8 (0.5)	(-3.7, -1.9)			
>= 65 years	Week 4	CR845	90	77 (85.6)	-3.0 (0.6)	(-4.2, -1.7)	-0.7 (0.8)	(-2.3, 0.9)	0.390
		Placebo	83	79 (95.2)	-2.3 (0.6)	(-3.5, -1.1)			
< 65 years	Week 8	CR845	147	125 (85.0)	-4.6 (0.5)	(-5.6, -3.7)	-0.1 (0.6)	(-1.2, 1.1)	0.929
		Placebo	153	140 (91.5)	-4.6 (0.5)	(-5.5, -3.6)			
>= 65 years	Week 8	CR845	90	76 (84.4)	-3.9 (0.6)	(-5.1, -2.7)	-0.6 (0.8)	(-2.2, 0.9)	0.418
		Placebo	83	77 (92.8)	-3.3 (0.6)	(-4.4, -2.1)			
< 65 years	Week 10	CR845	147	128 (87.1)	-5.2 (0.5)	(-6.1, -4.2)	-0.7 (0.6)	(-1.8, 0.4)	0.217
		Placebo	153	138 (90.2)	-4.5 (0.5)	(-5.4, -3.5)			
>= 65 years	Week 10	CR845	90	72 (80.0)	-4.9 (0.6)	(-6.1, -3.7)	-1.7 (0.8)	(-3.2, -0.1)	0.032 *
		Placebo	83	74 (89.2)	-3.3 (0.6)	(-4.4, -2.1)			
< 65 years	Week 12	CR845	147	128 (87.1)	-5.5 (0.5)	(-6.5, -4.5)	-0.3 (0.6)	(-1.5, 0.8)	0.574
		Placebo	153	139 (90.8)	-5.1 (0.5)	(-6.1, -4.2)			
>= 65 years	Week 12	CR845	90	73 (81.1)	-4.8 (0.6)	(-6.0, -3.6)	-1.2 (0.8)	(-2.8, 0.3)	0.119
		Placebo	83	76 (91.6)	-3.6 (0.6)	(-4.8, -2.4)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table BT2SMC_ISCB: Change from baseline in Skindex-10 mood/emotional distress score - MMRM results by sex
ITT

Change from baseline in Skindex-10 mood/emotional distress score					Repeated measures analysis					
					Change from Baseline		Treatment Difference			
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value	
B: Sex									0.003	i
Male	Week 4	CR845	137	122 (89.1)	-2.7 (0.5)	(-3.6, -1.7)	-0.4 (0.6)	(-1.6, 0.7)	0.453	
		Placebo	139	127 (91.4)	-2.2 (0.5)	(-3.2, -1.3)				
Female	Week 4	CR845	100	86 (86.0)	-4.6 (0.6)	(-5.8, -3.5)	-1.8 (0.7)	(-3.3, -0.4)	0.013	*
		Placebo	97	92 (94.8)	-2.8 (0.6)	(-3.9, -1.7)				
Male	Week 8	CR845	137	119 (86.9)	-3.1 (0.5)	(-4.0, -2.1)	0.9 (0.6)	(-0.3, 2.0)	0.129	
		Placebo	139	129 (92.8)	-3.9 (0.5)	(-4.8, -3.0)				
Female	Week 8	CR845	100	82 (82.0)	-5.8 (0.6)	(-7.0, -4.6)	-1.8 (0.8)	(-3.3, -0.3)	0.017	*
		Placebo	97	88 (90.7)	-4.0 (0.6)	(-5.2, -2.8)				
Male	Week 10	CR845	137	115 (83.9)	-3.7 (0.5)	(-4.6, -2.7)	0.3 (0.6)	(-0.9, 1.4)	0.654	
		Placebo	139	122 (87.8)	-3.9 (0.5)	(-4.8, -3.0)				
Female	Week 10	CR845	100	85 (85.0)	-6.7 (0.6)	(-7.9, -5.6)	-2.8 (0.7)	(-4.3, -1.4)	<0.001	*
		Placebo	97	90 (92.8)	-3.9 (0.6)	(-5.0, -2.7)				
Male	Week 12	CR845	137	116 (84.7)	-4.1 (0.5)	(-5.0, -3.1)	0.4 (0.6)	(-0.8, 1.5)	0.504	
		Placebo	139	124 (89.2)	-4.4 (0.5)	(-5.4, -3.5)				
Female	Week 12	CR845	100	85 (85.0)	-6.5 (0.6)	(-7.8, -5.3)	-2.1 (0.8)	(-3.6, -0.5)	0.011	*
		Placebo	97	91 (93.8)	-4.5 (0.6)	(-5.7, -3.3)				

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table BT2SMC_ISCC: Change from baseline in Skindex-10 mood/emotional distress score - MMRM results by race
ITT

Change from baseline in Skindex-10 mood/emotional distress score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
C: Race									0.117
Black/African American	Week 4	CR845	53	43 (81.1)	-2.7 (0.7)	(-4.1, -1.3)	-0.2 (1.0)	(-2.2, 1.9)	0.880
		Placebo	38	33 (86.8)	-2.5 (0.8)	(-4.1, -1.0)			
White	Week 4	CR845	164	148 (90.2)	-3.7 (0.5)	(-4.7, -2.8)	-1.4 (0.6)	(-2.5, -0.3)	0.013 *
		Placebo	169	161 (95.3)	-2.4 (0.5)	(-3.3, -1.4)			
Other	Week 4	CR845	20	17 (85.0)	-3.3 (1.3)	(-5.9, -0.6)	-0.4 (1.4)	(-3.2, 2.3)	0.742
		Placebo	29	25 (86.2)	-2.8 (1.2)	(-5.1, -0.5)			
Black/African American	Week 8	CR845	53	44 (83.0)	-3.6 (0.7)	(-5.1, -2.1)	1.2 (1.1)	(-1.0, 3.3)	0.287
		Placebo	38	35 (92.1)	-4.8 (0.8)	(-6.4, -3.1)			
White	Week 8	CR845	164	140 (85.4)	-4.4 (0.5)	(-5.3, -3.5)	-0.8 (0.5)	(-1.8, 0.3)	0.168
		Placebo	169	157 (92.9)	-3.7 (0.5)	(-4.6, -2.8)			
Other	Week 8	CR845	20	17 (85.0)	-4.1 (1.4)	(-6.9, -1.3)	0.6 (1.5)	(-2.4, 3.6)	0.689
		Placebo	29	25 (86.2)	-4.7 (1.2)	(-7.1, -2.3)			
Black/African American	Week 10	CR845	53	42 (79.2)	-3.4 (0.7)	(-4.9, -1.9)	1.7 (1.1)	(-0.4, 3.9)	0.105
		Placebo	38	34 (89.5)	-5.2 (0.8)	(-6.8, -3.5)			
White	Week 10	CR845	164	142 (86.6)	-5.3 (0.5)	(-6.2, -4.4)	-1.7 (0.5)	(-2.7, -0.6)	0.002 *
		Placebo	169	154 (91.1)	-3.6 (0.4)	(-4.5, -2.7)			
Other	Week 10	CR845	20	16 (80.0)	-6.0 (1.5)	(-9.1, -2.9)	-2.2 (1.7)	(-5.6, 1.2)	0.190
		Placebo	29	24 (82.8)	-3.8 (1.3)	(-6.4, -1.1)			
Black/African American	Week 12	CR845	53	43 (81.1)	-4.6 (0.8)	(-6.2, -3.1)	1.7 (1.1)	(-0.5, 4.0)	0.122
		Placebo	38	36 (94.7)	-6.3 (0.8)	(-8.0, -4.7)			
White	Week 12	CR845	164	142 (86.6)	-5.3 (0.5)	(-6.2, -4.4)	-1.3 (0.6)	(-2.4, -0.2)	0.017 *
		Placebo	169	156 (92.3)	-4.0 (0.5)	(-4.9, -3.1)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table BT2SMC_ISCC: Change from baseline in Skindex-10 mood/emotional distress score - MMRM results by race
ITT

Change from baseline in Skindex-10 mood/emotional distress score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Other	Week 12	CR845	20	16 (80.0)	-4.8 (1.6)	(-8.0, -1.6)	-0.2 (1.8)	(-3.8, 3.4)	0.924
		Placebo	29	23 (79.3)	-4.6 (1.4)	(-7.4, -1.9)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table BT2SMC_ISCD: Change from baseline in Skindex-10 mood/emotional distress score - MMRM results by baseline WI-NRS
ITT

Change from baseline in Skindex-10 mood/emotional distress score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
D: Baseline worst itching NRS score (WI-NRS)									0.292
>= 4 to < 7	Week 4	CR845	102	94 (92.2)	-4.1 (0.5)	(-5.1, -3.1)	-1.4 (0.6)	(-2.5, -0.2)	0.026 *
		Placebo	113	107 (94.7)	-2.7 (0.5)	(-3.7, -1.7)			
>= 7	Week 4	CR845	135	114 (84.4)	-3.2 (0.5)	(-4.2, -2.3)	-0.8 (0.6)	(-2.1, 0.4)	0.191
		Placebo	123	112 (91.1)	-2.4 (0.5)	(-3.4, -1.4)			
>= 4 to < 7	Week 8	CR845	102	93 (91.2)	-4.3 (0.6)	(-5.3, -3.2)	-0.8 (0.6)	(-2.1, 0.5)	0.215
		Placebo	113	104 (92.0)	-3.5 (0.5)	(-4.5, -2.4)			
>= 7	Week 8	CR845	135	108 (80.0)	-4.4 (0.5)	(-5.4, -3.4)	0.2 (0.7)	(-1.1, 1.5)	0.753
		Placebo	123	113 (91.9)	-4.6 (0.5)	(-5.6, -3.6)			
>= 4 to < 7	Week 10	CR845	102	90 (88.2)	-5.2 (0.5)	(-6.3, -4.2)	-1.3 (0.6)	(-2.5, -0.1)	0.035 *
		Placebo	113	100 (88.5)	-3.9 (0.5)	(-4.9, -2.9)			
>= 7	Week 10	CR845	135	110 (81.5)	-5.0 (0.5)	(-6.0, -4.0)	-0.9 (0.7)	(-2.2, 0.4)	0.167
		Placebo	123	112 (91.1)	-4.1 (0.5)	(-5.1, -3.1)			
>= 4 to < 7	Week 12	CR845	102	90 (88.2)	-5.3 (0.6)	(-6.4, -4.2)	-1.3 (0.6)	(-2.6, -0.1)	0.036 *
		Placebo	113	101 (89.4)	-4.0 (0.5)	(-5.0, -2.9)			
>= 7	Week 12	CR845	135	111 (82.2)	-5.2 (0.5)	(-6.2, -4.2)	-0.1 (0.7)	(-1.4, 1.2)	0.884
		Placebo	123	114 (92.7)	-5.1 (0.5)	(-6.1, -4.1)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table BT2SMC_ISCE: Change from baseline in Skindex-10 mood/emotional distress score - MMRM results by specific medical condition
ITT

Change from baseline in Skindex-10 mood/emotional distress score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
E: Presence of specific medical conditions									0.698
No	Week 4	CR845	195	171 (87.7)	-3.4 (0.4)	(-4.1, -2.6)	-1.0 (0.5)	(-2.0, -0.1)	0.037 *
		Placebo	199	187 (94.0)	-2.3 (0.3)	(-3.0, -1.6)			
Yes	Week 4	CR845	42	37 (88.1)	-4.2 (0.9)	(-5.9, -2.5)	-1.2 (1.3)	(-3.7, 1.3)	0.354
		Placebo	37	32 (86.5)	-3.0 (0.9)	(-4.9, -1.2)			
No	Week 8	CR845	195	166 (85.1)	-4.1 (0.4)	(-4.8, -3.4)	-0.2 (0.5)	(-1.2, 0.8)	0.710
		Placebo	199	183 (92.0)	-3.9 (0.3)	(-4.6, -3.2)			
Yes	Week 8	CR845	42	35 (83.3)	-4.8 (0.9)	(-6.6, -3.1)	-0.8 (1.3)	(-3.3, 1.7)	0.517
		Placebo	37	34 (91.9)	-4.0 (0.9)	(-5.8, -2.2)			
No	Week 10	CR845	195	166 (85.1)	-4.7 (0.4)	(-5.5, -4.0)	-0.9 (0.5)	(-1.8, 0.1)	0.087
		Placebo	199	177 (88.9)	-3.9 (0.4)	(-4.6, -3.2)			
Yes	Week 10	CR845	42	34 (81.0)	-6.1 (0.9)	(-7.8, -4.3)	-2.3 (1.2)	(-4.7, 0.2)	0.068
		Placebo	37	35 (94.6)	-3.8 (0.9)	(-5.5, -2.1)			
No	Week 12	CR845	195	166 (85.1)	-5.0 (0.4)	(-5.8, -4.3)	-0.6 (0.5)	(-1.6, 0.4)	0.218
		Placebo	199	181 (91.0)	-4.4 (0.4)	(-5.1, -3.7)			
Yes	Week 12	CR845	42	35 (83.3)	-5.6 (0.9)	(-7.4, -3.8)	-1.0 (1.3)	(-3.6, 1.6)	0.443
		Placebo	37	34 (91.9)	-4.6 (0.9)	(-6.5, -2.8)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor previous use of anti-itch medication is also included in the model.
Source Data: askin, created on: 17FEB2022

Table BT2SMC_ISCF: Change from baseline in Skindex-10 mood/emotional distress score - MMRM results by use of concomitant itch medication
ITT

Change from baseline in Skindex-10 mood/emotional distress score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
F: Use of concomitant itch medication									0.768
No	Week 4	CR845	150	136 (90.7)	-3.2 (0.5)	(-4.2, -2.3)	-0.9 (0.6)	(-2.1, 0.2)	0.104
		Placebo	151	141 (93.4)	-2.3 (0.5)	(-3.2, -1.4)			
Yes	Week 4	CR845	87	72 (82.8)	-4.1 (0.6)	(-5.2, -2.9)	-1.2 (0.8)	(-2.7, 0.3)	0.113
		Placebo	85	78 (91.8)	-2.9 (0.6)	(-4.0, -1.7)			
No	Week 8	CR845	150	134 (89.3)	-4.0 (0.5)	(-4.9, -3.0)	-0.2 (0.6)	(-1.3, 1.0)	0.785
		Placebo	151	138 (91.4)	-3.8 (0.5)	(-4.8, -2.9)			
Yes	Week 8	CR845	87	67 (77.0)	-4.7 (0.6)	(-5.9, -3.6)	-0.4 (0.8)	(-1.9, 1.1)	0.588
		Placebo	85	79 (92.9)	-4.3 (0.6)	(-5.4, -3.2)			
No	Week 10	CR845	150	128 (85.3)	-4.6 (0.5)	(-5.5, -3.6)	-1.1 (0.6)	(-2.2, 0.1)	0.072
		Placebo	151	136 (90.1)	-3.5 (0.5)	(-4.5, -2.6)			
Yes	Week 10	CR845	87	72 (82.8)	-5.7 (0.6)	(-6.8, -4.6)	-1.1 (0.7)	(-2.5, 0.4)	0.149
		Placebo	85	76 (89.4)	-4.6 (0.6)	(-5.7, -3.5)			
No	Week 12	CR845	150	131 (87.3)	-4.8 (0.5)	(-5.8, -3.9)	-0.5 (0.6)	(-1.7, 0.6)	0.377
		Placebo	151	139 (92.1)	-4.3 (0.5)	(-5.3, -3.4)			
Yes	Week 12	CR845	87	70 (80.5)	-5.7 (0.6)	(-6.9, -4.5)	-0.9 (0.8)	(-2.5, 0.6)	0.248
		Placebo	85	76 (89.4)	-4.8 (0.6)	(-6.0, -3.6)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor presence of medical condition is also included in the model.
Source Data: askin, created on: 17FEB2022

Table BT2SMC_ISCG: Change from baseline in Skindex-10 mood/emotional distress score - MMRM results by region
ITT

Change from baseline in Skindex-10 mood/emotional distress score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
G: Region									0.448
USA	Week 4	CR845	146	126 (86.3)	-3.3 (0.5)	(-4.3, -2.4)	-1.3 (0.6)	(-2.5, -0.1)	0.031 *
		Placebo	133	120 (90.2)	-2.0 (0.5)	(-3.0, -1.0)			
Asia	Week 4	CR845	8	8 (100.0)	-6.1 (1.5)	(-9.3, -2.9)	-1.7 (2.0)	(-5.9, 2.4)	0.389
		Placebo	12	12 (100.0)	-4.4 (1.3)	(-7.1, -1.7)			
Eastern Europe	Week 4	CR845	54	52 (96.3)	-3.0 (0.7)	(-4.4, -1.5)	-0.1 (0.8)	(-1.7, 1.5)	0.916
		Placebo	60	59 (98.3)	-2.9 (0.7)	(-4.2, -1.5)			
Western Europe/European origin	Week 4	CR845	29	22 (75.9)	-5.8 (1.1)	(-8.1, -3.5)	-1.5 (1.5)	(-4.5, 1.5)	0.317
		Placebo	31	28 (90.3)	-4.3 (1.0)	(-6.4, -2.3)			
USA	Week 8	CR845	146	122 (83.6)	-4.0 (0.5)	(-4.9, -3.0)	0.2 (0.6)	(-1.0, 1.5)	0.691
		Placebo	133	122 (91.7)	-4.2 (0.5)	(-5.2, -3.2)			
Asia	Week 8	CR845	8	7 (87.5)	-6.1 (1.4)	(-9.1, -3.1)	0.6 (1.8)	(-3.2, 4.5)	0.725
		Placebo	12	12 (100.0)	-6.7 (1.1)	(-9.1, -4.4)			
Eastern Europe	Week 8	CR845	54	49 (90.7)	-4.5 (0.8)	(-6.0, -3.0)	-1.4 (0.8)	(-3.0, 0.3)	0.110
		Placebo	60	58 (96.7)	-3.2 (0.7)	(-4.6, -1.8)			
Western Europe/European origin	Week 8	CR845	29	23 (79.3)	-5.7 (1.1)	(-7.9, -3.6)	-0.8 (1.4)	(-3.7, 2.1)	0.591
		Placebo	31	25 (80.6)	-5.0 (1.0)	(-7.1, -2.9)			
USA	Week 10	CR845	146	124 (84.9)	-4.3 (0.5)	(-5.2, -3.4)	0.1 (0.6)	(-1.1, 1.3)	0.880
		Placebo	133	120 (90.2)	-4.4 (0.5)	(-5.4, -3.4)			
Asia	Week 10	CR845	8	7 (87.5)	-8.6 (1.7)	(-12.3, -4.9)	-1.8 (2.2)	(-6.5, 3.0)	0.442
		Placebo	12	11 (91.7)	-6.9 (1.4)	(-9.8, -3.9)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table BT2SMC_ISCG: Change from baseline in Skindex-10 mood/emotional distress score - MMRM results by region
ITT

Change from baseline in Skindex-10 mood/emotional distress score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Eastern Europe	Week 10	CR845	54	47 (87.0)	-5.5 (0.8)	(-6.9, -4.0)	-2.6 (0.8)	(-4.2, -0.9)	0.002 *
		Placebo	60	58 (96.7)	-2.9 (0.7)	(-4.3, -1.5)			
Western Europe/European origin	Week 10	CR845	29	22 (75.9)	-7.6 (1.1)	(-9.8, -5.4)	-3.6 (1.5)	(-6.5, -0.7)	0.017 *
		Placebo	31	23 (74.2)	-4.0 (1.0)	(-6.1, -1.9)			
USA	Week 12	CR845	146	125 (85.6)	-4.8 (0.5)	(-5.7, -3.8)	0.2 (0.6)	(-1.0, 1.5)	0.690
		Placebo	133	124 (93.2)	-5.0 (0.5)	(-6.0, -4.1)			
Asia	Week 12	CR845	8	7 (87.5)	-7.9 (1.4)	(-11.0, -4.9)	-1.0 (1.8)	(-4.9, 2.9)	0.593
		Placebo	12	11 (91.7)	-6.9 (1.2)	(-9.4, -4.5)			
Eastern Europe	Week 12	CR845	54	47 (87.0)	-5.2 (0.8)	(-6.7, -3.7)	-1.6 (0.8)	(-3.3, 0.1)	0.060
		Placebo	60	56 (93.3)	-3.6 (0.7)	(-5.0, -2.2)			
Western Europe/European origin	Week 12	CR845	29	22 (75.9)	-7.1 (1.2)	(-9.6, -4.6)	-3.1 (1.7)	(-6.4, 0.2)	0.067
		Placebo	31	24 (77.4)	-4.0 (1.2)	(-6.4, -1.6)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table BT2SMC_ISCH: Change from baseline in Skindex-10 mood/emotional distress score - MMRM results by dialysis method
ITT

Change from baseline in Skindex-10 mood/emotional distress score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
H: Dialysis method									0.462
Hemodialysis (HD)	Week 4	CR845	222	195 (87.8)	-3.5 (0.4)	(-4.3, -2.8)	-1.3 (0.5)	(-2.2, -0.3)	0.009 *
		Placebo	199	183 (92.0)	-2.3 (0.4)	(-3.0, -1.5)			
Hemodiafiltration (HDF)	Week 4	CR845	15	13 (86.7)	-5.1 (2.3)	(-9.7, -0.5)	-0.8 (1.5)	(-3.7, 2.2)	0.597
		Placebo	37	36 (97.3)	-4.3 (1.7)	(-7.8, -0.8)			
Hemodialysis (HD)	Week 8	CR845	222	188 (84.7)	-4.3 (0.4)	(-5.0, -3.5)	-0.3 (0.5)	(-1.3, 0.6)	0.503
		Placebo	199	183 (92.0)	-4.0 (0.4)	(-4.7, -3.2)			
Hemodiafiltration (HDF)	Week 8	CR845	15	13 (86.7)	-5.4 (2.4)	(-10.2, -0.6)	-0.7 (1.7)	(-4.0, 2.7)	0.686
		Placebo	37	34 (91.9)	-4.7 (1.8)	(-8.3, -1.1)			
Hemodialysis (HD)	Week 10	CR845	222	188 (84.7)	-4.9 (0.4)	(-5.7, -4.2)	-0.8 (0.5)	(-1.8, 0.1)	0.088
		Placebo	199	181 (91.0)	-4.1 (0.4)	(-4.8, -3.3)			
Hemodiafiltration (HDF)	Week 10	CR845	15	12 (80.0)	-7.8 (2.4)	(-12.6, -3.0)	-4.2 (1.7)	(-7.5, -0.8)	0.016 *
		Placebo	37	31 (83.8)	-3.6 (1.8)	(-7.2, -0.0)			
Hemodialysis (HD)	Week 12	CR845	222	188 (84.7)	-5.1 (0.4)	(-5.9, -4.3)	-0.4 (0.5)	(-1.4, 0.6)	0.391
		Placebo	199	182 (91.5)	-4.7 (0.4)	(-5.5, -3.9)			
Hemodiafiltration (HDF)	Week 12	CR845	15	13 (86.7)	-7.5 (2.4)	(-12.2, -2.7)	-3.3 (1.7)	(-6.6, 0.0)	0.051
		Placebo	37	33 (89.2)	-4.2 (1.8)	(-7.8, -0.5)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table BT2SSC_ISCA: Change from baseline in Skindex-10 social functioning score - MMRM results by age
ITT

Change from baseline in Skindex-10 social functioning score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
A: Age									0.998
< 65 years	Week 4	CR845	147	133 (90.5)	-3.4 (0.6)	(-4.6, -2.1)	0.1 (0.8)	(-1.4, 1.6)	0.867
		Placebo	153	141 (92.2)	-3.5 (0.6)	(-4.7, -2.2)			
>= 65 years	Week 4	CR845	90	78 (86.7)	-3.1 (0.7)	(-4.6, -1.6)	0.6 (1.0)	(-1.3, 2.5)	0.515
		Placebo	83	79 (95.2)	-3.7 (0.7)	(-5.2, -2.3)			
< 65 years	Week 8	CR845	147	129 (87.8)	-4.6 (0.6)	(-5.8, -3.3)	0.2 (0.7)	(-1.3, 1.6)	0.798
		Placebo	153	142 (92.8)	-4.7 (0.6)	(-6.0, -3.5)			
>= 65 years	Week 8	CR845	90	76 (84.4)	-4.1 (0.7)	(-5.5, -2.6)	-0.5 (0.9)	(-2.4, 1.3)	0.570
		Placebo	83	76 (91.6)	-3.5 (0.7)	(-5.0, -2.1)			
< 65 years	Week 10	CR845	147	130 (88.4)	-5.0 (0.6)	(-6.3, -3.8)	-0.6 (0.8)	(-2.1, 0.9)	0.435
		Placebo	153	139 (90.8)	-4.4 (0.6)	(-5.7, -3.2)			
>= 65 years	Week 10	CR845	90	74 (82.2)	-4.7 (0.7)	(-6.1, -3.3)	-0.7 (0.9)	(-2.5, 1.2)	0.470
		Placebo	83	72 (86.7)	-4.0 (0.7)	(-5.4, -2.6)			
< 65 years	Week 12	CR845	147	128 (87.1)	-5.1 (0.7)	(-6.4, -3.8)	-0.2 (0.8)	(-1.8, 1.3)	0.794
		Placebo	153	140 (91.5)	-4.9 (0.6)	(-6.2, -3.7)			
>= 65 years	Week 12	CR845	90	74 (82.2)	-4.4 (0.7)	(-5.7, -3.0)	-0.1 (0.9)	(-1.9, 1.7)	0.906
		Placebo	83	74 (89.2)	-4.3 (0.7)	(-5.6, -2.9)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table BT2SSC_ISCB: Change from baseline in Skindex-10 social functioning score - MMRM results by sex
ITT

Change from baseline in Skindex-10 social functioning score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
B: Sex									0.005 i
Male	Week 4	CR845	137	124 (90.5)	-2.6 (0.6)	(-3.8, -1.4)	1.5 (0.8)	(0.1, 3.0)	0.043 *
		Placebo	139	128 (92.1)	-4.1 (0.6)	(-5.3, -2.9)			
Female	Week 4	CR845	100	87 (87.0)	-4.0 (0.7)	(-5.5, -2.6)	-1.4 (0.9)	(-3.3, 0.4)	0.125
		Placebo	97	92 (94.8)	-2.6 (0.7)	(-4.0, -1.1)			
Male	Week 8	CR845	137	122 (89.1)	-3.5 (0.6)	(-4.7, -2.3)	1.1 (0.7)	(-0.3, 2.6)	0.130
		Placebo	139	130 (93.5)	-4.6 (0.6)	(-5.8, -3.4)			
Female	Week 8	CR845	100	83 (83.0)	-5.4 (0.7)	(-6.8, -3.9)	-1.7 (0.9)	(-3.5, 0.2)	0.075
		Placebo	97	88 (90.7)	-3.7 (0.7)	(-5.2, -2.3)			
Male	Week 10	CR845	137	117 (85.4)	-4.0 (0.6)	(-5.3, -2.8)	0.5 (0.8)	(-1.0, 2.0)	0.500
		Placebo	139	124 (89.2)	-4.5 (0.6)	(-5.8, -3.3)			
Female	Week 10	CR845	100	87 (87.0)	-5.9 (0.7)	(-7.3, -4.5)	-2.2 (0.9)	(-4.0, -0.5)	0.014 *
		Placebo	97	87 (89.7)	-3.7 (0.7)	(-5.1, -2.3)			
Male	Week 12	CR845	137	117 (85.4)	-3.9 (0.6)	(-5.2, -2.7)	0.9 (0.8)	(-0.5, 2.4)	0.212
		Placebo	139	125 (89.9)	-4.9 (0.6)	(-6.1, -3.7)			
Female	Week 12	CR845	100	85 (85.0)	-5.9 (0.7)	(-7.4, -4.5)	-1.7 (1.0)	(-3.6, 0.2)	0.084
		Placebo	97	89 (91.8)	-4.3 (0.8)	(-5.7, -2.8)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table BT2SSC_ISCC: Change from baseline in Skindex-10 social functioning score - MMRM results by race
ITT

Change from baseline in Skindex-10 social functioning score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
C: Race									0.256
Black/African American	Week 4	CR845	53	44 (83.0)	-2.4 (1.0)	(-4.3, -0.5)	2.7 (1.4)	(-0.0, 5.5)	0.050
		Placebo	38	35 (92.1)	-5.1 (1.0)	(-7.2, -3.1)			
White	Week 4	CR845	164	150 (91.5)	-3.5 (0.6)	(-4.7, -2.3)	-0.6 (0.7)	(-2.0, 0.8)	0.425
		Placebo	169	160 (94.7)	-2.9 (0.6)	(-4.1, -1.8)			
Other	Week 4	CR845	20	17 (85.0)	-2.1 (1.7)	(-5.5, 1.3)	2.7 (1.8)	(-0.9, 6.3)	0.136
		Placebo	29	25 (86.2)	-4.8 (1.5)	(-7.8, -1.8)			
Black/African American	Week 8	CR845	53	45 (84.9)	-4.6 (0.9)	(-6.5, -2.8)	-0.5 (1.3)	(-3.1, 2.1)	0.710
		Placebo	38	37 (97.4)	-4.1 (1.0)	(-6.1, -2.1)			
White	Week 8	CR845	164	143 (87.2)	-4.2 (0.6)	(-5.4, -3.0)	-0.2 (0.7)	(-1.6, 1.1)	0.726
		Placebo	169	157 (92.9)	-3.9 (0.6)	(-5.1, -2.8)			
Other	Week 8	CR845	20	17 (85.0)	-4.1 (1.6)	(-7.4, -0.9)	2.5 (1.7)	(-0.8, 5.9)	0.135
		Placebo	29	24 (82.8)	-6.7 (1.4)	(-9.6, -3.8)			
Black/African American	Week 10	CR845	53	42 (79.2)	-4.1 (0.9)	(-6.0, -2.3)	0.1 (1.3)	(-2.5, 2.7)	0.945
		Placebo	38	36 (94.7)	-4.2 (1.0)	(-6.2, -2.3)			
White	Week 10	CR845	164	146 (89.0)	-4.9 (0.6)	(-6.0, -3.7)	-0.9 (0.7)	(-2.3, 0.4)	0.174
		Placebo	169	153 (90.5)	-3.9 (0.6)	(-5.1, -2.8)			
Other	Week 10	CR845	20	16 (80.0)	-5.8 (2.0)	(-9.7, -1.8)	0.4 (2.2)	(-4.1, 4.9)	0.850
		Placebo	29	22 (75.9)	-6.2 (1.7)	(-9.7, -2.7)			
Black/African American	Week 12	CR845	53	43 (81.1)	-4.7 (0.9)	(-6.5, -2.8)	1.3 (1.3)	(-1.4, 4.0)	0.337
		Placebo	38	37 (97.4)	-6.0 (1.0)	(-8.0, -3.9)			
White	Week 12	CR845	164	143 (87.2)	-4.9 (0.6)	(-6.0, -3.7)	-0.8 (0.7)	(-2.2, 0.6)	0.273
		Placebo	169	155 (91.7)	-4.1 (0.6)	(-5.2, -2.9)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table BT2SSC_ISCC: Change from baseline in Skindex-10 social functioning score - MMRM results by race
ITT

Change from baseline in Skindex-10 social functioning score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Other	Week 12	CR845	20	16 (80.0)	-4.1 (1.9)	(-7.9, -0.3)	2.3 (2.1)	(-2.0, 6.6)	0.282
		Placebo	29	22 (75.9)	-6.4 (1.7)	(-9.7, -3.0)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table BT2SSC_ISCD: Change from baseline in Skindex-10 social functioning score - MMRM results by baseline WI-NRS
ITT

Change from baseline in Skindex-10 social functioning score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
D: Baseline worst itching NRS score (WI-NRS)									0.145
>= 4 to < 7	Week 4	CR845	102	94 (92.2)	-4.2 (0.7)	(-5.4, -2.9)	-0.5 (0.7)	(-2.0, 1.0)	0.492
		Placebo	113	108 (95.6)	-3.6 (0.6)	(-4.9, -2.4)			
>= 7	Week 4	CR845	135	117 (86.7)	-2.8 (0.7)	(-4.1, -1.5)	0.8 (0.9)	(-0.9, 2.6)	0.332
		Placebo	123	112 (91.1)	-3.6 (0.7)	(-5.0, -2.3)			
>= 4 to < 7	Week 8	CR845	102	93 (91.2)	-5.3 (0.7)	(-6.6, -4.0)	-1.1 (0.7)	(-2.6, 0.4)	0.135
		Placebo	113	105 (92.9)	-4.2 (0.6)	(-5.4, -2.9)			
>= 7	Week 8	CR845	135	112 (83.0)	-3.9 (0.7)	(-5.2, -2.6)	0.7 (0.9)	(-0.9, 2.4)	0.391
		Placebo	123	113 (91.9)	-4.6 (0.7)	(-5.9, -3.3)			
>= 4 to < 7	Week 10	CR845	102	91 (89.2)	-5.4 (0.7)	(-6.7, -4.0)	-0.8 (0.8)	(-2.4, 0.7)	0.288
		Placebo	113	101 (89.4)	-4.5 (0.6)	(-5.8, -3.3)			
>= 7	Week 10	CR845	135	113 (83.7)	-4.8 (0.6)	(-6.1, -3.5)	-0.6 (0.8)	(-2.2, 1.1)	0.490
		Placebo	123	110 (89.4)	-4.2 (0.7)	(-5.5, -2.9)			
>= 4 to < 7	Week 12	CR845	102	90 (88.2)	-5.6 (0.7)	(-6.9, -4.2)	-1.3 (0.8)	(-2.8, 0.3)	0.108
		Placebo	113	102 (90.3)	-4.3 (0.6)	(-5.6, -3.0)			
>= 7	Week 12	CR845	135	112 (83.0)	-4.6 (0.7)	(-5.9, -3.2)	0.7 (0.9)	(-1.1, 2.4)	0.453
		Placebo	123	112 (91.1)	-5.2 (0.7)	(-6.6, -3.9)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table BT2SSC_ISCE: Change from baseline in Skindex-10 social functioning score - MMRM results by specific medical condition
ITT

Change from baseline in Skindex-10 social functioning score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
E: Presence of specific medical conditions									0.923
No	Week 4	CR845	195	174 (89.2)	-2.8 (0.5)	(-3.7, -1.9)	0.2 (0.6)	(-1.1, 1.4)	0.797
		Placebo	199	186 (93.5)	-2.9 (0.4)	(-3.8, -2.1)			
Yes	Week 4	CR845	42	37 (88.1)	-4.5 (1.1)	(-6.7, -2.3)	0.5 (1.6)	(-2.7, 3.7)	0.745
		Placebo	37	34 (91.9)	-5.1 (1.1)	(-7.3, -2.8)			
No	Week 8	CR845	195	170 (87.2)	-4.0 (0.5)	(-4.9, -3.1)	-0.1 (0.6)	(-1.3, 1.1)	0.866
		Placebo	199	182 (91.5)	-3.9 (0.4)	(-4.8, -3.0)			
Yes	Week 8	CR845	42	35 (83.3)	-5.1 (1.1)	(-7.4, -2.8)	-0.4 (1.6)	(-3.6, 2.9)	0.816
		Placebo	37	36 (97.3)	-4.7 (1.1)	(-7.0, -2.5)			
No	Week 10	CR845	195	169 (86.7)	-4.5 (0.5)	(-5.4, -3.6)	-0.5 (0.6)	(-1.8, 0.7)	0.384
		Placebo	199	176 (88.4)	-3.9 (0.4)	(-4.8, -3.1)			
Yes	Week 10	CR845	42	35 (83.3)	-5.9 (1.1)	(-8.2, -3.7)	-1.6 (1.6)	(-4.8, 1.6)	0.326
		Placebo	37	35 (94.6)	-4.3 (1.1)	(-6.6, -2.1)			
No	Week 12	CR845	195	167 (85.6)	-4.5 (0.5)	(-5.4, -3.6)	-0.2 (0.6)	(-1.5, 1.0)	0.730
		Placebo	199	179 (89.9)	-4.3 (0.4)	(-5.2, -3.4)			
Yes	Week 12	CR845	42	35 (83.3)	-5.7 (1.2)	(-8.1, -3.3)	-0.5 (1.7)	(-3.9, 3.0)	0.785
		Placebo	37	35 (94.6)	-5.2 (1.2)	(-7.6, -2.8)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor previous use of anti-itch medication is also included in the model.
Source Data: askin, created on: 17FEB2022

Table BT2SSC_ISCF: Change from baseline in Skindex-10 social functioning score - MMRM results by use of concomitant itch medication
ITT

Change from baseline in Skindex-10 social functioning score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
F: Use of concomitant itch medication									0.272
No	Week 4	CR845	150	138 (92.0)	-2.8 (0.6)	(-4.0, -1.6)	0.7 (0.7)	(-0.7, 2.2)	0.310
		Placebo	151	143 (94.7)	-3.5 (0.6)	(-4.7, -2.4)			
Yes	Week 4	CR845	87	73 (83.9)	-4.0 (0.8)	(-5.5, -2.5)	-0.6 (1.0)	(-2.6, 1.3)	0.537
		Placebo	85	77 (90.6)	-3.4 (0.8)	(-4.9, -1.9)			
No	Week 8	CR845	150	135 (90.0)	-3.8 (0.6)	(-4.9, -2.6)	0.5 (0.7)	(-0.9, 1.9)	0.501
		Placebo	151	141 (93.4)	-4.2 (0.6)	(-5.4, -3.1)			
Yes	Week 8	CR845	87	70 (80.5)	-5.4 (0.8)	(-6.9, -3.8)	-1.1 (1.0)	(-3.1, 0.9)	0.273
		Placebo	85	77 (90.6)	-4.3 (0.8)	(-5.8, -2.8)			
No	Week 10	CR845	150	131 (87.3)	-4.4 (0.6)	(-5.6, -3.2)	-0.6 (0.7)	(-2.1, 0.8)	0.395
		Placebo	151	138 (91.4)	-3.8 (0.6)	(-5.0, -2.6)			
Yes	Week 10	CR845	87	73 (83.9)	-5.7 (0.8)	(-7.2, -4.2)	-0.7 (1.0)	(-2.7, 1.2)	0.469
		Placebo	85	73 (85.9)	-5.0 (0.8)	(-6.5, -3.5)			
No	Week 12	CR845	150	132 (88.0)	-4.2 (0.6)	(-5.4, -3.0)	0.3 (0.8)	(-1.2, 1.8)	0.686
		Placebo	151	140 (92.7)	-4.5 (0.6)	(-5.7, -3.3)			
Yes	Week 12	CR845	87	70 (80.5)	-6.0 (0.8)	(-7.5, -4.5)	-1.1 (1.0)	(-3.1, 0.8)	0.246
		Placebo	85	74 (87.1)	-4.9 (0.7)	(-6.4, -3.4)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor presence of medical condition is also included in the model.
Source Data: askin, created on: 17FEB2022

Table BT2SSC_ISCG: Change from baseline in Skindex-10 social functioning score - MMRM results by region
ITT

Change from baseline in Skindex-10 social functioning score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
G: Region									0.369
USA	Week 4	CR845	146	129 (88.4)	-3.0 (0.6)	(-4.2, -1.8)	0.5 (0.8)	(-1.1, 2.1)	0.525
		Placebo	133	121 (91.0)	-3.5 (0.7)	(-4.8, -2.2)			
Asia	Week 4	CR845	8	8 (100.0)	-5.8 (1.8)	(-9.5, -2.1)	-1.2 (2.3)	(-6.1, 3.6)	0.604
		Placebo	12	12 (100.0)	-4.6 (1.5)	(-7.7, -1.5)			
Eastern Europe	Week 4	CR845	54	52 (96.3)	-2.6 (1.0)	(-4.7, -0.6)	-0.0 (1.1)	(-2.2, 2.2)	0.999
		Placebo	60	59 (98.3)	-2.6 (0.9)	(-4.5, -0.8)			
Western Europe/European origin	Week 4	CR845	29	22 (75.9)	-5.8 (1.4)	(-8.6, -2.9)	0.2 (1.8)	(-3.4, 3.9)	0.900
		Placebo	31	28 (90.3)	-6.0 (1.3)	(-8.6, -3.4)			
USA	Week 8	CR845	146	128 (87.7)	-4.0 (0.6)	(-5.2, -2.8)	0.3 (0.8)	(-1.2, 1.8)	0.674
		Placebo	133	124 (93.2)	-4.4 (0.6)	(-5.6, -3.1)			
Asia	Week 8	CR845	8	7 (87.5)	-7.7 (1.5)	(-10.8, -4.6)	-0.4 (1.9)	(-4.4, 3.6)	0.840
		Placebo	12	12 (100.0)	-7.3 (1.1)	(-9.8, -4.9)			
Eastern Europe	Week 8	CR845	54	48 (88.9)	-4.5 (1.0)	(-6.6, -2.4)	-1.2 (1.1)	(-3.4, 1.1)	0.299
		Placebo	60	58 (96.7)	-3.3 (1.0)	(-5.2, -1.4)			
Western Europe/European origin	Week 8	CR845	29	22 (75.9)	-5.6 (1.4)	(-8.4, -2.8)	0.1 (1.8)	(-3.6, 3.8)	0.958
		Placebo	31	24 (77.4)	-5.7 (1.3)	(-8.4, -3.1)			
USA	Week 10	CR845	146	127 (87.0)	-4.2 (0.6)	(-5.4, -3.0)	0.5 (0.8)	(-1.0, 2.1)	0.502
		Placebo	133	121 (91.0)	-4.7 (0.6)	(-5.9, -3.4)			
Asia	Week 10	CR845	8	7 (87.5)	-10.2 (1.7)	(-13.9, -6.5)	-3.3 (2.3)	(-8.1, 1.5)	0.169
		Placebo	12	11 (91.7)	-6.9 (1.4)	(-9.9, -3.9)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table BT2SSC_ISCG: Change from baseline in Skindex-10 social functioning score - MMRM results by region
ITT

Change from baseline in Skindex-10 social functioning score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Eastern Europe	Week 10	CR845	54	48 (88.9)	-5.0 (1.0)	(-7.0, -3.0)	-1.9 (1.1)	(-4.1, 0.2)	0.080
		Placebo	60	58 (96.7)	-3.1 (0.9)	(-4.9, -1.2)			
Western Europe/European origin	Week 10	CR845	29	22 (75.9)	-8.0 (1.4)	(-10.8, -5.2)	-3.4 (1.9)	(-7.2, 0.4)	0.078
		Placebo	31	21 (67.7)	-4.6 (1.4)	(-7.4, -1.8)			
USA	Week 12	CR845	146	126 (86.3)	-4.5 (0.6)	(-5.8, -3.3)	0.9 (0.8)	(-0.6, 2.5)	0.234
		Placebo	133	124 (93.2)	-5.5 (0.6)	(-6.7, -4.2)			
Asia	Week 12	CR845	8	7 (87.5)	-8.5 (1.7)	(-12.1, -5.0)	-1.8 (2.2)	(-6.4, 2.9)	0.432
		Placebo	12	11 (91.7)	-6.8 (1.4)	(-9.7, -3.9)			
Eastern Europe	Week 12	CR845	54	47 (87.0)	-4.7 (1.0)	(-6.8, -2.6)	-1.8 (1.1)	(-4.1, 0.4)	0.114
		Placebo	60	55 (91.7)	-2.9 (1.0)	(-4.8, -1.0)			
Western Europe/European origin	Week 12	CR845	29	22 (75.9)	-6.5 (1.5)	(-9.4, -3.5)	-1.8 (2.0)	(-5.7, 2.2)	0.369
		Placebo	31	24 (77.4)	-4.7 (1.4)	(-7.5, -1.8)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table BT2SSC_ISCH: Change from baseline in Skindex-10 social functioning score - MMRM results by dialysis method
ITT

Change from baseline in Skindex-10 social functioning score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
H: Dialysis method									0.441
Hemodialysis (HD)	Week 4	CR845	222	198 (89.2)	-3.4 (0.5)	(-4.3, -2.4)	0.3 (0.6)	(-1.0, 1.5)	0.672
		Placebo	199	183 (92.0)	-3.6 (0.5)	(-4.6, -2.6)			
Hemodiafiltration (HDF)	Week 4	CR845	15	13 (86.7)	-2.0 (2.6)	(-7.3, 3.3)	-0.3 (1.9)	(-4.1, 3.6)	0.896
		Placebo	37	37 (100.0)	-1.7 (1.9)	(-5.6, 2.1)			
Hemodialysis (HD)	Week 8	CR845	222	192 (86.5)	-4.5 (0.5)	(-5.4, -3.5)	-0.1 (0.6)	(-1.3, 1.1)	0.857
		Placebo	199	183 (92.0)	-4.4 (0.5)	(-5.4, -3.4)			
Hemodiafiltration (HDF)	Week 8	CR845	15	13 (86.7)	-2.8 (2.7)	(-8.1, 2.6)	-0.1 (2.0)	(-4.1, 3.8)	0.948
		Placebo	37	35 (94.6)	-2.6 (1.9)	(-6.5, 1.2)			
Hemodialysis (HD)	Week 10	CR845	222	192 (86.5)	-4.9 (0.5)	(-5.9, -4.0)	-0.4 (0.6)	(-1.6, 0.8)	0.517
		Placebo	199	179 (89.9)	-4.5 (0.5)	(-5.5, -3.5)			
Hemodiafiltration (HDF)	Week 10	CR845	15	12 (80.0)	-4.8 (2.7)	(-10.2, 0.6)	-3.1 (2.0)	(-7.1, 1.0)	0.132
		Placebo	37	32 (86.5)	-1.7 (1.9)	(-5.6, 2.2)			
Hemodialysis (HD)	Week 12	CR845	222	189 (85.1)	-5.0 (0.5)	(-6.0, -4.0)	0.1 (0.6)	(-1.1, 1.4)	0.838
		Placebo	199	180 (90.5)	-5.1 (0.5)	(-6.1, -4.1)			
Hemodiafiltration (HDF)	Week 12	CR845	15	13 (86.7)	-2.8 (2.7)	(-8.3, 2.6)	-1.8 (2.0)	(-5.9, 2.4)	0.393
		Placebo	37	34 (91.9)	-1.1 (1.9)	(-5.0, 2.8)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin, created on: 17FEB2022

Table BT2STCD15_ISPA: Decrease of Skindex-10 total score of at least 15 points by age
ITT

Decrease of Skindex-10 total score of at least 15 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	A: Age										0.980
	< 65 years	147	127 (86.4)	69 (46.9) [38.7, 55.3]	153	137 (89.5)	55 (35.9) [28.4, 44.1]	1.306 [0.994, 1.715]	1.576 [0.992, 2.503]	11.0 [-0.8, 22.7]	0.054
	>= 65 years	90	72 (80.0)	38 (42.2) [31.9, 53.1]	83	73 (88.0)	27 (32.5) [22.6, 43.7]	1.298 [0.876, 1.923]	1.516 [0.814, 2.821]	9.7 [-5.8, 25.2]	0.190

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table BT2STCD15_ISPB: Decrease of Skindex-10 total score of at least 15 points by sex
ITT

Decrease of Skindex-10 total score of at least 15 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	B: Sex										0.080	
	Male	137	114 (83.2)	56 (40.9) [32.6, 49.6]	139	122 (87.8)	52 (37.4) [29.4, 46.0]	1.093 [0.814, 1.467]	1.157 [0.713, 1.876]	3.5 [-8.8, 15.7]	0.556	
	Female	100	85 (85.0)	51 (51.0) [40.8, 61.1]	97	88 (90.7)	30 (30.9) [21.9, 41.1]	1.649 [1.157, 2.350]	2.324 [1.298, 4.161]	20.1 [5.6, 34.5]	0.004	*

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table BT2STCD15_ISPC: Decrease of Skindex-10 total score of at least 15 points by race
ITT

Decrease of Skindex-10 total score of at least 15 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	C: Race										0.427	
	Black/African American	53	41 (77.4)	22 (41.5) [28.1, 55.9]	38	35 (92.1)	16 (42.1) [26.3, 59.2]	0.986 [0.603, 1.611]	0.976 [0.419, 2.271]	-0.6 [-23.4, 22.2]	0.955	
	White	164	142 (86.6)	77 (47.0) [39.1, 54.9]	169	153 (90.5)	56 (33.1) [26.1, 40.8]	1.417 [1.083, 1.854]	1.786 [1.146, 2.783]	13.8 [2.8, 24.8]	0.010	*
	Other	20	16 (80.0)	8 (40.0) [19.1, 63.9]	29	22 (75.9)	10 (34.5) [17.9, 54.3]	1.160 [0.556, 2.418]	1.267 [0.390, 4.112]	5.5 [-26.3, 37.3]	0.697	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table BT2STCD15_ISPD: Decrease of Skindex-10 total score of at least 15 points by baseline WI-NRS
ITT

Decrease of Skindex-10 total score of at least 15 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.001	i
	>= 4 to < 7	102	90 (88.2)	53 (52.0) [41.8, 62.0]	113	101 (89.4)	29 (25.7) [17.9, 34.7]	2.025 [1.405, 2.917]	3.133 [1.765, 5.560]	26.3 [12.8, 39.8]	<0.001	*
	>= 7	135	109 (80.7)	54 (40.0) [31.7, 48.8]	123	109 (88.6)	53 (43.1) [34.2, 52.3]	0.928 [0.695, 1.240]	0.881 [0.536, 1.446]	-3.1 [-15.9, 9.7]	0.616	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table BT2STCD15_ISPE: Decrease of Skindex-10 total score of at least 15 points by specific medical condition
ITT

Decrease of Skindex-10 total score of at least 15 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	E: Presence of specific medical conditions										0.355	
	No	195	164 (84.1)	88 (45.1) [38.0, 52.4]	199	176 (88.4)	66 (33.2) [26.7, 40.2]	1.361 [1.059, 1.748]	1.657 [1.102, 2.493]	12.0 [1.9, 22.0]	0.015	*
	Yes	42	35 (83.3)	19 (45.2) [29.8, 61.3]	37	34 (91.9)	16 (43.2) [27.1, 60.5]	1.046 [0.636, 1.720]	1.084 [0.445, 2.640]	2.0 [-22.5, 26.5]	0.860	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table BT2STCD15_ISPF: Decrease of Skindex-10 total score of at least 15 points by use of concomitant itch medication
ITT

Decrease of Skindex-10 total score of at least 15 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	F: Use of concomitant itch medication										0.283	
	No	150	129 (86.0)	66 (44.0) [35.9, 52.3]	151	137 (90.7)	56 (37.1) [29.4, 45.3]	1.186 [0.901, 1.562]	1.333 [0.840, 2.115]	6.9 [-4.8, 18.6]	0.223	
	Yes	87	70 (80.5)	41 (47.1) [36.3, 58.1]	85	73 (85.9)	26 (30.6) [21.0, 41.5]	1.541 [1.043, 2.276]	2.023 [1.083, 3.777]	16.5 [1.0, 32.1]	0.027	*

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table BT2STCD15_ISPG: Decrease of Skindex-10 total score of at least 15 points by region
ITT

Decrease of Skindex-10 total score of at least 15 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	G: Region										0.319	
	USA	146	123 (84.2)	65 (44.5) [36.3, 53.0]	133	122 (91.7)	52 (39.1) [30.8, 47.9]	1.139 [0.862, 1.505]	1.250 [0.776, 2.015]	5.4 [-6.9, 17.7]	0.360	
	Asia	8	7 (87.5)	6 (75.0) [34.9, 96.8]	12	11 (91.7)	5 (41.7) [15.2, 72.3]	1.800 [0.825, 3.926]	4.200 [0.586, 30.095]	33.3 [-18.1, 84.7]	0.197	#
	Eastern Europe	54	47 (87.0)	24 (44.4) [30.9, 58.6]	60	55 (91.7)	14 (23.3) [13.4, 36.0]	1.905 [1.102, 3.292]	2.629 [1.177, 5.872]	21.1 [2.3, 39.9]	0.017	*
	Western Europe/European origin	29	22 (75.9)	12 (41.4) [23.5, 61.1]	31	22 (71.0)	11 (35.5) [19.2, 54.6]	1.166 [0.613, 2.217]	1.283 [0.452, 3.641]	5.9 [-22.0, 33.8]	0.642	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table BT2STCD15_ISPH: Decrease of Skindex-10 total score of at least 15 points by dialysis method
ITT

Decrease of Skindex-10 total score of at least 15 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	H: Dialysis method										0.369	
	Hemodialysis (HD)	222	186 (83.8)	101 (45.5) [38.8, 52.3]	199	178 (89.4)	74 (37.2) [30.5, 44.3]	1.223 [0.971, 1.541]	1.410 [0.954, 2.083]	8.3 [-1.5, 18.2]	0.085	
	Hemodiafiltration (HDF)	15	13 (86.7)	6 (40.0) [16.3, 67.7]	37	32 (86.5)	8 (21.6) [9.8, 38.2]	1.850 [0.773, 4.425]	2.417 [0.661, 8.832]	18.4 [-14.4, 51.2]	0.190	#

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table BT2SDCD3_ISPA: Decrease of Skindex-10 disease score of at least 3 points by age
ITT

Decrease of Skindex-10 disease score of at least 3 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	A: Age										0.464
	< 65 years	147	128 (87.1)	87 (59.2) [50.8, 67.2]	153	139 (90.8)	87 (56.9) [48.6, 64.8]	1.041 [0.859, 1.262]	1.100 [0.695, 1.740]	2.3 [-9.5, 14.2]	0.684
	>= 65 years	90	73 (81.1)	49 (54.4) [43.6, 65.0]	83	75 (90.4)	49 (59.0) [47.7, 69.7]	0.922 [0.711, 1.197]	0.829 [0.454, 1.515]	-4.6 [-20.5, 11.3]	0.544

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table BT2SDCD3_ISPB: Decrease of Skindex-10 disease score of at least 3 points by sex
ITT

Decrease of Skindex-10 disease score of at least 3 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	B: Sex										0.074
	Male	137	115 (83.9)	70 (51.1) [42.4, 59.7]	139	124 (89.2)	81 (58.3) [49.6, 66.6]	0.877 [0.707, 1.088]	0.748 [0.465, 1.203]	-7.2 [-19.6, 5.3]	0.232
	Female	100	86 (86.0)	66 (66.0) [55.8, 75.2]	97	90 (92.8)	55 (56.7) [46.3, 66.7]	1.164 [0.931, 1.456]	1.482 [0.833, 2.639]	9.3 [-5.3, 23.9]	0.181

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table BT2SDCD3_ISPC: Decrease of Skindex-10 disease score of at least 3 points by race
ITT

Decrease of Skindex-10 disease score of at least 3 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	C: Race										0.246
	Black/African American	53	41 (77.4)	27 (50.9) [36.8, 64.9]	38	35 (92.1)	24 (63.2) [46.0, 78.2]	0.807 [0.563, 1.155]	0.606 [0.259, 1.419]	-12.2 [-34.9, 10.4]	0.250
	White	164	144 (87.8)	99 (60.4) [52.4, 67.9]	169	156 (92.3)	94 (55.6) [47.8, 63.2]	1.085 [0.904, 1.303]	1.215 [0.786, 1.879]	4.7 [-6.4, 15.9]	0.381
	Other	20	16 (80.0)	10 (50.0) [27.2, 72.8]	29	23 (79.3)	18 (62.1) [42.3, 79.3]	0.806 [0.478, 1.358]	0.611 [0.193, 1.937]	-12.1 [-44.4, 20.3]	0.406

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table BT2SDCD3_ISPD: Decrease of Skindex-10 disease score of at least 3 points by baseline WI-NRS
ITT

Decrease of Skindex-10 disease score of at least 3 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.108
	>= 4 to < 7	102	90 (88.2)	63 (61.8) [51.6, 71.2]	113	102 (90.3)	61 (54.0) [44.4, 63.4]	1.144 [0.910, 1.438]	1.377 [0.799, 2.373]	7.8 [-6.3, 21.9]	0.250
	>= 7	135	111 (82.2)	73 (54.1) [45.3, 62.7]	123	112 (91.1)	75 (61.0) [51.8, 69.6]	0.887 [0.719, 1.094]	0.754 [0.459, 1.237]	-6.9 [-19.7, 5.9]	0.264

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table BT2SDCD3_ISPE: Decrease of Skindex-10 disease score of at least 3 points by specific medical condition
ITT

Decrease of Skindex-10 disease score of at least 3 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	E: Presence of specific medical conditions										0.316
	No	195	166 (85.1)	112 (57.4) [50.2, 64.5]	199	180 (90.5)	111 (55.8) [48.6, 62.8]	1.030 [0.866, 1.224]	1.070 [0.718, 1.594]	1.7 [-8.6, 12.0]	0.740
	Yes	42	35 (83.3)	24 (57.1) [41.0, 72.3]	37	34 (91.9)	25 (67.6) [50.2, 82.0]	0.846 [0.599, 1.193]	0.640 [0.255, 1.607]	-10.4 [-34.2, 13.4]	0.344

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table BT2SDCD3_ISPF: Decrease of Skindex-10 disease score of at least 3 points by use of concomitant itch medication
ITT

Decrease of Skindex-10 disease score of at least 3 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	F: Use of concomitant itch medication										0.566
	No	150	130 (86.7)	85 (56.7) [48.3, 64.7]	151	139 (92.1)	83 (55.0) [46.7, 63.1]	1.031 [0.843, 1.261]	1.071 [0.680, 1.689]	1.7 [-10.2, 13.6]	0.767
	Yes	87	71 (81.6)	51 (58.6) [47.6, 69.1]	85	75 (88.2)	53 (62.4) [51.2, 72.6]	0.940 [0.738, 1.197]	0.855 [0.464, 1.577]	-3.7 [-19.5, 12.0]	0.618

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table BT2SDCD3_ISPG: Decrease of Skindex-10 disease score of at least 3 points by region
ITT

Decrease of Skindex-10 disease score of at least 3 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	G: Region										0.633	
	USA	146	125 (85.6)	83 (56.8) [48.4, 65.0]	133	124 (93.2)	81 (60.9) [52.1, 69.2]	0.933 [0.767, 1.136]	0.846 [0.524, 1.364]	-4.1 [-16.3, 8.2]	0.493	
	Asia	8	7 (87.5)	5 (62.5) [24.5, 91.5]	12	11 (91.7)	9 (75.0) [42.8, 94.5]	0.833 [0.445, 1.562]	0.556 [0.080, 3.858]	-12.5 [-64.5, 39.5]	0.642	#
	Eastern Europe	54	47 (87.0)	32 (59.3) [45.0, 72.4]	60	56 (93.3)	31 (51.7) [38.4, 64.8]	1.147 [0.825, 1.595]	1.361 [0.648, 2.859]	7.6 [-12.4, 27.6]	0.418	
	Western Europe/European origin	29	22 (75.9)	16 (55.2) [35.7, 73.6]	31	23 (74.2)	15 (48.4) [30.2, 66.9]	1.140 [0.699, 1.861]	1.313 [0.475, 3.625]	6.8 [-21.8, 35.4]	0.602	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table BT2SDCD3_ISPH: Decrease of Skindex-10 disease score of at least 3 points by dialysis method
ITT

Decrease of Skindex-10 disease score of at least 3 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	H: Dialysis method										0.280
	Hemodialysis (HD)	222	188 (84.7)	127 (57.2) [50.4, 63.8]	199	182 (91.5)	119 (59.8) [52.6, 66.7]	0.957 [0.814, 1.124]	0.899 [0.609, 1.325]	-2.6 [-12.5, 7.3]	0.591
	Hemodiafiltration (HDF)	15	13 (86.7)	9 (60.0) [32.3, 83.7]	37	32 (86.5)	17 (45.9) [29.5, 63.1]	1.306 [0.760, 2.244]	1.765 [0.522, 5.969]	14.1 [-20.2, 48.3]	0.363

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table BT2SMCD3_ISPA: Decrease of Skindex-10 mood/emotional distress score of at least 3 points by age
ITT

Decrease of Skindex-10 mood/emotional distress score of at least 3 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	A: Age										0.554
	< 65 years	147	128 (87.1)	90 (61.2) [52.8, 69.1]	153	139 (90.8)	92 (60.1) [51.9, 67.9]	1.018 [0.849, 1.222]	1.047 [0.659, 1.664]	1.1 [-10.6, 12.8]	0.847
	>= 65 years	90	73 (81.1)	49 (54.4) [43.6, 65.0]	83	76 (91.6)	40 (48.2) [37.1, 59.4]	1.130 [0.843, 1.513]	1.285 [0.707, 2.336]	6.3 [-9.8, 22.3]	0.412

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table BT2SMCD3_ISPB: Decrease of Skindex-10 mood/emotional distress score of at least 3 points by sex
ITT

Decrease of Skindex-10 mood/emotional distress score of at least 3 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	B: Sex										0.501
	Male	137	116 (84.7)	78 (56.9) [48.2, 65.4]	139	124 (89.2)	79 (56.8) [48.2, 65.2]	1.002 [0.816, 1.230]	1.004 [0.624, 1.617]	0.1 [-12.3, 12.5]	0.987
	Female	100	85 (85.0)	61 (61.0) [50.7, 70.6]	97	91 (93.8)	53 (54.6) [44.2, 64.8]	1.116 [0.879, 1.419]	1.299 [0.737, 2.289]	6.4 [-8.4, 21.1]	0.367

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table BT2SMCD3_ISPC: Decrease of Skindex-10 mood/emotional distress score of at least 3 points by race
ITT

Decrease of Skindex-10 mood/emotional distress score of at least 3 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	C: Race										0.008	i
	Black/African American	53	43 (81.1)	27 (50.9) [36.8, 64.9]	38	36 (94.7)	29 (76.3) [59.8, 88.6]	0.668 [0.486, 0.918]	0.322 [0.128, 0.810]	-25.4 [-46.7, -4.0]	0.015	*
	White	164	142 (86.6)	103 (62.8) [54.9, 70.2]	169	156 (92.3)	89 (52.7) [44.9, 60.4]	1.193 [0.991, 1.435]	1.518 [0.980, 2.351]	10.1 [-1.0, 21.3]	0.062	
	Other	20	16 (80.0)	9 (45.0) [23.1, 68.5]	29	23 (79.3)	14 (48.3) [29.4, 67.5]	0.932 [0.505, 1.722]	0.877 [0.280, 2.749]	-3.3 [-35.9, 29.3]	0.823	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table BT2SMCD3_ISPD: Decrease of Skindex-10 mood/emotional distress score of at least 3 points by baseline WI-NRS
ITT

Decrease of Skindex-10 mood/emotional distress score of at least 3 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.002	i
	>= 4 to < 7	102	90 (88.2)	66 (64.7) [54.6, 73.9]	113	101 (89.4)	53 (46.9) [37.5, 56.5]	1.380 [1.082, 1.759]	2.075 [1.199, 3.594]	17.8 [3.8, 31.8]	0.009	*
	>= 7	135	111 (82.2)	73 (54.1) [45.3, 62.7]	123	114 (92.7)	79 (64.2) [55.1, 72.7]	0.842 [0.687, 1.032]	0.656 [0.398, 1.082]	-10.2 [-22.9, 2.6]	0.098	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table BT2SMCD3_ISPE: Decrease of Skindex-10 mood/emotional distress score of at least 3 points by specific medical condition
ITT

Decrease of Skindex-10 mood/emotional distress score of at least 3 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	E: Presence of specific medical conditions										0.814
	No	195	166 (85.1)	113 (57.9) [50.7, 65.0]	199	181 (91.0)	111 (55.8) [48.6, 62.8]	1.039 [0.875, 1.234]	1.093 [0.733, 1.628]	2.2 [-8.1, 12.5]	0.664
	Yes	42	35 (83.3)	26 (61.9) [45.6, 76.4]	37	34 (91.9)	21 (56.8) [39.5, 72.9]	1.091 [0.755, 1.576]	1.238 [0.503, 3.047]	5.1 [-19.1, 29.4]	0.644

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table BT2SMCD3_ISPF: Decrease of Skindex-10 mood/emotional distress score of at least 3 points by use of concomitant itch medication
ITT

Decrease of Skindex-10 mood/emotional distress score of at least 3 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	F: Use of concomitant itch medication										0.107
	No	150	131 (87.3)	94 (62.7) [54.4, 70.4]	151	139 (92.1)	82 (54.3) [46.0, 62.4]	1.154 [0.953, 1.398]	1.412 [0.891, 2.238]	8.4 [-3.4, 20.1]	0.142
	Yes	87	70 (80.5)	45 (51.7) [40.8, 62.6]	85	76 (89.4)	50 (58.8) [47.6, 69.4]	0.879 [0.671, 1.152]	0.750 [0.410, 1.370]	-7.1 [-23.1, 8.9]	0.351

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table BT2SMCD3_ISPG: Decrease of Skindex-10 mood/emotional distress score of at least 3 points by region
ITT

Decrease of Skindex-10 mood/emotional distress score of at least 3 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	G: Region										0.920	
	USA	146	125 (85.6)	86 (58.9) [50.5, 67.0]	133	124 (93.2)	77 (57.9) [49.0, 66.4]	1.017 [0.834, 1.241]	1.042 [0.647, 1.679]	1.0 [-11.3, 13.3]	0.865	
	Asia	8	7 (87.5)	6 (75.0) [34.9, 96.8]	12	11 (91.7)	8 (66.7) [34.9, 90.1]	1.125 [0.639, 1.981]	1.500 [0.203, 11.088]	8.3 [-42.2, 58.9]	1.000	#
	Eastern Europe	54	47 (87.0)	31 (57.4) [43.2, 70.8]	60	56 (93.3)	33 (55.0) [41.6, 67.9]	1.044 [0.755, 1.444]	1.103 [0.525, 2.314]	2.4 [-17.6, 22.4]	0.797	
	Western Europe/European origin	29	22 (75.9)	16 (55.2) [35.7, 73.6]	31	24 (77.4)	14 (45.2) [27.3, 64.0]	1.222 [0.735, 2.030]	1.495 [0.540, 4.136]	10.0 [-18.5, 38.5]	0.442	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table BT2SMCD3_ISPH: Decrease of Skindex-10 mood/emotional distress score of at least 3 points by dialysis method
ITT

Decrease of Skindex-10 mood/emotional distress score of at least 3 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	H: Dialysis method										0.229
	Hemodialysis (HD)	222	188 (84.7)	128 (57.7) [50.9, 64.2]	199	182 (91.5)	112 (56.3) [49.1, 63.3]	1.024 [0.867, 1.210]	1.058 [0.719, 1.557]	1.4 [-8.6, 11.3]	0.776
	Hemodiafiltration (HDF)	15	13 (86.7)	11 (73.3) [44.9, 92.2]	37	33 (89.2)	20 (54.1) [36.9, 70.5]	1.357 [0.886, 2.077]	2.338 [0.628, 8.701]	19.3 [-12.9, 51.5]	0.204

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table BT2SSCD4_ISPA: Decrease of Skindex-10 social functioning score of at least 4 points by age
ITT

Decrease of Skindex-10 social functioning score of at least 4 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	A: Age										0.868
	< 65 years	147	128 (87.1)	69 (46.9) [38.7, 55.3]	153	140 (91.5)	66 (43.1) [35.2, 51.4]	1.088 [0.847, 1.398]	1.166 [0.740, 1.838]	3.8 [-8.1, 15.7]	0.509
	>= 65 years	90	74 (82.2)	41 (45.6) [35.0, 56.4]	83	74 (89.2)	36 (43.4) [32.5, 54.7]	1.050 [0.752, 1.467]	1.092 [0.599, 1.991]	2.2 [-13.8, 18.2]	0.774

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table BT2SSCD4_ISPB: Decrease of Skindex-10 social functioning score of at least 4 points by sex
ITT

Decrease of Skindex-10 social functioning score of at least 4 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	B: Sex										0.286
	Male	137	117 (85.4)	63 (46.0) [37.4, 54.7]	139	125 (89.9)	65 (46.8) [38.3, 55.4]	0.983 [0.763, 1.267]	0.969 [0.604, 1.556]	-0.8 [-13.3, 11.7]	0.897
	Female	100	85 (85.0)	47 (47.0) [36.9, 57.2]	97	89 (91.8)	37 (38.1) [28.5, 48.6]	1.232 [0.888, 1.710]	1.438 [0.815, 2.537]	8.9 [-5.9, 23.6]	0.210

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table BT2SSCD4_ISPC: Decrease of Skindex-10 social functioning score of at least 4 points by race
ITT

Decrease of Skindex-10 social functioning score of at least 4 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	C: Race										0.206
	Black/African American	53	43 (81.1)	22 (41.5) [28.1, 55.9]	38	37 (97.4)	21 (55.3) [38.3, 71.4]	0.751 [0.489, 1.153]	0.575 [0.248, 1.332]	-13.8 [-36.7, 9.1]	0.197
	White	164	143 (87.2)	79 (48.2) [40.3, 56.1]	169	155 (91.7)	70 (41.4) [33.9, 49.2]	1.163 [0.915, 1.478]	1.314 [0.852, 2.027]	6.8 [-4.5, 18.0]	0.216
	Other	20	16 (80.0)	9 (45.0) [23.1, 68.5]	29	22 (75.9)	11 (37.9) [20.7, 57.7]	1.186 [0.606, 2.323]	1.339 [0.421, 4.258]	7.1 [-25.2, 39.4]	0.624

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table BT2SSCD4_ISPD: Decrease of Skindex-10 social functioning score of at least 4 points by baseline WI-NRS
ITT

		CR845			Placebo						
Decrease of Skindex-10 social functioning score of at least 4 points		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.013 i
	>= 4 to < 7	102	90 (88.2)	56 (54.9) [44.7, 64.8]	113	102 (90.3)	44 (38.9) [29.9, 48.6]	1.410 [1.055, 1.885]	1.909 [1.109, 3.287]	16.0 [1.8, 30.1]	0.019 *
	>= 7	135	112 (83.0)	54 (40.0) [31.7, 48.8]	123	112 (91.1)	58 (47.2) [38.1, 56.4]	0.848 [0.642, 1.121]	0.747 [0.456, 1.224]	-7.2 [-20.0, 5.7]	0.248

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table BT2SSCD4_ISPE: Decrease of Skindex-10 social functioning score of at least 4 points by specific medical condition
ITT

Decrease of Skindex-10 social functioning score of at least 4 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	E: Presence of specific medical conditions										0.843
	No	195	167 (85.6)	89 (45.6) [38.5, 52.9]	199	179 (89.9)	84 (42.2) [35.3, 49.4]	1.081 [0.865, 1.352]	1.149 [0.772, 1.712]	3.4 [-6.9, 13.7]	0.493
	Yes	42	35 (83.3)	21 (50.0) [34.2, 65.8]	37	35 (94.6)	18 (48.6) [31.9, 65.6]	1.028 [0.656, 1.609]	1.056 [0.436, 2.555]	1.4 [-23.3, 26.0]	0.905

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table BT2SSCD4_ISPF: Decrease of Skindex-10 social functioning score of at least 4 points by use of concomitant itch medication
ITT

Decrease of Skindex-10 social functioning score of at least 4 points		CR845 N	CR845 nval	CR845 n (%) [95 % CI]	Placebo N	Placebo nval	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	F: Use of concomitant itch medication										0.169
	No	150	132 (88.0)	64 (42.7) [34.6, 51.0]	151	140 (92.7)	67 (44.4) [36.3, 52.7]	0.962 [0.743, 1.244]	0.933 [0.591, 1.472]	-1.7 [-13.6, 10.2]	0.766
	Yes	87	70 (80.5)	46 (52.9) [41.9, 63.7]	85	74 (87.1)	35 (41.2) [30.6, 52.4]	1.284 [0.930, 1.773]	1.603 [0.877, 2.930]	11.7 [-4.3, 27.7]	0.126

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table BT2SSCD4_ISPG: Decrease of Skindex-10 social functioning score of at least 4 points by region
ITT

Decrease of Skindex-10 social functioning score of at least 4 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	G: Region										0.333	
	USA	146	126 (86.3)	68 (46.6) [38.3, 55.0]	133	124 (93.2)	63 (47.4) [38.7, 56.2]	0.983 [0.766, 1.262]	0.969 [0.605, 1.551]	-0.8 [-13.2, 11.7]	0.895	
	Asia	8	7 (87.5)	7 (87.5) [47.3, 99.7]	12	11 (91.7)	6 (50.0) [21.1, 78.9]	1.750 [0.938, 3.264]	7.000 [0.647, 75.735]	37.5 [-9.3, 84.3]	0.158	#
	Eastern Europe	54	47 (87.0)	23 (42.6) [29.2, 56.8]	60	55 (91.7)	20 (33.3) [21.7, 46.7]	1.278 [0.796, 2.051]	1.484 [0.693, 3.176]	9.3 [-10.3, 28.8]	0.311	
	Western Europe/European origin	29	22 (75.9)	12 (41.4) [23.5, 61.1]	31	24 (77.4)	13 (41.9) [24.5, 60.9]	0.987 [0.542, 1.797]	0.977 [0.350, 2.730]	-0.6 [-28.9, 27.7]	0.965	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table BT2SSCD4_ISPH: Decrease of Skindex-10 social functioning score of at least 4 points by dialysis method
ITT

Decrease of Skindex-10 social functioning score of at least 4 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	H: Dialysis method										0.655
	Hemodialysis (HD)	222	189 (85.1)	105 (47.3) [40.6, 54.1]	199	180 (90.5)	88 (44.2) [37.2, 51.4]	1.070 [0.868, 1.318]	1.132 [0.771, 1.662]	3.1 [-6.9, 13.1]	0.528
	Hemodiafiltration (HDF)	15	13 (86.7)	5 (33.3) [11.8, 61.6]	37	34 (91.9)	14 (37.8) [22.5, 55.2]	0.881 [0.386, 2.013]	0.821 [0.232, 2.903]	-4.5 [-37.7, 28.7]	0.762

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin, created on: 17FEB2022

Table BT2A_SSIA: Incidence of TEAEs by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
A: Age								0.093
< 65 years	146	98 (67.1) [58.9, 74.7]	153	85 (55.6) [47.3, 63.6]	1.208 [1.008, 1.449]	1.633 [1.021, 2.613]	11.6 [-0.1, 23.2]	0.041 *
>= 65 years	89	62 (69.7) [59.0, 79.0]	83	60 (72.3) [61.4, 81.6]	0.964 [0.796, 1.167]	0.880 [0.455, 1.703]	-2.6 [-17.4, 12.1]	0.705

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSIB: Incidence of TEAEs by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
B: Sex								0.419
Male	135	86 (63.7) [55.0, 71.8]	139	84 (60.4) [51.8, 68.6]	1.054 [0.876, 1.269]	1.149 [0.705, 1.873]	3.3 [-8.9, 15.5]	0.578
Female	100	74 (74.0) [64.3, 82.3]	97	61 (62.9) [52.5, 72.5]	1.177 [0.971, 1.426]	1.680 [0.915, 3.084]	11.1 [-2.8, 25.0]	0.094

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSIC: Incidence of TEAEs by race
SAF-S

	CR845		Placebo					
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
C: Race								0.242
Black/African American	53	40 (75.5) [61.7, 86.2]	38	31 (81.6) [65.7, 92.3]	0.925 [0.746, 1.147]	0.695 [0.248, 1.949]	-6.1 [-25.3, 13.1]	0.490
White	162	103 (63.6) [55.7, 71.0]	169	93 (55.0) [47.2, 62.7]	1.155 [0.966, 1.382]	1.427 [0.918, 2.217]	8.6 [-2.6, 19.7]	0.114
Other	20	17 (85.0) [62.1, 96.8]	29	21 (72.4) [52.8, 87.3]	1.174 [0.878, 1.569]	2.159 [0.495, 9.417]	12.6 [-14.2, 39.4]	0.488 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSID: Incidence of TEAEs by baseline WI-NRS
SAF-S

	CR845		Placebo					
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)								0.057
>= 4 to < 7	101	71 (70.3) [60.4, 79.0]	113	62 (54.9) [45.2, 64.2]	1.281 [1.039, 1.580]	1.947 [1.106, 3.426]	15.4 [1.7, 29.2]	0.020 *
>= 7	134	89 (66.4) [57.8, 74.3]	123	83 (67.5) [58.4, 75.6]	0.984 [0.829, 1.169]	0.953 [0.566, 1.604]	-1.1 [-13.4, 11.2]	0.857

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSIE: Incidence of TEAEs by specific medical condition
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
E: Presence of specific medical conditions								0.041 i
No	194	130 (67.0) [59.9, 73.6]	199	114 (57.3) [50.1, 64.3]	1.170 [1.001, 1.366]	1.515 [1.005, 2.283]	9.7 [-0.3, 19.8]	0.047 *
Yes	41	30 (73.2) [57.1, 85.8]	37	31 (83.8) [68.0, 93.8]	0.873 [0.692, 1.103]	0.528 [0.173, 1.608]	-10.6 [-31.2, 10.0]	0.260

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSIF: Incidence of TEAEs by use of concomitant itch medication
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
F: Use of concomitant itch medication								0.009 i
No	148	99 (66.9) [58.7, 74.4]	151	79 (52.3) [44.0, 60.5]	1.279 [1.058, 1.546]	1.841 [1.153, 2.941]	14.6 [2.9, 26.2]	0.010 *
Yes	87	61 (70.1) [59.4, 79.5]	85	66 (77.6) [67.3, 86.0]	0.903 [0.755, 1.079]	0.675 [0.340, 1.342]	-7.5 [-21.8, 6.7]	0.263

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSIG: Incidence of TEAEs by region
SAF-S

	CR845		Placebo						
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
G: Region								0.344	
USA	145	101 (69.7) [61.5, 77.0]	133	76 (57.1) [48.3, 65.7]	1.219 [1.016, 1.463]	1.722 [1.051, 2.819]	12.5 [0.5, 24.5]	0.031	*
Asia	8	8 (100.0) [63.1, 100.0]	12	11 (91.7) [61.5, 99.8]	1.091 [0.920, 1.294]	2.217 + [0.080, 61.403]	8.3 [-17.7, 34.4]	1.000	#
Eastern Europe	54	27 (50.0) [36.1, 63.9]	60	35 (58.3) [44.9, 70.9]	0.857 [0.609, 1.206]	0.714 [0.341, 1.497]	-8.3 [-28.4, 11.7]	0.375	
Western Europe/European origin	28	24 (85.7) [67.3, 96.0]	31	23 (74.2) [55.4, 88.1]	1.155 [0.894, 1.494]	2.087 [0.552, 7.887]	11.5 [-12.0, 35.1]	0.276	

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSIH: Incidence of TEAEs by dialysis method
SAF-S

	CR845		Placebo					
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
H: Dialysis method								0.562
Hemodialysis (HD)	220	153 (69.5) [63.0, 75.6]	199	126 (63.3) [56.2, 70.0]	1.098 [0.958, 1.260]	1.323 [0.881, 1.987]	6.2 [-3.3, 15.8]	0.178
Hemodiafiltration (HDF)	15	7 (46.7) [21.3, 73.4]	37	19 (51.4) [34.4, 68.1]	0.909 [0.486, 1.698]	0.829 [0.249, 2.757]	-4.7 [-39.3, 29.9]	0.762

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AS_SSIA: Incidence of serious TEAEs by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Serious TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
A: Age								0.515
< 65 years	146	34 (23.3) [16.7, 31.0]	153	34 (22.2) [15.9, 29.6]	1.048 [0.690, 1.591]	1.063 [0.619, 1.825]	1.1 [-9.1, 11.2]	0.826
>= 65 years	89	24 (27.0) [18.1, 37.4]	83	17 (20.5) [12.4, 30.8]	1.317 [0.764, 2.270]	1.433 [0.705, 2.914]	6.5 [-7.3, 20.3]	0.320

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AS_SSIB: Incidence of serious TEAEs by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Serious TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
B: Sex								0.955
Male	135	33 (24.4) [17.5, 32.6]	139	30 (21.6) [15.1, 29.4]	1.133 [0.734, 1.748]	1.175 [0.669, 2.065]	2.9 [-7.8, 13.6]	0.574
Female	100	25 (25.0) [16.9, 34.7]	97	21 (21.6) [13.9, 31.2]	1.155 [0.694, 1.920]	1.206 [0.622, 2.339]	3.4 [-9.5, 16.2]	0.579

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AS_SSIC: Incidence of serious TEAEs by race
SAF-S

	CR845		Placebo					
Serious TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
C: Race								0.161
Black/African American	53	18 (34.0) [21.5, 48.3]	38	12 (31.6) [17.5, 48.7]	1.075 [0.590, 1.960]	1.114 [0.458, 2.712]	2.4 [-19.4, 24.2]	0.813
White	162	34 (21.0) [15.0, 28.1]	169	37 (21.9) [15.9, 28.9]	0.959 [0.634, 1.448]	0.948 [0.560, 1.602]	-0.9 [-10.4, 8.5]	0.841
Other	20	6 (30.0) [11.9, 54.3]	29	2 (6.9) [0.8, 22.8]	4.350 [0.975, 19.407]	5.786 [1.030, 32.491]	23.1 [-3.2, 49.4]	0.050 *

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AS_SSID: Incidence of serious TEAEs by baseline WI-NRS
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Serious TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)								0.973
>= 4 to < 7	101	21 (20.8) [13.4, 30.0]	113	21 (18.6) [11.9, 27.0]	1.119 [0.651, 1.924]	1.150 [0.586, 2.259]	2.2 [-9.4, 13.8]	0.685
>= 7	134	37 (27.6) [20.2, 36.0]	123	30 (24.4) [17.1, 33.0]	1.132 [0.748, 1.714]	1.182 [0.676, 2.069]	3.2 [-8.3, 14.7]	0.558

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AS_SSIE: Incidence of serious TEAEs by specific medical condition
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Serious TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
E: Presence of specific medical conditions								0.514
No	194	44 (22.7) [17.0, 29.2]	199	42 (21.1) [15.7, 27.4]	1.075 [0.740, 1.562]	1.097 [0.680, 1.769]	1.6 [-7.1, 10.3]	0.706
Yes	41	14 (34.1) [20.1, 50.6]	37	9 (24.3) [11.8, 41.2]	1.404 [0.690, 2.855]	1.613 [0.599, 4.343]	9.8 [-12.8, 32.4]	0.345

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AS_SSIF: Incidence of serious TEAEs by use of concomitant itch medication
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Serious TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
F: Use of concomitant itch medication								0.108
No	148	40 (27.0) [20.1, 34.9]	151	29 (19.2) [13.3, 26.4]	1.407 [0.924, 2.144]	1.558 [0.905, 2.684]	7.8 [-2.4, 18.0]	0.109
Yes	87	18 (20.7) [12.7, 30.7]	85	22 (25.9) [17.0, 36.5]	0.799 [0.463, 1.381]	0.747 [0.367, 1.520]	-5.2 [-19.0, 8.6]	0.422

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AS_SSIG: Incidence of serious TEAEs by region
SAF-S

	CR845		Placebo					
Serious TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
G: Region								0.072
USA	145	43 (29.7) [22.4, 37.8]	133	31 (23.3) [16.4, 31.4]	1.272 [0.855, 1.893]	1.387 [0.811, 2.374]	6.3 [-4.7, 17.4]	0.233
Asia	8	0 (0.0) [0.0, 36.9]	12	2 (16.7) [2.1, 48.4]	0.289 + [0.016, 5.330]	0.247 + [0.010, 5.871]	-16.7 [-48.2, 14.8]	0.495 #
Eastern Europe	54	5 (9.3) [3.1, 20.3]	60	13 (21.7) [12.1, 34.2]	0.427 [0.163, 1.120]	0.369 [0.122, 1.115]	-12.4 [-27.1, 2.3]	0.071
Western Europe/European origin	28	10 (35.7) [18.6, 55.9]	31	5 (16.1) [5.5, 33.7]	2.214 [0.861, 5.692]	2.889 [0.844, 9.886]	19.6 [-5.8, 45.0]	0.087

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AS_SSIH: Incidence of serious TEAEs by dialysis method
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Serious TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
H: Dialysis method								0.234
Hemodialysis (HD)	220	53 (24.1) [18.6, 30.3]	199	45 (22.6) [17.0, 29.1]	1.065 [0.752, 1.509]	1.086 [0.690, 1.710]	1.5 [-7.1, 10.1]	0.722
Hemodiafiltration (HDF)	15	5 (33.3) [11.8, 61.6]	37	6 (16.2) [6.2, 32.0]	2.056 [0.738, 5.723]	2.583 [0.647, 10.314]	17.1 [-14.2, 48.5]	0.260 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AC_SSIA: Incidence of severe TEAEs by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Severe TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
A: Age								0.388
< 65 years	146	24 (16.4) [10.8, 23.5]	153	22 (14.4) [9.2, 21.0]	1.143 [0.671, 1.947]	1.171 [0.625, 2.197]	2.1 [-6.8, 10.9]	0.622
>= 65 years	89	15 (16.9) [9.8, 26.3]	83	8 (9.6) [4.3, 18.1]	1.749 [0.782, 3.908]	1.900 [0.760, 4.750]	7.2 [-4.0, 18.4]	0.166

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AC_SSIB: Incidence of severe TEAEs by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Severe TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
B: Sex								0.517
Male	135	20 (14.8) [9.3, 21.9]	139	18 (12.9) [7.9, 19.7]	1.144 [0.633, 2.066]	1.169 [0.589, 2.322]	1.9 [-7.1, 10.8]	0.656
Female	100	19 (19.0) [11.8, 28.1]	97	12 (12.4) [6.6, 20.6]	1.536 [0.789, 2.991]	1.662 [0.758, 3.640]	6.6 [-4.5, 17.7]	0.203

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AC_SSIC: Incidence of severe TEAEs by race
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Severe TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
C: Race								0.185
Black/African American	53	14 (26.4) [15.3, 40.3]	38	6 (15.8) [6.0, 31.3]	1.673 [0.707, 3.957]	1.915 [0.660, 5.551]	10.6 [-8.2, 29.5]	0.230
White	162	21 (13.0) [8.2, 19.1]	169	23 (13.6) [8.8, 19.7]	0.952 [0.549, 1.652]	0.945 [0.501, 1.784]	-0.6 [-8.6, 7.3]	0.863
Other	20	4 (20.0) [5.7, 43.7]	29	1 (3.4) [0.1, 17.8]	5.800 [0.699, 48.126]	7.000 [0.719, 68.148]	16.6 [-6.4, 39.5]	0.144 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AC_SSID: Incidence of severe TEAEs by baseline WI-NRS
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Severe TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)								0.662
>= 4 to < 7	101	12 (11.9) [6.3, 19.8]	113	12 (10.6) [5.6, 17.8]	1.119 [0.526, 2.378]	1.135 [0.485, 2.653]	1.3 [-8.2, 10.7]	0.771
>= 7	134	27 (20.1) [13.7, 27.9]	123	18 (14.6) [8.9, 22.1]	1.377 [0.799, 2.372]	1.472 [0.765, 2.832]	5.5 [-4.5, 15.5]	0.246

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AC_SSIE: Incidence of severe TEAEs by specific medical condition
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Severe TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
E: Presence of specific medical conditions								0.429
No	194	32 (16.5) [11.6, 22.5]	199	27 (13.6) [9.1, 19.1]	1.216 [0.758, 1.950]	1.258 [0.722, 2.193]	2.9 [-4.6, 10.5]	0.417
Yes	41	7 (17.1) [7.2, 32.1]	37	3 (8.1) [1.7, 21.9]	2.106 [0.587, 7.554]	2.333 [0.556, 9.786]	9.0 [-8.1, 26.0]	0.317 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AC_SSIF: Incidence of severe TEAEs by use of concomitant itch medication
SAF-S

	CR845		Placebo					
Severe TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
F: Use of concomitant itch medication								0.257
No	148	24 (16.2) [10.7, 23.2]	151	15 (9.9) [5.7, 15.9]	1.632 [0.892, 2.986]	1.755 [0.881, 3.497]	6.3 [-2.0, 14.6]	0.107
Yes	87	15 (17.2) [10.0, 26.8]	85	15 (17.6) [10.2, 27.4]	0.977 [0.510, 1.872]	0.972 [0.442, 2.137]	-0.4 [-12.9, 12.1]	0.944

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AC_SSIG: Incidence of severe TEAEs by region
SAF-S

	CR845		Placebo					
Severe TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
G: Region								0.314
USA	145	27 (18.6) [12.6, 25.9]	133	19 (14.3) [8.8, 21.4]	1.303 [0.761, 2.232]	1.373 [0.723, 2.606]	4.3 [-5.1, 13.7]	0.332
Asia	8	0 (0.0) [0.0, 36.9]	12	1 (8.3) [0.2, 38.5]	0.481 + [0.022, 10.536]	0.451 + [0.016, 12.488]	-8.3 [-34.4, 17.7]	1.000 #
Eastern Europe	54	4 (7.4) [2.1, 17.9]	60	7 (11.7) [4.8, 22.6]	0.635 [0.197, 2.050]	0.606 [0.167, 2.196]	-4.3 [-16.7, 8.2]	0.444
Western Europe/European origin	28	8 (28.6) [13.2, 48.7]	31	3 (9.7) [2.0, 25.8]	2.952 [0.868, 10.046]	3.733 [0.880, 15.847]	18.9 [-4.2, 42.0]	0.065

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AC_SSIH: Incidence of severe TEAEs by dialysis method
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Severe TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
H: Dialysis method								0.598
Hemodialysis (HD)	220	36 (16.4) [11.7, 21.9]	199	26 (13.1) [8.7, 18.6]	1.252 [0.785, 1.997]	1.302 [0.755, 2.246]	3.3 [-3.9, 10.5]	0.343
Hemodiafiltration (HDF)	15	3 (20.0) [4.3, 48.1]	37	4 (10.8) [3.0, 25.4]	1.850 [0.469, 7.291]	2.063 [0.402, 10.593]	9.2 [-18.1, 36.5]	0.397 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AN_SSIA: Incidence of non-severe TEAEs by age
SAF-S

	CR845		Placebo						
Non-severe TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
A: Age								0.035	i
< 65 years	146	97 (66.4) [58.2, 74.0]	153	80 (52.3) [44.1, 60.4]	1.271 [1.050, 1.537]	1.806 [1.132, 2.883]	14.2 [2.5, 25.8]	0.013	*
>= 65 years	89	61 (68.5) [57.8, 78.0]	83	60 (72.3) [61.4, 81.6]	0.948 [0.781, 1.151]	0.835 [0.433, 1.610]	-3.7 [-18.5, 11.0]	0.592	

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AN_SSIB: Incidence of non-severe TEAEs by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Non-severe TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
B: Sex								0.456
Male	135	85 (63.0) [54.2, 71.1]	139	81 (58.3) [49.6, 66.6]	1.080 [0.893, 1.308]	1.217 [0.749, 1.978]	4.7 [-7.6, 17.0]	0.428
Female	100	73 (73.0) [63.2, 81.4]	97	59 (60.8) [50.4, 70.6]	1.200 [0.983, 1.465]	1.741 [0.955, 3.176]	12.2 [-1.9, 26.2]	0.070

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AN_SSIC: Incidence of non-severe TEAEs by race
SAF-S

	CR845		Placebo						
Non-severe TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
C: Race								0.157	
Black/African American	53	38 (71.7) [57.7, 83.2]	38	30 (78.9) [62.7, 90.4]	0.908 [0.717, 1.150]	0.676 [0.253, 1.805]	-7.2 [-27.3, 12.8]	0.435	
White	162	103 (63.6) [55.7, 71.0]	169	89 (52.7) [44.9, 60.4]	1.207 [1.004, 1.452]	1.569 [1.011, 2.437]	10.9 [-0.2, 22.1]	0.045	*
Other	20	17 (85.0) [62.1, 96.8]	29	21 (72.4) [52.8, 87.3]	1.174 [0.878, 1.569]	2.159 [0.495, 9.417]	12.6 [-14.2, 39.4]	0.488	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AN_SSID: Incidence of non-severe TEAEs by baseline WI-NRS
SAF-S

	CR845		Placebo					
Non-severe TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)								0.048 i
>= 4 to < 7	101	71 (70.3) [60.4, 79.0]	113	60 (53.1) [43.5, 62.5]	1.324 [1.068, 1.641]	2.091 [1.189, 3.676]	17.2 [3.5, 30.9]	0.010 *
>= 7	134	87 (64.9) [56.2, 73.0]	123	80 (65.0) [55.9, 73.4]	0.998 [0.834, 1.195]	0.995 [0.596, 1.662]	-0.1 [-12.6, 12.3]	0.985

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AN_SSIE: Incidence of non-severe TEAEs by specific medical condition
SAF-S

	CR845		Placebo						
		n (%)		n (%)	RR	OR	RD		
Non-severe TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value	
E: Presence of specific medical conditions								0.059	
No	194	128 (66.0) [58.8, 72.6]	199	110 (55.3) [48.1, 62.3]	1.194 [1.016, 1.402]	1.569 [1.044, 2.359]	10.7 [0.6, 20.8]	0.030	*
Yes	41	30 (73.2) [57.1, 85.8]	37	30 (81.1) [64.8, 92.0]	0.902 [0.708, 1.150]	0.636 [0.217, 1.863]	-7.9 [-29.0, 13.2]	0.411	

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AN_SSIF: Incidence of non-severe TEAEs by use of concomitant itch medication
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Non-severe TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
F: Use of concomitant itch medication								0.015 i
No	148	97 (65.5) [57.3, 73.2]	151	76 (50.3) [42.1, 58.6]	1.302 [1.069, 1.586]	1.877 [1.178, 2.990]	15.2 [3.5, 26.9]	0.008 *
Yes	87	61 (70.1) [59.4, 79.5]	85	64 (75.3) [64.7, 84.0]	0.931 [0.775, 1.119]	0.770 [0.393, 1.510]	-5.2 [-19.6, 9.3]	0.447

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AN_SSIG: Incidence of non-severe TEAEs by region
SAF-S

	CR845		Placebo						
Non-severe TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
G: Region								0.234	
USA	145	99 (68.3) [60.0, 75.7]	133	71 (53.4) [44.5, 62.1]	1.279 [1.054, 1.552]	1.879 [1.153, 3.062]	14.9 [2.8, 27.0]	0.011	*
Asia	8	8 (100.0) [63.1, 100.0]	12	11 (91.7) [61.5, 99.8]	1.091 [0.920, 1.294]	2.217 + [0.080, 61.403]	8.3 [-17.7, 34.4]	1.000	#
Eastern Europe	54	27 (50.0) [36.1, 63.9]	60	35 (58.3) [44.9, 70.9]	0.857 [0.609, 1.206]	0.714 [0.341, 1.497]	-8.3 [-28.4, 11.7]	0.375	
Western Europe/European origin	28	24 (85.7) [67.3, 96.0]	31	23 (74.2) [55.4, 88.1]	1.155 [0.894, 1.494]	2.087 [0.552, 7.887]	11.5 [-12.0, 35.1]	0.276	

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AN_SSIH: Incidence of non-severe TEAEs by dialysis method
SAF-S

	CR845		Placebo					
Non-severe TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
H: Dialysis method								0.508
Hemodialysis (HD)	220	151 (68.6) [62.1, 74.7]	199	121 (60.8) [53.7, 67.6]	1.129 [0.978, 1.302]	1.411 [0.943, 2.110]	7.8 [-1.8, 17.5]	0.094
Hemodiafiltration (HDF)	15	7 (46.7) [21.3, 73.4]	37	19 (51.4) [34.4, 68.1]	0.909 [0.486, 1.698]	0.829 [0.249, 2.757]	-4.7 [-39.3, 29.9]	0.762

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AT_SSIA: Incidence of TEAEs leading to study drug discontinuation by age
SAF-S

TEAEs leading to study drug discontinuation	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
A: Age								0.691	
< 65 years	146	5 (3.4) [1.1, 7.8]	153	4 (2.6) [0.7, 6.6]	1.310 [0.359, 4.783]	1.321 [0.348, 5.018]	0.8 [-3.7, 5.4]	0.745	#
>= 65 years	89	8 (9.0) [4.0, 16.9]	83	4 (4.8) [1.3, 11.9]	1.865 [0.583, 5.964]	1.951 [0.565, 6.738]	4.2 [-4.5, 12.9]	0.285	

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AT_SSIB: Incidence of TEAEs leading to study drug discontinuation by sex
SAF-S

TEAEs leading to study drug discontinuation	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
B: Sex								0.219	
Male	135	6 (4.4) [1.6, 9.4]	139	6 (4.3) [1.6, 9.2]	1.030 [0.341, 3.113]	1.031 [0.324, 3.280]	0.1 [-5.4, 5.7]	0.959	
Female	100	7 (7.0) [2.9, 13.9]	97	2 (2.1) [0.3, 7.3]	3.395 [0.723, 15.939]	3.575 [0.724, 17.660]	4.9 [-1.8, 11.7]	0.170	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AT_SSIC: Incidence of TEAEs leading to study drug discontinuation by race
SAF-S

	CR845		Placebo					
TEAEs leading to study drug discontinuation	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
C: Race								0.938
Black/African American	53	1 (1.9) [0.0, 10.1]	38	0 (0.0) [0.0, 9.3]	2.167 + [0.091, 51.789]	2.200 + [0.087, 55.477]	1.9 [-4.0, 7.8]	1.000 #
White	162	9 (5.6) [2.6, 10.3]	169	6 (3.6) [1.3, 7.6]	1.565 [0.570, 4.297]	1.598 [0.556, 4.595]	2.0 [-3.1, 7.1]	0.381
Other	20	3 (15.0) [3.2, 37.9]	29	2 (6.9) [0.8, 22.8]	2.175 [0.399, 11.859]	2.382 [0.360, 15.759]	8.1 [-14.3, 30.5]	0.387 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AT_SSID: Incidence of TEAEs leading to study drug discontinuation by baseline WI-NRS
SAF-S

TEAEs leading to study drug discontinuation	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
D: Baseline worst itching NRS score (WI-NRS)								0.066	
>= 4 to < 7	101	1 (1.0) [0.0, 5.4]	113	4 (3.5) [1.0, 8.8]	0.280 [0.032, 2.462]	0.273 [0.030, 2.479]	-2.5 [-7.4, 2.3]	0.373	#
>= 7	134	12 (9.0) [4.7, 15.1]	123	4 (3.3) [0.9, 8.1]	2.754 [0.912, 8.312]	2.926 [0.918, 9.329]	5.7 [-0.8, 12.2]	0.059	

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AT_SSIE: Incidence of TEAEs leading to study drug discontinuation by specific medical condition
SAF-S

TEAEs leading to study drug discontinuation	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
E: Presence of specific medical conditions								0.466	
No	194	11 (5.7) [2.9, 9.9]	199	8 (4.0) [1.8, 7.8]	1.410 [0.580, 3.431]	1.435 [0.565, 3.648]	1.7 [-3.1, 6.4]	0.446	
Yes	41	2 (4.9) [0.6, 16.5]	37	0 (0.0) [0.0, 9.5]	4.524 + [0.224, 91.272]	4.747 + [0.221, 102.161]	4.9 [-4.3, 14.0]	0.495	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AT_SSIF: Incidence of TEAEs leading to study drug discontinuation by use of concomitant itch medication
SAF-S

TEAEs leading to study drug discontinuation	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
F: Use of concomitant itch medication								0.822	
No	148	7 (4.7) [1.9, 9.5]	151	4 (2.6) [0.7, 6.6]	1.785 [0.534, 5.972]	1.824 [0.523, 6.368]	2.1 [-2.9, 7.0]	0.340	
Yes	87	6 (6.9) [2.6, 14.4]	85	4 (4.7) [1.3, 11.6]	1.466 [0.429, 5.011]	1.500 [0.408, 5.516]	2.2 [-5.9, 10.3]	0.747	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AT_SSIG: Incidence of TEAEs leading to study drug discontinuation by region
SAF-S

TEAEs leading to study drug discontinuation	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
G: Region		n<10 for all subgroups						NE
USA	145	5 (3.4) [1.1, 7.9]	133	3 (2.3) [0.5, 6.5]				
Asia	8	0 (0.0) [0.0, 36.9]	12	0 (0.0) [0.0, 26.5]				
Eastern Europe	54	3 (5.6) [1.2, 15.4]	60	2 (3.3) [0.4, 11.5]				
Western Europe/European origin	28	5 (17.9) [6.1, 36.9]	31	3 (9.7) [2.0, 25.8]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AT_SSIH: Incidence of TEAEs leading to study drug discontinuation by dialysis method
SAF-S

TEAEs leading to study drug discontinuation	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
H: Dialysis method								0.765	
Hemodialysis (HD)	220	12 (5.5) [2.8, 9.3]	199	6 (3.0) [1.1, 6.4]	1.809 [0.692, 4.730]	1.856 [0.683, 5.041]	2.4 [-1.9, 6.7]	0.219	
Hemodiafiltration (HDF)	15	1 (6.7) [0.2, 31.9]	37	2 (5.4) [0.7, 18.2]	1.233 [0.121, 12.604]	1.250 [0.105, 14.914]	1.3 [-18.0, 20.5]	1.000	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSA: TEAEs - significant SOC and PT by age
SAF-S

	CR845		Placebo						
		n (%)		n (%)	RR	OR	RD		
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value	
SOC: Gastrointestinal disorders									
A: Age								0.140	
< 65 years	146	30 (20.5) [14.3, 28.0]	153	25 (16.3) [10.9, 23.2]	1.258 [0.778, 2.032]	1.324 [0.736, 2.382]	4.2 [-5.3, 13.7]	0.349	
>= 65 years	89	27 (30.3) [21.0, 41.0]	83	11 (13.3) [6.8, 22.5]	2.289 [1.214, 4.316]	2.850 [1.308, 6.212]	17.1 [3.9, 30.3]	0.007	*

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSA: TEAEs - significant SOC and PT by age
SAF-S

	CR845		Placebo						
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
PT: Diarrhoea									
A: Age								0.028	i
< 65 years	146	9 (6.2) [2.9, 11.4]	153	13 (8.5) [4.6, 14.1]	0.726 [0.320, 1.646]	0.707 [0.293, 1.709]	-2.3 [-8.9, 4.2]	0.441	
>= 65 years	89	10 (11.2) [5.5, 19.7]	83	0 (0.0) [0.0, 4.3]	19.600 + [1.167, 329.290]	22.057 + [1.271, 382.689]	11.2 [3.5, 19.0]	0.002	*

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSA: TEAEs - significant SOC and PT by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Injury, poisoning and procedural complications								
A: Age								0.819
< 65 years	146	30 (20.5) [14.3, 28.0]	153	28 (18.3) [12.5, 25.4]	1.123 [0.707, 1.783]	1.155 [0.651, 2.049]	2.2 [-7.4, 11.9]	0.624
>= 65 years	89	21 (23.6) [15.2, 33.8]	83	16 (19.3) [11.4, 29.4]	1.224 [0.687, 2.181]	1.293 [0.622, 2.691]	4.3 [-9.1, 17.7]	0.492

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSA: TEAEs - significant SOC and PT by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Nervous system disorders								
A: Age								0.154
< 65 years	146	23 (15.8) [10.3, 22.7]	153	13 (8.5) [4.6, 14.1]	1.854 [0.976, 3.520]	2.014 [0.978, 4.145]	7.3 [-0.8, 15.3]	0.054
>= 65 years	89	23 (25.8) [17.1, 36.2]	83	21 (25.3) [16.4, 36.0]	1.021 [0.613, 1.702]	1.029 [0.518, 2.042]	0.5 [-13.7, 14.8]	0.935

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSA: TEAEs - significant SOC and PT by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
PT: Dizziness								
A: Age								0.983
< 65 years	146	5 (3.4) [1.1, 7.8]	153	5 (3.3) [1.1, 7.5]	1.048 [0.310, 3.545]	1.050 [0.297, 3.704]	0.2 [-4.6, 4.9]	1.000 #
>= 65 years	89	8 (9.0) [4.0, 16.9]	83	7 (8.4) [3.5, 16.6]	1.066 [0.404, 2.810]	1.072 [0.371, 3.100]	0.6 [-9.0, 10.1]	0.898

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSA: TEAEs - significant SOC and PT by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Skin and subcutaneous tissue disorders								
A: Age								0.237
< 65 years	146	8 (5.5) [2.4, 10.5]	153	4 (2.6) [0.7, 6.6]	2.096 [0.645, 6.811]	2.159 [0.636, 7.332]	2.9 [-2.3, 8.0]	0.208
>= 65 years	89	5 (5.6) [1.8, 12.6]	83	6 (7.2) [2.7, 15.1]	0.777 [0.246, 2.451]	0.764 [0.224, 2.604]	-1.6 [-10.1, 6.9]	0.667

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSB: TEAEs - significant SOC and PT by sex
SAF-S

	CR845		Placebo						
		n (%)		n (%)	RR	OR	RD		
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value	
SOC: Gastrointestinal disorders									
B: Sex								0.425	
Male	135	32 (23.7) [16.8, 31.8]	139	18 (12.9) [7.9, 19.7]	1.830 [1.081, 3.099]	2.088 [1.107, 3.939]	10.8 [0.9, 20.6]	0.021	*
Female	100	25 (25.0) [16.9, 34.7]	97	18 (18.6) [11.4, 27.7]	1.347 [0.787, 2.306]	1.463 [0.739, 2.897]	6.4 [-6.1, 18.9]	0.275	

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSB: TEAEs - significant SOC and PT by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
PT: Diarrhoea								
B: Sex								0.370
Male	135	10 (7.4)	139	5 (3.6)	2.059	2.144	3.8	0.166
		[3.6, 13.2]		[1.2, 8.2]	[0.723, 5.867]	[0.713, 6.446]	[-2.3, 9.9]	
Female	100	9 (9.0)	97	8 (8.2)	1.091	1.100	0.8	0.851
		[4.2, 16.4]		[3.6, 15.6]	[0.439, 2.712]	[0.406, 2.979]	[-8.1, 9.6]	

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSB: TEAEs - significant SOC and PT by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Injury, poisoning and procedural complications								
B: Sex								0.261
Male	135	30 (22.2) [15.5, 30.2]	139	22 (15.8) [10.2, 23.0]	1.404 [0.855, 2.307]	1.519 [0.826, 2.796]	6.4 [-3.6, 16.4]	0.178
Female	100	21 (21.0) [13.5, 30.3]	97	22 (22.7) [14.8, 32.3]	0.926 [0.546, 1.571]	0.906 [0.461, 1.782]	-1.7 [-14.2, 10.9]	0.776

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSB: TEAEs - significant SOC and PT by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Nervous system disorders								
B: Sex								0.769
Male	135	25 (18.5) [12.4, 26.1]	139	20 (14.4) [9.0, 21.3]	1.287 [0.751, 2.205]	1.352 [0.711, 2.571]	4.1 [-5.4, 13.6]	0.357
Female	100	21 (21.0) [13.5, 30.3]	97	14 (14.4) [8.1, 23.0]	1.455 [0.786, 2.694]	1.576 [0.750, 3.313]	6.6 [-5.1, 18.2]	0.229

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSB: TEAEs - significant SOC and PT by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
PT: Dizziness								
B: Sex								0.284
Male	135	9 (6.7) [3.1, 12.3]	139	6 (4.3) [1.6, 9.2]	1.544 [0.565, 4.221]	1.583 [0.548, 4.576]	2.4 [-3.8, 8.5]	0.393
Female	100	4 (4.0) [1.1, 9.9]	97	6 (6.2) [2.3, 13.0]	0.647 [0.188, 2.221]	0.632 [0.173, 2.312]	-2.2 [-9.3, 5.0]	0.533 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSB: TEAEs - significant SOC and PT by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Skin and subcutaneous tissue disorders								
B: Sex								0.548
Male	135	6 (4.4) [1.6, 9.4]	139	6 (4.3) [1.6, 9.2]	1.030 [0.341, 3.113]	1.031 [0.324, 3.280]	0.1 [-5.4, 5.7]	0.959
Female	100	7 (7.0) [2.9, 13.9]	97	4 (4.1) [1.1, 10.2]	1.698 [0.513, 5.615]	1.750 [0.496, 6.180]	2.9 [-4.5, 10.3]	0.381

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSC: TEAEs - significant SOC and PT by race
SAF-S

	CR845		Placebo					
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
SOC: Gastrointestinal disorders								
C: Race								0.561
Black/African American	53	16 (30.2) [18.3, 44.3]	38	5 (13.2) [4.4, 28.1]	2.294 [0.920, 5.721]	2.854 [0.942, 8.647]	17.0 [-1.6, 35.7]	0.059
White	162	33 (20.4) [14.5, 27.4]	169	25 (14.8) [9.8, 21.1]	1.377 [0.858, 2.210]	1.473 [0.832, 2.609]	5.6 [-3.2, 14.4]	0.183
Other	20	8 (40.0) [19.1, 63.9]	29	6 (20.7) [8.0, 39.7]	1.933 [0.792, 4.718]	2.556 [0.719, 9.081]	19.3 [-11.0, 49.6]	0.146

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSC: TEAEs - significant SOC and PT by race
SAF-S

	CR845		Placebo						
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
PT: Diarrhoea									
C: Race								0.772	
Black/African American	53	4 (7.5) [2.1, 18.2]	38	2 (5.3) [0.6, 17.7]	1.434 [0.277, 7.433]	1.469 [0.255, 8.465]	2.3 [-10.0, 14.6]	1.000	#
White	162	15 (9.3) [5.3, 14.8]	169	10 (5.9) [2.9, 10.6]	1.565 [0.724, 3.382]	1.622 [0.707, 3.724]	3.3 [-3.0, 9.7]	0.251	
Other	20	0 (0.0) [0.0, 16.8]	29	1 (3.4) [0.1, 17.8]	0.476 + [0.020, 11.131]	0.463 + [0.018, 11.958]	-3.4 [-14.3, 7.4]	1.000	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSC: TEAEs - significant SOC and PT by race
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Injury, poisoning and procedural complications								
C: Race								0.901
Black/African American	53	9 (17.0) [8.1, 29.8]	38	6 (15.8) [6.0, 31.3]	1.075 [0.418, 2.768]	1.091 [0.353, 3.373]	1.2 [-16.4, 18.8]	0.881
White	162	38 (23.5) [17.2, 30.7]	169	32 (18.9) [13.3, 25.7]	1.239 [0.816, 1.882]	1.312 [0.773, 2.227]	4.5 [-4.9, 13.9]	0.315
Other	20	4 (20.0) [5.7, 43.7]	29	6 (20.7) [8.0, 39.7]	0.967 [0.312, 2.991]	0.958 [0.232, 3.953]	-0.7 [-27.8, 26.4]	1.000 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSC: TEAEs - significant SOC and PT by race
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Nervous system disorders								
C: Race								0.274
Black/African American	53	15 (28.3) [16.8, 42.3]	38	10 (26.3) [13.4, 43.1]	1.075 [0.543, 2.130]	1.105 [0.433, 2.822]	2.0 [-18.8, 22.8]	0.835
White	162	23 (14.2) [9.2, 20.5]	169	20 (11.8) [7.4, 17.7]	1.200 [0.686, 2.098]	1.233 [0.649, 2.343]	2.4 [-5.5, 10.2]	0.523
Other	20	8 (40.0) [19.1, 63.9]	29	4 (13.8) [3.9, 31.7]	2.900 [1.008, 8.341]	4.167 [1.044, 16.622]	26.2 [-2.9, 55.3]	0.048 *

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSC: TEAEs - significant SOC and PT by race
SAF-S

	CR845		Placebo					
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
PT: Dizziness								
C: Race								0.551
Black/African American	53	6 (11.3) [4.3, 23.0]	38	2 (5.3) [0.6, 17.7]	2.151 [0.459, 10.085]	2.298 [0.438, 12.063]	6.1 [-7.3, 19.4]	0.461 #
White	162	5 (3.1) [1.0, 7.1]	169	7 (4.1) [1.7, 8.3]	0.745 [0.241, 2.300]	0.737 [0.229, 2.371]	-1.1 [-5.7, 3.6]	0.608
Other	20	2 (10.0) [1.2, 31.7]	29	3 (10.3) [2.2, 27.4]	0.967 [0.177, 5.271]	0.963 [0.146, 6.358]	-0.3 [-21.8, 21.1]	1.000 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSC: TEAEs - significant SOC and PT by race
SAF-S

	CR845		Placebo						
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
SOC: Skin and subcutaneous tissue disorders									
C: Race								0.447	
Black/African American	53	3 (5.7) [1.2, 15.7]	38	0 (0.0) [0.0, 9.3]	5.056 + [0.269, 95.098]	5.337 + [0.268, 106.411]	5.7 [-2.8, 14.1]	0.262	#
White	162	9 (5.6) [2.6, 10.3]	169	7 (4.1) [1.7, 8.3]	1.341 [0.512, 3.517]	1.361 [0.495, 3.746]	1.4 [-3.8, 6.7]	0.550	
Other	20	1 (5.0) [0.1, 24.9]	29	3 (10.3) [2.2, 27.4]	0.483 [0.054, 4.320]	0.456 [0.044, 4.732]	-5.3 [-24.2, 13.5]	0.636	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSD: TEAEs - significant SOC and PT by baseline WI-NRS
SAF-S

	CR845		Placebo						
		n (%)		n (%)	RR	OR	RD		
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value	
SOC: Gastrointestinal disorders									
D: Baseline worst itching NRS score (WI-NRS)								0.525	
>= 4 to < 7	101	26 (25.7) [17.6, 35.4]	113	16 (14.2) [8.3, 22.0]	1.818 [1.036, 3.189]	2.102 [1.052, 4.198]	11.6 [-0.0, 23.2]	0.034	*
>= 7	134	31 (23.1) [16.3, 31.2]	123	20 (16.3) [10.2, 24.0]	1.423 [0.858, 2.360]	1.550 [0.830, 2.896]	6.9 [-3.6, 17.3]	0.168	

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSD: TEAEs - significant SOC and PT by baseline WI-NRS
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
PT: Diarrhoea								
D: Baseline worst itching NRS score (WI-NRS)								0.484
>= 4 to < 7	101	7 (6.9) [2.8, 13.8]	113	7 (6.2) [2.5, 12.3]	1.119 [0.406, 3.080]	1.128 [0.381, 3.333]	0.7 [-6.9, 8.3]	0.828
>= 7	134	12 (9.0) [4.7, 15.1]	123	6 (4.9) [1.8, 10.3]	1.836 [0.711, 4.742]	1.918 [0.697, 5.278]	4.1 [-2.9, 11.0]	0.202

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSD: TEAEs - significant SOC and PT by baseline WI-NRS
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Injury, poisoning and procedural complications								
D: Baseline worst itching NRS score (WI-NRS)								0.477
>= 4 to < 7	101	24 (23.8) [15.9, 33.3]	113	20 (17.7) [11.2, 26.0]	1.343 [0.791, 2.279]	1.449 [0.745, 2.821]	6.1 [-5.8, 17.9]	0.274
>= 7	134	27 (20.1) [13.7, 27.9]	123	24 (19.5) [12.9, 27.6]	1.033 [0.631, 1.690]	1.041 [0.563, 1.923]	0.6 [-9.9, 11.2]	0.898

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSD: TEAEs - significant SOC and PT by baseline WI-NRS
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Nervous system disorders								
D: Baseline worst itching NRS score (WI-NRS)								0.180
>= 4 to < 7	101	19 (18.8) [11.7, 27.8]	113	11 (9.7) [5.0, 16.8]	1.932 [0.967, 3.862]	2.149 [0.968, 4.769]	9.1 [-1.2, 19.4]	0.057
>= 7	134	27 (20.1) [13.7, 27.9]	123	23 (18.7) [12.2, 26.7]	1.078 [0.654, 1.776]	1.097 [0.591, 2.038]	1.5 [-9.0, 11.9]	0.770

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSD: TEAEs - significant SOC and PT by baseline WI-NRS
SAF-S

	CR845		Placebo						
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
PT: Dizziness									
D: Baseline worst itching NRS score (WI-NRS)								0.335	
>= 4 to < 7	101	5 (5.0) [1.6, 11.2]	113	3 (2.7) [0.6, 7.6]	1.865 [0.457, 7.607]	1.910 [0.445, 8.201]	2.3 [-3.8, 8.4]	0.480	#
>= 7	134	8 (6.0) [2.6, 11.4]	123	9 (7.3) [3.4, 13.4]	0.816 [0.325, 2.048]	0.804 [0.300, 2.155]	-1.3 [-8.2, 5.5]	0.665	

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSD: TEAEs - significant SOC and PT by baseline WI-NRS
SAF-S

	CR845		Placebo						
		n (%)		n (%)	RR	OR	RD		
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value	
SOC: Skin and subcutaneous tissue disorders									
D: Baseline worst itching NRS score (WI-NRS)								0.589	
>= 4 to < 7	101	6 (5.9) [2.2, 12.5]	113	4 (3.5) [1.0, 8.8]	1.678 [0.487, 5.778]	1.721 [0.472, 6.282]	2.4 [-4.3, 9.1]	0.522	#
>= 7	134	7 (5.2) [2.1, 10.5]	123	6 (4.9) [1.8, 10.3]	1.071 [0.370, 3.099]	1.075 [0.351, 3.291]	0.3 [-5.8, 6.5]	0.900	

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSE: TEAEs - significant SOC and PT by specific medical condition
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Gastrointestinal disorders								
E: Presence of specific medical conditions								0.368
No	194	47 (24.2) [18.4, 30.9]	199	28 (14.1) [9.6, 19.7]	1.722 [1.127, 2.631]	1.953 [1.164, 3.275]	10.2 [1.9, 18.4]	0.011 *
Yes	41	10 (24.4) [12.4, 40.3]	37	8 (21.6) [9.8, 38.2]	1.128 [0.499, 2.553]	1.169 [0.406, 3.371]	2.8 [-18.5, 24.0]	0.773

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSE: TEAEs - significant SOC and PT by specific medical condition
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
PT: Diarrhoea								
E: Presence of specific medical conditions								0.566
No	194	16 (8.2) [4.8, 13.0]	199	12 (6.0) [3.2, 10.3]	1.368 [0.664, 2.815]	1.401 [0.645, 3.044]	2.2 [-3.4, 7.8]	0.394
Yes	41	3 (7.3) [1.5, 19.9]	37	1 (2.7) [0.1, 14.2]	2.707 [0.294, 24.905]	2.842 [0.282, 28.593]	4.6 [-7.5, 16.7]	0.617 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSE: TEAEs - significant SOC and PT by specific medical condition
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Injury, poisoning and procedural complications								
E: Presence of specific medical conditions								0.905
No	194	39 (20.1) [14.7, 26.4]	199	35 (17.6) [12.6, 23.6]	1.143 [0.758, 1.725]	1.179 [0.711, 1.956]	2.5 [-5.7, 10.8]	0.524
Yes	41	12 (29.3) [16.1, 45.5]	37	9 (24.3) [11.8, 41.2]	1.203 [0.573, 2.525]	1.287 [0.470, 3.528]	4.9 [-17.3, 27.1]	0.625

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSE: TEAEs - significant SOC and PT by specific medical condition
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Nervous system disorders								
E: Presence of specific medical conditions								0.211
No	194	35 (18.0) [12.9, 24.2]	199	23 (11.6) [7.5, 16.8]	1.561 [0.959, 2.542]	1.684 [0.954, 2.973]	6.5 [-1.0, 14.0]	0.070
Yes	41	11 (26.8) [14.2, 42.9]	37	11 (29.7) [15.9, 47.0]	0.902 [0.445, 1.831]	0.867 [0.323, 2.326]	-2.9 [-25.5, 19.7]	0.778

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSE: TEAEs - significant SOC and PT by specific medical condition
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
PT: Dizziness								
E: Presence of specific medical conditions								0.460
No	194	10 (5.2) [2.5, 9.3]	199	8 (4.0) [1.8, 7.8]	1.282 [0.517, 3.180]	1.298 [0.501, 3.360]	1.1 [-3.5, 5.8]	0.591
Yes	41	3 (7.3) [1.5, 19.9]	37	4 (10.8) [3.0, 25.4]	0.677 [0.162, 2.827]	0.651 [0.136, 3.124]	-3.5 [-18.9, 11.9]	0.702 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSE: TEAEs - significant SOC and PT by specific medical condition
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Skin and subcutaneous tissue disorders								
E: Presence of specific medical conditions								0.957
No	194	10 (5.2) [2.5, 9.3]	199	8 (4.0) [1.8, 7.8]	1.282 [0.517, 3.180]	1.298 [0.501, 3.360]	1.1 [-3.5, 5.8]	0.591
Yes	41	3 (7.3) [1.5, 19.9]	37	2 (5.4) [0.7, 18.2]	1.354 [0.239, 7.659]	1.382 [0.218, 8.762]	1.9 [-11.5, 15.3]	1.000 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSF: TEAEs - significant SOC and PT by use of concomitant itch medication
SAF-S

	CR845		Placebo						
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
SOC: Gastrointestinal disorders									
F: Use of concomitant itch medication								0.447	
No	148	32 (21.6) [15.3, 29.1]	151	18 (11.9) [7.2, 18.2]	1.814 [1.066, 3.085]	2.038 [1.087, 3.823]	9.7 [0.6, 18.8]	0.025	*
Yes	87	25 (28.7) [19.5, 39.4]	85	18 (21.2) [13.1, 31.4]	1.357 [0.801, 2.298]	1.501 [0.747, 3.015]	7.6 [-6.5, 21.6]	0.254	

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSF: TEAEs - significant SOC and PT by use of concomitant itch medication
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
PT: Diarrhoea								
F: Use of concomitant itch medication								0.544
No	148	12 (8.1) [4.3, 13.7]	151	7 (4.6) [1.9, 9.3]	1.749 [0.708, 4.320]	1.815 [0.694, 4.746]	3.5 [-2.7, 9.7]	0.219
Yes	87	7 (8.0) [3.3, 15.9]	85	6 (7.1) [2.6, 14.7]	1.140 [0.399, 3.253]	1.152 [0.371, 3.580]	1.0 [-8.1, 10.0]	0.807

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSF: TEAEs - significant SOC and PT by use of concomitant itch medication
SAF-S

	CR845		Placebo						
		n (%)		n (%)	RR	OR	RD		
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value	
SOC: Injury, poisoning and procedural complications									
F: Use of concomitant itch medication								0.016	i
No	148	35 (23.6) [17.1, 31.3]	151	21 (13.9) [8.8, 20.5]	1.700 [1.040, 2.779]	1.917 [1.056, 3.483]	9.7 [0.3, 19.2]	0.031	*
Yes	87	16 (18.4) [10.9, 28.1]	85	23 (27.1) [18.0, 37.8]	0.680 [0.387, 1.194]	0.607 [0.295, 1.252]	-8.7 [-22.3, 5.0]	0.176	

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSF: TEAEs - significant SOC and PT by use of concomitant itch medication
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Nervous system disorders								
F: Use of concomitant itch medication								0.964
No	148	25 (16.9) [11.2, 23.9]	151	19 (12.6) [7.7, 19.0]	1.342 [0.773, 2.331]	1.412 [0.741, 2.692]	4.3 [-4.4, 13.0]	0.294
Yes	87	21 (24.1) [15.6, 34.5]	85	15 (17.6) [10.2, 27.4]	1.368 [0.757, 2.471]	1.485 [0.706, 3.122]	6.5 [-6.8, 19.8]	0.297

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSF: TEAEs - significant SOC and PT by use of concomitant itch medication
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
PT: Dizziness								
F: Use of concomitant itch medication								0.800
No	148	7 (4.7) [1.9, 9.5]	151	6 (4.0) [1.5, 8.4]	1.190 [0.410, 3.458]	1.200 [0.394, 3.658]	0.8 [-4.5, 6.1]	0.749
Yes	87	6 (6.9) [2.6, 14.4]	85	6 (7.1) [2.6, 14.7]	0.977 [0.328, 2.910]	0.975 [0.302, 3.153]	-0.2 [-8.9, 8.6]	0.967

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSF: TEAEs - significant SOC and PT by use of concomitant itch medication
SAF-S

	CR845		Placebo						
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
SOC: Skin and subcutaneous tissue disorders									
F: Use of concomitant itch medication								0.367	
No	148	4 (2.7) [0.7, 6.8]	151	5 (3.3) [1.1, 7.6]	0.816 [0.224, 2.980]	0.811 [0.213, 3.082]	-0.6 [-5.1, 3.9]	1.000	#
Yes	87	9 (10.3) [4.8, 18.7]	85	5 (5.9) [1.9, 13.2]	1.759 [0.614, 5.033]	1.846 [0.592, 5.754]	4.5 [-4.8, 13.7]	0.286	

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSG: TEAEs - significant SOC and PT by region
SAF-S

	CR845		Placebo						
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
SOC: Gastrointestinal disorders									
G: Region								0.168	
USA	145	36 (24.8) [18.0, 32.7]	133	16 (12.0) [7.0, 18.8]	2.064 [1.203, 3.541]	2.415 [1.268, 4.599]	12.8 [3.1, 22.5]	0.006	*
Asia	8	5 (62.5) [24.5, 91.5]	12	2 (16.7) [2.1, 48.4]	3.750 [0.949, 14.821]	8.333 [1.034, 67.142]	45.8 [-4.2, 95.9]	0.062	#
Eastern Europe	54	6 (11.1) [4.2, 22.6]	60	7 (11.7) [4.8, 22.6]	0.952 [0.341, 2.659]	0.946 [0.297, 3.014]	-0.6 [-14.0, 12.9]	0.926	
Western Europe/European origin	28	10 (35.7) [18.6, 55.9]	31	11 (35.5) [19.2, 54.6]	1.006 [0.506, 2.001]	1.010 [0.347, 2.937]	0.2 [-27.6, 28.1]	0.985	

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSG: TEAEs - significant SOC and PT by region
SAF-S

	CR845		Placebo						
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
PT: Diarrhoea									
G: Region								0.861	
USA	145	13 (9.0) [4.9, 14.8]	133	7 (5.3) [2.1, 10.5]	1.703 [0.701, 4.141]	1.773 [0.685, 4.587]	3.7 [-3.0, 10.4]	0.234	
Asia	8	0 (0.0) [0.0, 36.9]	12	1 (8.3) [0.2, 38.5]	0.481 + [0.022, 10.536]	0.451 + [0.016, 12.488]	-8.3 [-34.4, 17.7]	1.000	#
Eastern Europe	54	3 (5.6) [1.2, 15.4]	60	3 (5.0) [1.0, 13.9]	1.111 [0.234, 5.274]	1.118 [0.216, 5.786]	0.6 [-9.4, 10.5]	1.000	#
Western Europe/European origin	28	3 (10.7) [2.3, 28.2]	31	2 (6.5) [0.8, 21.4]	1.661 [0.299, 9.225]	1.740 [0.269, 11.261]	4.3 [-13.5, 22.0]	0.661	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSG: TEAEs - significant SOC and PT by region
SAF-S

	CR845		Placebo						
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
SOC: Injury, poisoning and procedural complications									
G: Region								0.223	
USA	145	30 (20.7) [14.4, 28.2]	133	23 (17.3) [11.3, 24.8]	1.196 [0.733, 1.952]	1.248 [0.683, 2.280]	3.4 [-6.5, 13.3]	0.472	
Asia	8	1 (12.5) [0.3, 52.7]	12	3 (25.0) [5.5, 57.2]	0.500 [0.063, 3.998]	0.429 [0.036, 5.063]	-12.5 [-56.5, 31.5]	0.619	#
Eastern Europe	54	10 (18.5) [9.3, 31.4]	60	14 (23.3) [13.4, 36.0]	0.794 [0.385, 1.636]	0.747 [0.300, 1.856]	-4.8 [-21.5, 11.8]	0.531	
Western Europe/European origin	28	10 (35.7) [18.6, 55.9]	31	4 (12.9) [3.6, 29.8]	2.768 [0.977, 7.838]	3.750 [1.018, 13.814]	22.8 [-1.9, 47.5]	0.041	*

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSG: TEAEs - significant SOC and PT by region
SAF-S

	CR845		Placebo						
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
SOC: Nervous system disorders									
G: Region								0.725	
USA	145	31 (21.4) [15.0, 29.0]	133	19 (14.3) [8.8, 21.4]	1.497 [0.889, 2.518]	1.632 [0.871, 3.055]	7.1 [-2.6, 16.8]	0.125	
Asia	8	2 (25.0) [3.2, 65.1]	12	1 (8.3) [0.2, 38.5]	3.000 [0.323, 27.831]	3.667 [0.273, 49.288]	16.7 [-27.6, 60.9]	0.537	#
Eastern Europe	54	4 (7.4) [2.1, 17.9]	60	5 (8.3) [2.8, 18.4]	0.889 [0.252, 3.141]	0.880 [0.224, 3.461]	-0.9 [-12.6, 10.7]	1.000	#
Western Europe/European origin	28	9 (32.1) [15.9, 52.4]	31	9 (29.0) [14.2, 48.0]	1.107 [0.513, 2.391]	1.158 [0.382, 3.511]	3.1 [-23.8, 30.1]	0.797	

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSG: TEAEs - significant SOC and PT by region
SAF-S

	CR845		Placebo						
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
PT: Dizziness									
G: Region								0.608	
USA	145	9 (6.2) [2.9, 11.5]	133	5 (3.8) [1.2, 8.6]	1.651 [0.568, 4.802]	1.694 [0.553, 5.190]	2.4 [-3.4, 8.3]	0.352	
Asia	8	1 (12.5) [0.3, 52.7]	12	1 (8.3) [0.2, 38.5]	1.500 [0.109, 20.675]	1.571 [0.084, 29.409]	4.2 [-34.0, 42.3]	1.000	#
Eastern Europe	54	0 (0.0) [0.0, 6.6]	60	2 (3.3) [0.4, 11.5]	0.222 + [0.011, 4.520]	0.215 + [0.010, 4.573]	-3.3 [-9.6, 3.0]	0.497	#
Western Europe/European origin	28	3 (10.7) [2.3, 28.2]	31	4 (12.9) [3.6, 29.8]	0.830 [0.203, 3.391]	0.810 [0.165, 3.983]	-2.2 [-22.0, 17.7]	1.000	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSG: TEAEs - significant SOC and PT by region
SAF-S

	CR845		Placebo						
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
SOC: Skin and subcutaneous tissue disorders									
G: Region								0.183	
USA	145	8 (5.5) [2.4, 10.6]	133	1 (0.8) [0.0, 4.1]	7.338 [0.930, 57.890]	7.708 [0.951, 62.478]	4.8 [0.0, 9.5]	0.038	*
Asia	8	0 (0.0) [0.0, 36.9]	12	3 (25.0) [5.5, 57.2]	0.206 + [0.012, 3.527]	0.160 + [0.007, 3.560]	-25.0 [-59.9, 9.9]	0.242	#
Eastern Europe	54	1 (1.9) [0.0, 9.9]	60	2 (3.3) [0.4, 11.5]	0.556 [0.052, 5.956]	0.547 [0.048, 6.210]	-1.5 [-9.0, 6.1]	1.000	#
Western Europe/European origin	28	4 (14.3) [4.0, 32.7]	31	4 (12.9) [3.6, 29.8]	1.107 [0.305, 4.015]	1.125 [0.253, 4.997]	1.4 [-19.5, 22.3]	1.000	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSH: TEAEs - significant SOC and PT by dialysis method
SAF-S

	CR845		Placebo						
		n (%)		n (%)	RR	OR	RD		
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value	
SOC: Gastrointestinal disorders									
H: Dialysis method								0.545	
Hemodialysis (HD)	220	55 (25.0) [19.4, 31.3]	199	31 (15.6) [10.8, 21.4]	1.605 [1.080, 2.385]	1.806 [1.107, 2.948]	9.4 [1.3, 17.5]	0.017	*
Hemodiafiltration (HDF)	15	2 (13.3) [1.7, 40.5]	37	5 (13.5) [4.5, 28.8]	0.987 [0.214, 4.539]	0.985 [0.169, 5.734]	-0.2 [-25.3, 24.9]	1.000	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSH: TEAEs - significant SOC and PT by dialysis method
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
PT: Diarrhoea								
H: Dialysis method								0.562
Hemodialysis (HD)	220	18 (8.2) [4.9, 12.6]	199	10 (5.0) [2.4, 9.0]	1.628 [0.770, 3.443]	1.684 [0.758, 3.741]	3.2 [-2.0, 8.4]	0.197
Hemodiafiltration (HDF)	15	1 (6.7) [0.2, 31.9]	37	3 (8.1) [1.7, 21.9]	0.822 [0.093, 7.290]	0.810 [0.077, 8.465]	-1.4 [-21.5, 18.6]	1.000 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSH: TEAEs - significant SOC and PT by dialysis method
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Injury, poisoning and procedural complications								
H: Dialysis method								0.860
Hemodialysis (HD)	220	49 (22.3) [17.0, 28.4]	199	39 (19.6) [14.3, 25.8]	1.136 [0.782, 1.652]	1.176 [0.733, 1.886]	2.7 [-5.6, 10.9]	0.503
Hemodiafiltration (HDF)	15	2 (13.3) [1.7, 40.5]	37	5 (13.5) [4.5, 28.8]	0.987 [0.214, 4.539]	0.985 [0.169, 5.734]	-0.2 [-25.3, 24.9]	1.000 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSH: TEAEs - significant SOC and PT by dialysis method
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Nervous system disorders								
H: Dialysis method								0.358
Hemodialysis (HD)	220	46 (20.9) [15.7, 26.9]	199	31 (15.6) [10.8, 21.4]	1.342 [0.888, 2.029]	1.433 [0.867, 2.368]	5.3 [-2.5, 13.2]	0.160
Hemodiafiltration (HDF)	15	0 (0.0) [0.0, 21.8]	37	3 (8.1) [1.7, 21.9]	0.339 + [0.019, 6.197]	0.318 + [0.015, 6.536]	-8.1 [-21.6, 5.4]	0.548 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSH: TEAEs - significant SOC and PT by dialysis method
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
PT: Dizziness								
H: Dialysis method								0.382
Hemodialysis (HD)	220	13 (5.9) [3.2, 9.9]	199	9 (4.5) [2.1, 8.4]	1.307 [0.571, 2.990]	1.326 [0.554, 3.172]	1.4 [-3.3, 6.1]	0.526
Hemodiafiltration (HDF)	15	0 (0.0) [0.0, 21.8]	37	3 (8.1) [1.7, 21.9]	0.339 + [0.019, 6.197]	0.318 + [0.015, 6.536]	-8.1 [-21.6, 5.4]	0.548 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2A_SSSH: TEAEs - significant SOC and PT by dialysis method
SAF-S

	CR845		Placebo						
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
SOC: Skin and subcutaneous tissue disorders									
H: Dialysis method								0.763	
Hemodialysis (HD)	220	13 (5.9) [3.2, 9.9]	199	9 (4.5) [2.1, 8.4]	1.307 [0.571, 2.990]	1.326 [0.554, 3.172]	1.4 [-3.3, 6.1]	0.526	
Hemodiafiltration (HDF)	15	0 (0.0) [0.0, 21.8]	37	1 (2.7) [0.1, 14.2]	0.792 + [0.034, 18.416]	0.785 + [0.030, 20.352]	-2.7 [-12.6, 7.2]	1.000	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 17FEB2022

Table BT2AEG_SSIA: Incidence of AESI gait disturbance by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI gait disturbance	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
A: Age		n<10 for all subgroups						NE
< 65 years	146	4 (2.7) [0.8, 6.9]	153	1 (0.7) [0.0, 3.6]				
>= 65 years	89	4 (4.5) [1.2, 11.1]	83	1 (1.2) [0.0, 6.5]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEG_SSIB: Incidence of AESI gait disturbance by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI gait disturbance	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
B: Sex		n<10 for all subgroups						NE
Male	135	4 (3.0) [0.8, 7.4]	139	1 (0.7) [0.0, 3.9]				
Female	100	4 (4.0) [1.1, 9.9]	97	1 (1.0) [0.0, 5.6]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEG_SSIC: Incidence of AESI gait disturbance by race
SAF-S

	CR845		Placebo					
AESI gait disturbance	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
C: Race		n<10 for all subgroups						NE
Black/African American	53	3 (5.7) [1.2, 15.7]	38	0 (0.0) [0.0, 9.3]				
White	162	4 (2.5) [0.7, 6.2]	169	2 (1.2) [0.1, 4.2]				
Other	20	1 (5.0) [0.1, 24.9]	29	0 (0.0) [0.0, 11.9]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEG_SSID: Incidence of AESI gait disturbance by baseline WI-NRS
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI gait disturbance	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)		n<10 for all subgroups						NE
>= 4 to < 7	101	5 (5.0) [1.6, 11.2]	113	2 (1.8) [0.2, 6.2]				
>= 7	134	3 (2.2) [0.5, 6.4]	123	0 (0.0) [0.0, 3.0]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEG_SSIE: Incidence of AESI gait disturbance by specific medical condition
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI gait disturbance	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
E: Presence of specific medical conditions		n<10 for all subgroups						NE
No	194	6 (3.1) [1.1, 6.6]	199	2 (1.0) [0.1, 3.6]				
Yes	41	2 (4.9) [0.6, 16.5]	37	0 (0.0) [0.0, 9.5]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEG_SSIF: Incidence of AESI gait disturbance by use of concomitant itch medication
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI gait disturbance	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
F: Use of concomitant itch medication		n<10 for all subgroups						NE
No	148	5 (3.4) [1.1, 7.7]	151	1 (0.7) [0.0, 3.6]				
Yes	87	3 (3.4) [0.7, 9.7]	85	1 (1.2) [0.0, 6.4]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEG_SSIG: Incidence of AESI gait disturbance by region
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI gait disturbance	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
G: Region		n<10 for all subgroups						NE
USA	145	6 (4.1) [1.5, 8.8]	133	1 (0.8) [0.0, 4.1]				
Asia	8	0 (0.0) [0.0, 36.9]	12	0 (0.0) [0.0, 26.5]				
Eastern Europe	54	0 (0.0) [0.0, 6.6]	60	0 (0.0) [0.0, 6.0]				
Western Europe/European origin	28	2 (7.1) [0.9, 23.5]	31	1 (3.2) [0.1, 16.7]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEG_SSIH: Incidence of AESI gait disturbance by dialysis method
SAF-S

	CR845		Placebo					
AESI gait disturbance	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
H: Dialysis method								NE
Hemodialysis (HD)	220	8 (3.6) [1.6, 7.0]	199	2 (1.0) [0.1, 3.6]	3.618 [0.778, 16.837]	3.717 [0.780, 17.716]	2.6 [-0.7, 5.9]	0.110 #
Hemodiafiltration (HDF)	15	0 (0.0) [0.0, 21.8]	37	0 (0.0) [0.0, 9.5]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEGN_SSIA: Incidence of AESI gait disturbance - non-severe by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI gait disturbance - non-severe	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
A: Age		n<10 for all subgroups						NE
< 65 years	146	4 (2.7) [0.8, 6.9]	153	1 (0.7) [0.0, 3.6]				
>= 65 years	89	4 (4.5) [1.2, 11.1]	83	1 (1.2) [0.0, 6.5]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEGN_SSIB: Incidence of AESI gait disturbance - non-severe by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI gait disturbance - non-severe	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
B: Sex		n<10 for all subgroups						NE
Male	135	4 (3.0) [0.8, 7.4]	139	1 (0.7) [0.0, 3.9]				
Female	100	4 (4.0) [1.1, 9.9]	97	1 (1.0) [0.0, 5.6]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEGN_SSIC: Incidence of AESI gait disturbance - non-severe by race
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI gait disturbance - non-severe	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
C: Race		n<10 for all subgroups						NE
Black/African American	53	3 (5.7) [1.2, 15.7]	38	0 (0.0) [0.0, 9.3]				
White	162	4 (2.5) [0.7, 6.2]	169	2 (1.2) [0.1, 4.2]				
Other	20	1 (5.0) [0.1, 24.9]	29	0 (0.0) [0.0, 11.9]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEGN_SSID: Incidence of AESI gait disturbance - non-severe by baseline WI-NRS
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI gait disturbance - non-severe	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)		n<10 for all subgroups						NE
>= 4 to < 7	101	5 (5.0) [1.6, 11.2]	113	2 (1.8) [0.2, 6.2]				
>= 7	134	3 (2.2) [0.5, 6.4]	123	0 (0.0) [0.0, 3.0]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEGN_SSIE: Incidence of AESI gait disturbance - non-severe by specific medical condition
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI gait disturbance - non-severe	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
E: Presence of specific medical conditions		n<10 for all subgroups						NE
No	194	6 (3.1) [1.1, 6.6]	199	2 (1.0) [0.1, 3.6]				
Yes	41	2 (4.9) [0.6, 16.5]	37	0 (0.0) [0.0, 9.5]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEGN_SSIF: Incidence of AESI gait disturbance - non-severe by use of concomitant itch medication
SAF-S

	CR845		Placebo					
AESI gait disturbance - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
F: Use of concomitant itch medication		n<10 for all subgroups						NE
No	148	5 (3.4) [1.1, 7.7]	151	1 (0.7) [0.0, 3.6]				
Yes	87	3 (3.4) [0.7, 9.7]	85	1 (1.2) [0.0, 6.4]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEGN_SSIG: Incidence of AESI gait disturbance - non-severe by region
SAF-S

	CR845		Placebo					
AESI gait disturbance - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
G: Region		n<10 for all subgroups						NE
USA	145	6 (4.1) [1.5, 8.8]	133	1 (0.8) [0.0, 4.1]				
Asia	8	0 (0.0) [0.0, 36.9]	12	0 (0.0) [0.0, 26.5]				
Eastern Europe	54	0 (0.0) [0.0, 6.6]	60	0 (0.0) [0.0, 6.0]				
Western Europe/European origin	28	2 (7.1) [0.9, 23.5]	31	1 (3.2) [0.1, 16.7]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEGN_SSIH: Incidence of AESI gait disturbance - non-severe by dialysis method
SAF-S

	CR845		Placebo					
AESI gait disturbance - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
H: Dialysis method								NE
Hemodialysis (HD)	220	8 (3.6) [1.6, 7.0]	199	2 (1.0) [0.1, 3.6]	3.618 [0.778, 16.837]	3.717 [0.780, 17.716]	2.6 [-0.7, 5.9]	0.110 #
Hemodiafiltration (HDF)	15	0 (0.0) [0.0, 21.8]	37	0 (0.0) [0.0, 9.5]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEF_SSIA: Incidence of AESI falls/injuries by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI falls/injuries	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
A: Age								0.561
< 65 years	146	13 (8.9) [4.8, 14.7]	153	7 (4.6) [1.9, 9.2]	1.946 [0.799, 4.741]	2.039 [0.790, 5.263]	4.3 [-2.0, 10.7]	0.135
>= 65 years	89	10 (11.2) [5.5, 19.7]	83	7 (8.4) [3.5, 16.6]	1.332 [0.532, 3.338]	1.374 [0.498, 3.796]	2.8 [-7.2, 12.8]	0.540

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEF_SSIB: Incidence of AESI falls/injuries by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI falls/injuries	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
B: Sex								0.747
Male	135	14 (10.4) [5.8, 16.8]	139	8 (5.8) [2.5, 11.0]	1.802 [0.781, 4.156]	1.895 [0.768, 4.675]	4.6 [-2.6, 11.8]	0.161
Female	100	9 (9.0) [4.2, 16.4]	97	6 (6.2) [2.3, 13.0]	1.455 [0.538, 3.933]	1.500 [0.513, 4.387]	2.8 [-5.6, 11.2]	0.458

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEF_SSIC: Incidence of AESI falls/injuries by race
SAF-S

	CR845		Placebo						
AESI falls/injuries	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
C: Race								0.938	
Black/African American	53	5 (9.4) [3.1, 20.7]	38	2 (5.3) [0.6, 17.7]	1.792 [0.367, 8.755]	1.875 [0.344, 10.221]	4.2 [-8.7, 17.0]	0.695	#
White	162	15 (9.3) [5.3, 14.8]	169	10 (5.9) [2.9, 10.6]	1.565 [0.724, 3.382]	1.622 [0.707, 3.724]	3.3 [-3.0, 9.7]	0.251	
Other	20	3 (15.0) [3.2, 37.9]	29	2 (6.9) [0.8, 22.8]	2.175 [0.399, 11.859]	2.382 [0.360, 15.759]	8.1 [-14.3, 30.5]	0.387	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEF_SSID: Incidence of AESI falls/injuries by baseline WI-NRS
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI falls/injuries	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)								0.922
>= 4 to < 7	101	10 (9.9) [4.9, 17.5]	113	7 (6.2) [2.5, 12.3]	1.598 [0.632, 4.042]	1.664 [0.609, 4.549]	3.7 [-4.6, 12.0]	0.318
>= 7	134	13 (9.7) [5.3, 16.0]	123	7 (5.7) [2.3, 11.4]	1.705 [0.703, 4.133]	1.780 [0.686, 4.620]	4.0 [-3.2, 11.3]	0.231

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEF_SSIE: Incidence of AESI falls/injuries by specific medical condition
SAF-S

	CR845		Placebo					
AESI falls/injuries	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
E: Presence of specific medical conditions								0.956
No	194	16 (8.2) [4.8, 13.0]	199	10 (5.0) [2.4, 9.0]	1.641 [0.764, 3.527]	1.699 [0.751, 3.843]	3.2 [-2.2, 8.7]	0.199
Yes	41	7 (17.1) [7.2, 32.1]	37	4 (10.8) [3.0, 25.4]	1.579 [0.502, 4.964]	1.699 [0.454, 6.349]	6.3 [-11.6, 24.1]	0.430

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEF_SSIF: Incidence of AESI falls/injuries by use of concomitant itch medication
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI falls/injuries	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
F: Use of concomitant itch medication								0.311
No	148	15 (10.1) [5.8, 16.2]	151	7 (4.6) [1.9, 9.3]	2.186 [0.918, 5.208]	2.320 [0.918, 5.866]	5.5 [-1.1, 12.1]	0.069
Yes	87	8 (9.2) [4.1, 17.3]	85	7 (8.2) [3.4, 16.2]	1.117 [0.424, 2.944]	1.128 [0.390, 3.262]	1.0 [-8.6, 10.6]	0.824

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEF_SSIG: Incidence of AESI falls/injuries by region
SAF-S

	CR845		Placebo					
AESI falls/injuries	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
G: Region								0.582
USA	145	13 (9.0) [4.9, 14.8]	133	6 (4.5) [1.7, 9.6]	1.987 [0.778, 5.079]	2.085 [0.769, 5.653]	4.5 [-2.1, 11.0]	0.142
Asia	8	0 (0.0) [0.0, 36.9]	12	0 (0.0) [0.0, 26.5]				
Eastern Europe	54	3 (5.6) [1.2, 15.4]	60	4 (6.7) [1.8, 16.2]	0.833 [0.195, 3.557]	0.824 [0.176, 3.858]	-1.1 [-11.7, 9.4]	1.000 #
Western Europe/European origin	28	7 (25.0) [10.7, 44.9]	31	4 (12.9) [3.6, 29.8]	1.938 [0.634, 5.921]	2.250 [0.581, 8.717]	12.1 [-11.2, 35.4]	0.238

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEF_SSIH: Incidence of AESI falls/injuries by dialysis method
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI falls/injuries	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
H: Dialysis method								0.259
Hemodialysis (HD)	220	23 (10.5) [6.7, 15.3]	199	11 (5.5) [2.8, 9.7]	1.891 [0.946, 3.780]	1.995 [0.947, 4.206]	4.9 [-0.7, 10.5]	0.065
Hemodiafiltration (HDF)	15	0 (0.0) [0.0, 21.8]	37	3 (8.1) [1.7, 21.9]	0.339 + [0.019, 6.197]	0.318 + [0.015, 6.536]	-8.1 [-21.6, 5.4]	0.548 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEFN_SSIA: Incidence of AESI falls/injuries - non-severe by age
SAF-S

	CR845		Placebo					
AESI falls/injuries - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
A: Age								0.364
< 65 years	146	12 (8.2) [4.3, 13.9]	153	5 (3.3) [1.1, 7.5]	2.515 [0.908, 6.963]	2.651 [0.910, 7.721]	5.0 [-1.0, 10.9]	0.065
>= 65 years	89	10 (11.2) [5.5, 19.7]	83	7 (8.4) [3.5, 16.6]	1.332 [0.532, 3.338]	1.374 [0.498, 3.796]	2.8 [-7.2, 12.8]	0.540

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEFN_SSIB: Incidence of AESI falls/injuries - non-severe by sex
SAF-S

	CR845		Placebo					
AESI falls/injuries - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
B: Sex								0.920
Male	135	14 (10.4) [5.8, 16.8]	139	8 (5.8) [2.5, 11.0]	1.802 [0.781, 4.156]	1.895 [0.768, 4.675]	4.6 [-2.6, 11.8]	0.161
Female	100	8 (8.0) [3.5, 15.2]	97	4 (4.1) [1.1, 10.2]	1.940 [0.604, 6.234]	2.022 [0.588, 6.947]	3.9 [-3.8, 11.5]	0.257

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEFN_SSIC: Incidence of AESI falls/injuries - non-severe by race
SAF-S

	CR845		Placebo						
AESI falls/injuries - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
C: Race								0.792	
Black/African American	53	5 (9.4) [3.1, 20.7]	38	1 (2.6) [0.1, 13.8]	3.585 [0.436, 29.458]	3.854 [0.432, 34.418]	6.8 [-4.8, 18.4]	0.395	#
White	162	15 (9.3) [5.3, 14.8]	169	9 (5.3) [2.5, 9.9]	1.739 [0.783, 3.861]	1.814 [0.771, 4.271]	3.9 [-2.3, 10.1]	0.168	
Other	20	2 (10.0) [1.2, 31.7]	29	2 (6.9) [0.8, 22.8]	1.450 [0.222, 9.458]	1.500 [0.193, 11.637]	3.1 [-17.2, 23.4]	1.000	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEFN_SSID: Incidence of AESI falls/injuries - non-severe by baseline WI-NRS
SAF-S

	CR845		Placebo					
AESI falls/injuries - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)								0.647
>= 4 to < 7	101	10 (9.9) [4.9, 17.5]	113	7 (6.2) [2.5, 12.3]	1.598 [0.632, 4.042]	1.664 [0.609, 4.549]	3.7 [-4.6, 12.0]	0.318
>= 7	134	12 (9.0) [4.7, 15.1]	123	5 (4.1) [1.3, 9.2]	2.203 [0.799, 6.074]	2.321 [0.793, 6.791]	4.9 [-1.9, 11.6]	0.116

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEFN_SSIE: Incidence of AESI falls/injuries - non-severe by specific medical condition
SAF-S

	CR845		Placebo					
AESI falls/injuries - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
E: Presence of specific medical conditions								0.989
No	194	16 (8.2) [4.8, 13.0]	199	9 (4.5) [2.1, 8.4]	1.824 [0.826, 4.028]	1.898 [0.818, 4.404]	3.7 [-1.6, 9.1]	0.131
Yes	41	6 (14.6) [5.6, 29.2]	37	3 (8.1) [1.7, 21.9]	1.805 [0.486, 6.707]	1.943 [0.449, 8.400]	6.5 [-10.0, 23.0]	0.487 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEFN_SSIF: Incidence of AESI falls/injuries - non-severe by use of concomitant itch medication
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI falls/injuries - non-severe	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
F: Use of concomitant itch medication								0.258
No	148	15 (10.1) [5.8, 16.2]	151	6 (4.0) [1.5, 8.4]	2.551 [1.017, 6.395]	2.726 [1.027, 7.230]	6.2 [-0.3, 12.6]	0.037 *
Yes	87	7 (8.0) [3.3, 15.9]	85	6 (7.1) [2.6, 14.7]	1.140 [0.399, 3.253]	1.152 [0.371, 3.580]	1.0 [-8.1, 10.0]	0.807

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEFN_SSIG: Incidence of AESI falls/injuries - non-severe by region
SAF-S

	CR845		Placebo						
AESI falls/injuries - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
G: Region								0.384	
USA	145	13 (9.0) [4.9, 14.8]	133	4 (3.0) [0.8, 7.5]	2.981 [0.997, 8.917]	3.176 [1.009, 9.997]	6.0 [-0.2, 12.2]	0.039	*
Asia	8	0 (0.0) [0.0, 36.9]	12	0 (0.0) [0.0, 26.5]					
Eastern Europe	54	3 (5.6) [1.2, 15.4]	60	4 (6.7) [1.8, 16.2]	0.833 [0.195, 3.557]	0.824 [0.176, 3.858]	-1.1 [-11.7, 9.4]	1.000	#
Western Europe/European origin	28	6 (21.4) [8.3, 41.0]	31	4 (12.9) [3.6, 29.8]	1.661 [0.522, 5.284]	1.841 [0.461, 7.352]	8.5 [-14.1, 31.2]	0.494	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEFN_SSIH: Incidence of AESI falls/injuries - non-severe by dialysis method
SAF-S

	CR845		Placebo						
AESI falls/injuries - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
H: Dialysis method								0.221	
Hemodialysis (HD)	220	22 (10.0) [6.4, 14.7]	199	9 (4.5) [2.1, 8.4]	2.211 [1.043, 4.688]	2.346 [1.053, 5.224]	5.5 [0.1, 10.9]	0.033	*
Hemodiafiltration (HDF)	15	0 (0.0) [0.0, 21.8]	37	3 (8.1) [1.7, 21.9]	0.339 + [0.019, 6.197]	0.318 + [0.015, 6.536]	-8.1 [-21.6, 5.4]	0.548	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEV_SSIA: Incidence of AESI dizziness by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI dizziness	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
A: Age								0.882
< 65 years	146	5 (3.4) [1.1, 7.8]	153	5 (3.3) [1.1, 7.5]	1.048 [0.310, 3.545]	1.050 [0.297, 3.704]	0.2 [-4.6, 4.9]	1.000 #
>= 65 years	89	8 (9.0) [4.0, 16.9]	83	8 (9.6) [4.3, 18.1]	0.933 [0.367, 2.371]	0.926 [0.331, 2.591]	-0.6 [-10.5, 9.2]	0.884

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEV_SSIB: Incidence of AESI dizziness by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI dizziness	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
B: Sex								0.369
Male	135	9 (6.7) [3.1, 12.3]	139	7 (5.0) [2.0, 10.1]	1.324 [0.507, 3.454]	1.347 [0.487, 3.726]	1.6 [-4.7, 7.9]	0.566
Female	100	4 (4.0) [1.1, 9.9]	97	6 (6.2) [2.3, 13.0]	0.647 [0.188, 2.221]	0.632 [0.173, 2.312]	-2.2 [-9.3, 5.0]	0.533 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEV_SSIC: Incidence of AESI dizziness by race
SAF-S

	CR845		Placebo					
AESI dizziness	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
C: Race								0.467
Black/African American	53	6 (11.3) [4.3, 23.0]	38	2 (5.3) [0.6, 17.7]	2.151 [0.459, 10.085]	2.298 [0.438, 12.063]	6.1 [-7.3, 19.4]	0.461 #
White	162	5 (3.1) [1.0, 7.1]	169	8 (4.7) [2.1, 9.1]	0.652 [0.218, 1.952]	0.641 [0.205, 2.002]	-1.6 [-6.4, 3.1]	0.441
Other	20	2 (10.0) [1.2, 31.7]	29	3 (10.3) [2.2, 27.4]	0.967 [0.177, 5.271]	0.963 [0.146, 6.358]	-0.3 [-21.8, 21.1]	1.000 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEV_SSID: Incidence of AESI dizziness by baseline WI-NRS
SAF-S

	CR845		Placebo					
AESI dizziness	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)								0.504
>= 4 to < 7	101	5 (5.0) [1.6, 11.2]	113	4 (3.5) [1.0, 8.8]	1.399 [0.386, 5.066]	1.419 [0.370, 5.437]	1.4 [-5.0, 7.8]	0.738 #
>= 7	134	8 (6.0) [2.6, 11.4]	123	9 (7.3) [3.4, 13.4]	0.816 [0.325, 2.048]	0.804 [0.300, 2.155]	-1.3 [-8.2, 5.5]	0.665

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEV_SSIE: Incidence of AESI dizziness by specific medical condition
SAF-S

	CR845		Placebo					
AESI dizziness	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
E: Presence of specific medical conditions								0.543
No	194	10 (5.2) [2.5, 9.3]	199	9 (4.5) [2.1, 8.4]	1.140 [0.473, 2.744]	1.147 [0.456, 2.888]	0.6 [-4.1, 5.4]	0.771
Yes	41	3 (7.3) [1.5, 19.9]	37	4 (10.8) [3.0, 25.4]	0.677 [0.162, 2.827]	0.651 [0.136, 3.124]	-3.5 [-18.9, 11.9]	0.702 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEV_SSIF: Incidence of AESI dizziness by use of concomitant itch medication
SAF-S

	CR845		Placebo					
AESI dizziness	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
F: Use of concomitant itch medication								0.955
No	148	7 (4.7) [1.9, 9.5]	151	7 (4.6) [1.9, 9.3]	1.020 [0.367, 2.837]	1.021 [0.349, 2.987]	0.1 [-5.4, 5.6]	0.969
Yes	87	6 (6.9) [2.6, 14.4]	85	6 (7.1) [2.6, 14.7]	0.977 [0.328, 2.910]	0.975 [0.302, 3.153]	-0.2 [-8.9, 8.6]	0.967

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEV_SSIG: Incidence of AESI dizziness by region
SAF-S

	CR845		Placebo					
AESI dizziness	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
G: Region								0.526
USA	145	9 (6.2) [2.9, 11.5]	133	5 (3.8) [1.2, 8.6]	1.651 [0.568, 4.802]	1.694 [0.553, 5.190]	2.4 [-3.4, 8.3]	0.352
Asia	8	1 (12.5) [0.3, 52.7]	12	1 (8.3) [0.2, 38.5]	1.500 [0.109, 20.675]	1.571 [0.084, 29.409]	4.2 [-34.0, 42.3]	1.000 #
Eastern Europe	54	0 (0.0) [0.0, 6.6]	60	2 (3.3) [0.4, 11.5]	0.222 + [0.011, 4.520]	0.215 + [0.010, 4.573]	-3.3 [-9.6, 3.0]	0.497 #
Western Europe/European origin	28	3 (10.7) [2.3, 28.2]	31	5 (16.1) [5.5, 33.7]	0.664 [0.174, 2.529]	0.624 [0.135, 2.890]	-5.4 [-26.1, 15.3]	0.709 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEV_SSIH: Incidence of AESI dizziness by dialysis method
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI dizziness	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
H: Dialysis method								0.419
Hemodialysis (HD)	220	13 (5.9) [3.2, 9.9]	199	10 (5.0) [2.4, 9.0]	1.176 [0.527, 2.622]	1.187 [0.509, 2.771]	0.9 [-3.9, 5.7]	0.692
Hemodiafiltration (HDF)	15	0 (0.0) [0.0, 21.8]	37	3 (8.1) [1.7, 21.9]	0.339 + [0.019, 6.197]	0.318 + [0.015, 6.536]	-8.1 [-21.6, 5.4]	0.548 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEVN_SSIA: Incidence of AESI dizziness - non-severe by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI dizziness - non-severe	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
A: Age								0.896
< 65 years	146	4 (2.7) [0.8, 6.9]	153	5 (3.3) [1.1, 7.5]	0.838 [0.230, 3.061]	0.834 [0.219, 3.168]	-0.5 [-5.1, 4.0]	1.000 #
>= 65 years	89	8 (9.0) [4.0, 16.9]	83	8 (9.6) [4.3, 18.1]	0.933 [0.367, 2.371]	0.926 [0.331, 2.591]	-0.6 [-10.5, 9.2]	0.884

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEVN_SSIB: Incidence of AESI dizziness - non-severe by sex
SAF-S

	CR845		Placebo					
AESI dizziness - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
B: Sex								0.458
Male	135	8 (5.9) [2.6, 11.3]	139	7 (5.0) [2.0, 10.1]	1.177 [0.439, 3.155]	1.188 [0.419, 3.372]	0.9 [-5.2, 7.0]	0.747
Female	100	4 (4.0) [1.1, 9.9]	97	6 (6.2) [2.3, 13.0]	0.647 [0.188, 2.221]	0.632 [0.173, 2.312]	-2.2 [-9.3, 5.0]	0.533 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEVN_SSIC: Incidence of AESI dizziness - non-severe by race
SAF-S

	CR845		Placebo					
AESI dizziness - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
C: Race								0.588
Black/African American	53	5 (9.4) [3.1, 20.7]	38	2 (5.3) [0.6, 17.7]	1.792 [0.367, 8.755]	1.875 [0.344, 10.221]	4.2 [-8.7, 17.0]	0.695 #
White	162	5 (3.1) [1.0, 7.1]	169	8 (4.7) [2.1, 9.1]	0.652 [0.218, 1.952]	0.641 [0.205, 2.002]	-1.6 [-6.4, 3.1]	0.441
Other	20	2 (10.0) [1.2, 31.7]	29	3 (10.3) [2.2, 27.4]	0.967 [0.177, 5.271]	0.963 [0.146, 6.358]	-0.3 [-21.8, 21.1]	1.000 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEVN_SSID: Incidence of AESI dizziness - non-severe by baseline WI-NRS
SAF-S

	CR845		Placebo					
AESI dizziness - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)								0.411
>= 4 to < 7	101	5 (5.0) [1.6, 11.2]	113	4 (3.5) [1.0, 8.8]	1.399 [0.386, 5.066]	1.419 [0.370, 5.437]	1.4 [-5.0, 7.8]	0.738 #
>= 7	134	7 (5.2) [2.1, 10.5]	123	9 (7.3) [3.4, 13.4]	0.714 [0.274, 1.859]	0.698 [0.252, 1.935]	-2.1 [-8.8, 4.6]	0.489

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEVN_SSIE: Incidence of AESI dizziness - non-severe by specific medical condition
SAF-S

	CR845		Placebo					
AESI dizziness - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
E: Presence of specific medical conditions								0.630
No	194	9 (4.6) [2.1, 8.6]	199	9 (4.5) [2.1, 8.4]	1.026 [0.416, 2.529]	1.027 [0.399, 2.645]	0.1 [-4.5, 4.8]	0.956
Yes	41	3 (7.3) [1.5, 19.9]	37	4 (10.8) [3.0, 25.4]	0.677 [0.162, 2.827]	0.651 [0.136, 3.124]	-3.5 [-18.9, 11.9]	0.702 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEVN_SSIF: Incidence of AESI dizziness - non-severe by use of concomitant itch medication
SAF-S

	CR845		Placebo					
AESI dizziness - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
F: Use of concomitant itch medication								0.887
No	148	6 (4.1) [1.5, 8.6]	151	7 (4.6) [1.9, 9.3]	0.875 [0.301, 2.541]	0.869 [0.285, 2.650]	-0.6 [-5.9, 4.7]	0.806
Yes	87	6 (6.9) [2.6, 14.4]	85	6 (7.1) [2.6, 14.7]	0.977 [0.328, 2.910]	0.975 [0.302, 3.153]	-0.2 [-8.9, 8.6]	0.967

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEVN_SSIG: Incidence of AESI dizziness - non-severe by region
SAF-S

	CR845		Placebo						
AESI dizziness - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
G: Region								0.597	
USA	145	8 (5.5) [2.4, 10.6]	133	5 (3.8) [1.2, 8.6]	1.468 [0.492, 4.375]	1.495 [0.477, 4.688]	1.8 [-3.9, 7.4]	0.489	
Asia	8	1 (12.5) [0.3, 52.7]	12	1 (8.3) [0.2, 38.5]	1.500 [0.109, 20.675]	1.571 [0.084, 29.409]	4.2 [-34.0, 42.3]	1.000	#
Eastern Europe	54	0 (0.0) [0.0, 6.6]	60	2 (3.3) [0.4, 11.5]	0.222 + [0.011, 4.520]	0.215 + [0.010, 4.573]	-3.3 [-9.6, 3.0]	0.497	#
Western Europe/European origin	28	3 (10.7) [2.3, 28.2]	31	5 (16.1) [5.5, 33.7]	0.664 [0.174, 2.529]	0.624 [0.135, 2.890]	-5.4 [-26.1, 15.3]	0.709	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEVN_SSIH: Incidence of AESI dizziness - non-severe by dialysis method
SAF-S

	CR845		Placebo					
AESI dizziness - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
H: Dialysis method								0.450
Hemodialysis (HD)	220	12 (5.5) [2.8, 9.3]	199	10 (5.0) [2.4, 9.0]	1.085 [0.480, 2.457]	1.090 [0.460, 2.582]	0.4 [-4.3, 5.2]	0.844
Hemodiafiltration (HDF)	15	0 (0.0) [0.0, 21.8]	37	3 (8.1) [1.7, 21.9]	0.339 + [0.019, 6.197]	0.318 + [0.015, 6.536]	-8.1 [-21.6, 5.4]	0.548 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEO_SSIA: Incidence of AESI somnolence by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI somnolence	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
A: Age								0.874
< 65 years	146	4 (2.7) [0.8, 6.9]	153	2 (1.3) [0.2, 4.6]	2.096 [0.390, 11.270]	2.127 [0.384, 11.791]	1.4 [-2.4, 5.3]	0.439 #
>= 65 years	89	8 (9.0) [4.0, 16.9]	83	3 (3.6) [0.8, 10.2]	2.487 [0.683, 9.059]	2.634 [0.674, 10.286]	5.4 [-3.0, 13.7]	0.151

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEO_SSIB: Incidence of AESI somnolence by sex
SAF-S

	CR845		Placebo					
AESI somnolence	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
B: Sex		n<10 for all subgroups						NE
Male	135	7 (5.2) [2.1, 10.4]	139	2 (1.4) [0.2, 5.1]				
Female	100	5 (5.0) [1.6, 11.3]	97	3 (3.1) [0.6, 8.8]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEO_SSIC: Incidence of AESI somnolence by race
SAF-S

	CR845		Placebo					
AESI somnolence	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
C: Race		n<10 for all subgroups						NE
Black/African American	53	2 (3.8) [0.5, 13.0]	38	3 (7.9) [1.7, 21.4]				
White	162	7 (4.3) [1.8, 8.7]	169	1 (0.6) [0.0, 3.3]				
Other	20	3 (15.0) [3.2, 37.9]	29	1 (3.4) [0.1, 17.8]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEO_SSID: Incidence of AESI somnolence by baseline WI-NRS
SAF-S

	CR845		Placebo					
AESI somnolence	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)								0.102
>= 4 to < 7	101	6 (5.9) [2.2, 12.5]	113	0 (0.0) [0.0, 3.2]	14.529 + [0.829, 254.725]	15.450 + [0.859, 277.803]	5.9 [0.4, 11.5]	0.010 *
>= 7	134	6 (4.5) [1.7, 9.5]	123	5 (4.1) [1.3, 9.2]	1.101 [0.345, 3.518]	1.106 [0.329, 3.721]	0.4 [-5.3, 6.1]	0.871

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEO_SSIE: Incidence of AESI somnolence by specific medical condition
SAF-S

	CR845		Placebo						
AESI somnolence	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
E: Presence of specific medical conditions								0.255	
No	194	10 (5.2) [2.5, 9.3]	199	3 (1.5) [0.3, 4.3]	3.419 [0.955, 12.236]	3.551 [0.962, 13.104]	3.6 [-0.4, 7.7]	0.044	*
Yes	41	2 (4.9) [0.6, 16.5]	37	2 (5.4) [0.7, 18.2]	0.902 [0.134, 6.088]	0.897 [0.120, 6.714]	-0.5 [-12.9, 11.9]	1.000	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEO_SSIF: Incidence of AESI somnolence by use of concomitant itch medication
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI somnolence	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
F: Use of concomitant itch medication								0.280
No	148	6 (4.1) [1.5, 8.6]	151	4 (2.6) [0.7, 6.6]	1.530 [0.441, 5.313]	1.553 [0.429, 5.619]	1.4 [-3.3, 6.2]	0.538 #
Yes	87	6 (6.9) [2.6, 14.4]	85	1 (1.2) [0.0, 6.4]	5.862 [0.721, 47.670]	6.222 [0.733, 52.827]	5.7 [-1.2, 12.7]	0.118 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEO_SSIG: Incidence of AESI somnolence by region
SAF-S

	CR845		Placebo					
AESI somnolence	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
G: Region								0.690
USA	145	7 (4.8) [2.0, 9.7]	133	3 (2.3) [0.5, 6.5]	2.140 [0.565, 8.107]	2.198 [0.557, 8.681]	2.6 [-2.5, 7.6]	0.339 #
Asia	8	2 (25.0) [3.2, 65.1]	12	0 (0.0) [0.0, 26.5]	7.222 + [0.391, 133.240]	9.615 + [0.400, 231.416]	25.0 [-15.4, 65.4]	0.147 #
Eastern Europe	54	0 (0.0) [0.0, 6.6]	60	0 (0.0) [0.0, 6.0]				
Western Europe/European origin	28	3 (10.7) [2.3, 28.2]	31	2 (6.5) [0.8, 21.4]	1.661 [0.299, 9.225]	1.740 [0.269, 11.261]	4.3 [-13.5, 22.0]	0.661 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEO_SSIH: Incidence of AESI somnolence by dialysis method
SAF-S

	CR845		Placebo					
AESI somnolence	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
H: Dialysis method								NE
Hemodialysis (HD)	220	12 (5.5) [2.8, 9.3]	199	5 (2.5) [0.8, 5.8]	2.171 [0.779, 6.054]	2.238 [0.774, 6.470]	2.9 [-1.2, 7.1]	0.128
Hemodiafiltration (HDF)	15	0 (0.0) [0.0, 21.8]	37	0 (0.0) [0.0, 9.5]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEON_SSIA: Incidence of AESI somnolence - non-severe by age
SAF-S

	CR845		Placebo					
AESI somnolence - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
A: Age								0.874
< 65 years	146	4 (2.7) [0.8, 6.9]	153	2 (1.3) [0.2, 4.6]	2.096 [0.390, 11.270]	2.127 [0.384, 11.791]	1.4 [-2.4, 5.3]	0.439 #
>= 65 years	89	8 (9.0) [4.0, 16.9]	83	3 (3.6) [0.8, 10.2]	2.487 [0.683, 9.059]	2.634 [0.674, 10.286]	5.4 [-3.0, 13.7]	0.151

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEON_SSIB: Incidence of AESI somnolence - non-severe by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI somnolence - non-severe	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
B: Sex		n<10 for all subgroups						NE
Male	135	7 (5.2) [2.1, 10.4]	139	2 (1.4) [0.2, 5.1]				
Female	100	5 (5.0) [1.6, 11.3]	97	3 (3.1) [0.6, 8.8]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEON_SSIC: Incidence of AESI somnolence - non-severe by race
SAF-S

	CR845		Placebo					
AESI somnolence - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
C: Race		n<10 for all subgroups						NE
Black/African American	53	2 (3.8) [0.5, 13.0]	38	3 (7.9) [1.7, 21.4]				
White	162	7 (4.3) [1.8, 8.7]	169	1 (0.6) [0.0, 3.3]				
Other	20	3 (15.0) [3.2, 37.9]	29	1 (3.4) [0.1, 17.8]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEON_SSID: Incidence of AESI somnolence - non-severe by baseline WI-NRS
SAF-S

	CR845		Placebo					
AESI somnolence - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)								0.102
>= 4 to < 7	101	6 (5.9) [2.2, 12.5]	113	0 (0.0) [0.0, 3.2]	14.529 + [0.829, 254.725]	15.450 + [0.859, 277.803]	5.9 [0.4, 11.5]	0.010 *
>= 7	134	6 (4.5) [1.7, 9.5]	123	5 (4.1) [1.3, 9.2]	1.101 [0.345, 3.518]	1.106 [0.329, 3.721]	0.4 [-5.3, 6.1]	0.871

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEON_SSIE: Incidence of AESI somnolence - non-severe by specific medical condition
SAF-S

	CR845		Placebo						
AESI somnolence - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
E: Presence of specific medical conditions								0.255	
No	194	10 (5.2) [2.5, 9.3]	199	3 (1.5) [0.3, 4.3]	3.419 [0.955, 12.236]	3.551 [0.962, 13.104]	3.6 [-0.4, 7.7]	0.044	*
Yes	41	2 (4.9) [0.6, 16.5]	37	2 (5.4) [0.7, 18.2]	0.902 [0.134, 6.088]	0.897 [0.120, 6.714]	-0.5 [-12.9, 11.9]	1.000	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEON_SSIF: Incidence of AESI somnolence - non-severe by use of concomitant itch medication
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI somnolence - non-severe	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
F: Use of concomitant itch medication								0.280
No	148	6 (4.1) [1.5, 8.6]	151	4 (2.6) [0.7, 6.6]	1.530 [0.441, 5.313]	1.553 [0.429, 5.619]	1.4 [-3.3, 6.2]	0.538 #
Yes	87	6 (6.9) [2.6, 14.4]	85	1 (1.2) [0.0, 6.4]	5.862 [0.721, 47.670]	6.222 [0.733, 52.827]	5.7 [-1.2, 12.7]	0.118 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEON_SSIG: Incidence of AESI somnolence - non-severe by region
SAF-S

	CR845		Placebo					
AESI somnolence - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
G: Region								0.690
USA	145	7 (4.8) [2.0, 9.7]	133	3 (2.3) [0.5, 6.5]	2.140 [0.565, 8.107]	2.198 [0.557, 8.681]	2.6 [-2.5, 7.6]	0.339 #
Asia	8	2 (25.0) [3.2, 65.1]	12	0 (0.0) [0.0, 26.5]	7.222 + [0.391, 133.240]	9.615 + [0.400, 231.416]	25.0 [-15.4, 65.4]	0.147 #
Eastern Europe	54	0 (0.0) [0.0, 6.6]	60	0 (0.0) [0.0, 6.0]				
Western Europe/European origin	28	3 (10.7) [2.3, 28.2]	31	2 (6.5) [0.8, 21.4]	1.661 [0.299, 9.225]	1.740 [0.269, 11.261]	4.3 [-13.5, 22.0]	0.661 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEON_SSIH: Incidence of AESI somnolence - non-severe by dialysis method
SAF-S

	CR845		Placebo					
AESI somnolence - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
H: Dialysis method								NE
Hemodialysis (HD)	220	12 (5.5) [2.8, 9.3]	199	5 (2.5) [0.8, 5.8]	2.171 [0.779, 6.054]	2.238 [0.774, 6.470]	2.9 [-1.2, 7.1]	0.128
Hemodiafiltration (HDF)	15	0 (0.0) [0.0, 21.8]	37	0 (0.0) [0.0, 9.5]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEM_SSIA: Incidence of AESI mental status change by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI mental status change	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
A: Age		n<10 for all subgroups						NE
< 65 years	146	4 (2.7) [0.8, 6.9]	153	2 (1.3) [0.2, 4.6]				
>= 65 years	89	6 (6.7) [2.5, 14.1]	83	3 (3.6) [0.8, 10.2]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEM_SSIB: Incidence of AESI mental status change by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI mental status change	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
B: Sex								0.383
Male	135	8 (5.9) [2.6, 11.3]	139	3 (2.2) [0.4, 6.2]	2.746 [0.744, 10.131]	2.856 [0.741, 11.002]	3.8 [-1.6, 9.2]	0.113
Female	100	2 (2.0) [0.2, 7.0]	97	2 (2.1) [0.3, 7.3]	0.970 [0.139, 6.750]	0.969 [0.134, 7.022]	-0.1 [-5.0, 4.9]	1.000 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEM_SSIC: Incidence of AESI mental status change by race
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI mental status change	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
C: Race		n<10 for all subgroups						NE
Black/African American	53	4 (7.5) [2.1, 18.2]	38	2 (5.3) [0.6, 17.7]				
White	162	4 (2.5) [0.7, 6.2]	169	2 (1.2) [0.1, 4.2]				
Other	20	2 (10.0) [1.2, 31.7]	29	1 (3.4) [0.1, 17.8]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEM_SSID: Incidence of AESI mental status change by baseline WI-NRS
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI mental status change	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)		n<10 for all subgroups						NE
>= 4 to < 7	101	5 (5.0) [1.6, 11.2]	113	4 (3.5) [1.0, 8.8]				
>= 7	134	5 (3.7) [1.2, 8.5]	123	1 (0.8) [0.0, 4.4]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEM_SSIE: Incidence of AESI mental status change by specific medical condition
SAF-S

	CR845		Placebo						
AESI mental status change	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
E: Presence of specific medical conditions								0.235	
No	194	6 (3.1) [1.1, 6.6]	199	5 (2.5) [0.8, 5.8]	1.231 [0.382, 3.967]	1.238 [0.372, 4.126]	0.6 [-3.2, 4.4]	0.728	
Yes	41	4 (9.8) [2.7, 23.1]	37	0 (0.0) [0.0, 9.5]	8.143 + [0.453, 146.312]	9.000 + [0.468, 173.091]	9.8 [-1.9, 21.4]	0.117	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEM_SSIF: Incidence of AESI mental status change by use of concomitant itch medication
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI mental status change	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
F: Use of concomitant itch medication		n<10 for all subgroups						NE
No	148	7 (4.7) [1.9, 9.5]	151	2 (1.3) [0.2, 4.7]				
Yes	87	3 (3.4) [0.7, 9.7]	85	3 (3.5) [0.7, 10.0]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEM_SSIG: Incidence of AESI mental status change by region
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI mental status change	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
G: Region		n<10 for all subgroups						NE
USA	145	6 (4.1) [1.5, 8.8]	133	3 (2.3) [0.5, 6.5]				
Asia	8	0 (0.0) [0.0, 36.9]	12	1 (8.3) [0.2, 38.5]				
Eastern Europe	54	0 (0.0) [0.0, 6.6]	60	0 (0.0) [0.0, 6.0]				
Western Europe/European origin	28	4 (14.3) [4.0, 32.7]	31	1 (3.2) [0.1, 16.7]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEM_SSIH: Incidence of AESI mental status change by dialysis method
SAF-S

	CR845		Placebo					
AESI mental status change	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
H: Dialysis method								0.898
Hemodialysis (HD)	220	9 (4.1) [1.9, 7.6]	199	4 (2.0) [0.6, 5.1]	2.035 [0.637, 6.506]	2.079 [0.630, 6.861]	2.1 [-1.7, 5.8]	0.220
Hemodiafiltration (HDF)	15	1 (6.7) [0.2, 31.9]	37	1 (2.7) [0.1, 14.2]	2.467 [0.165, 36.928]	2.571 [0.150, 44.000]	4.0 [-14.4, 22.3]	0.498 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEMN_SSIA: Incidence of AESI mental status change - non-severe by age
SAF-S

AESI mental status change - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
A: Age		n<10 for all subgroups						NE
< 65 years	146	3 (2.1) [0.4, 5.9]	153	2 (1.3) [0.2, 4.6]				
>= 65 years	89	5 (5.6) [1.8, 12.6]	83	3 (3.6) [0.8, 10.2]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEMN_SSIB: Incidence of AESI mental status change - non-severe by sex
SAF-S

AESI mental status change - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
B: Sex		n<10 for all subgroups						NE
Male	135	6 (4.4) [1.6, 9.4]	139	3 (2.2) [0.4, 6.2]				
Female	100	2 (2.0) [0.2, 7.0]	97	2 (2.1) [0.3, 7.3]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEMN_SSIC: Incidence of AESI mental status change - non-severe by race
SAF-S

AESI mental status change - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
C: Race		n<10 for all subgroups						NE
Black/African American	53	2 (3.8) [0.5, 13.0]	38	2 (5.3) [0.6, 17.7]				
White	162	4 (2.5) [0.7, 6.2]	169	2 (1.2) [0.1, 4.2]				
Other	20	2 (10.0) [1.2, 31.7]	29	1 (3.4) [0.1, 17.8]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEMN_SSID: Incidence of AESI mental status change - non-severe by baseline WI-NRS
SAF-S

AESI mental status change - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)		n<10 for all subgroups						NE
>= 4 to < 7	101	4 (4.0) [1.1, 9.8]	113	4 (3.5) [1.0, 8.8]				
>= 7	134	4 (3.0) [0.8, 7.5]	123	1 (0.8) [0.0, 4.4]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEMN_SSIE: Incidence of AESI mental status change - non-severe by specific medical condition
SAF-S

AESI mental status change - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
E: Presence of specific medical conditions								0.261	
No	194	5 (2.6) [0.8, 5.9]	199	5 (2.5) [0.8, 5.8]	1.026 [0.302, 3.487]	1.026 [0.292, 3.603]	0.1 [-3.6, 3.7]	1.000	#
Yes	41	3 (7.3) [1.5, 19.9]	37	0 (0.0) [0.0, 9.5]	6.333 + [0.338, 118.670]	6.818 + [0.340, 136.552]	7.3 [-3.2, 17.9]	0.242	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEMN_SSIF: Incidence of AESI mental status change - non-severe by use of concomitant itch medication
SAF-S

AESI mental status change - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
F: Use of concomitant itch medication		n<10 for all subgroups						NE
No	148	6 (4.1) [1.5, 8.6]	151	2 (1.3) [0.2, 4.7]				
Yes	87	2 (2.3) [0.3, 8.1]	85	3 (3.5) [0.7, 10.0]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEMN_SSIG: Incidence of AESI mental status change - non-severe by region
SAF-S

AESI mental status change - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
G: Region		n<10 for all subgroups						NE
USA	145	4 (2.8) [0.8, 6.9]	133	3 (2.3) [0.5, 6.5]				
Asia	8	0 (0.0) [0.0, 36.9]	12	1 (8.3) [0.2, 38.5]				
Eastern Europe	54	0 (0.0) [0.0, 6.6]	60	0 (0.0) [0.0, 6.0]				
Western Europe/European origin	28	4 (14.3) [4.0, 32.7]	31	1 (3.2) [0.1, 16.7]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEMN_SSIH: Incidence of AESI mental status change - non-severe by dialysis method
SAF-S

AESI mental status change - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
H: Dialysis method								0.769	
Hemodialysis (HD)	220	7 (3.2) [1.3, 6.4]	199	4 (2.0) [0.6, 5.1]	1.583 [0.470, 5.327]	1.602 [0.462, 5.557]	1.2 [-2.3, 4.7]	0.454	
Hemodiafiltration (HDF)	15	1 (6.7) [0.2, 31.9]	37	1 (2.7) [0.1, 14.2]	2.467 [0.165, 36.928]	2.571 [0.150, 44.000]	4.0 [-14.4, 22.3]	0.498	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEU_SSIA: Incidence of AESI unusual feeling/sensation by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI unusual feeling/sensation	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
A: Age		n<10 for all subgroups						NE
< 65 years	146	7 (4.8) [1.9, 9.6]	153	2 (1.3) [0.2, 4.6]				
>= 65 years	89	4 (4.5) [1.2, 11.1]	83	4 (4.8) [1.3, 11.9]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEU_SSIB: Incidence of AESI unusual feeling/sensation by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI unusual feeling/sensation	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
B: Sex		n<10 for all subgroups						NE
Male	135	6 (4.4) [1.6, 9.4]	139	3 (2.2) [0.4, 6.2]				
Female	100	5 (5.0) [1.6, 11.3]	97	3 (3.1) [0.6, 8.8]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEU_SSIC: Incidence of AESI unusual feeling/sensation by race
SAF-S

	CR845		Placebo					
AESI unusual feeling/sensation	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
C: Race								0.650
Black/African American	53	4 (7.5) [2.1, 18.2]	38	1 (2.6) [0.1, 13.8]	2.868 [0.334, 24.654]	3.020 [0.324, 28.160]	4.9 [-6.1, 15.9]	0.396 #
White	162	7 (4.3) [1.8, 8.7]	169	4 (2.4) [0.6, 5.9]	1.826 [0.545, 6.119]	1.863 [0.535, 6.488]	2.0 [-2.5, 6.4]	0.322
Other	20	0 (0.0) [0.0, 16.8]	29	1 (3.4) [0.1, 17.8]	0.476 + [0.020, 11.131]	0.463 + [0.018, 11.958]	-3.4 [-14.3, 7.4]	1.000 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEU_SSID: Incidence of AESI unusual feeling/sensation by baseline WI-NRS
SAF-S

	CR845		Placebo					
AESI unusual feeling/sensation	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)								0.721
>= 4 to < 7	101	4 (4.0) [1.1, 9.8]	113	3 (2.7) [0.6, 7.6]	1.492 [0.342, 6.505]	1.512 [0.330, 6.925]	1.3 [-4.5, 7.1]	0.709 #
>= 7	134	7 (5.2) [2.1, 10.5]	123	3 (2.4) [0.5, 7.0]	2.142 [0.566, 8.100]	2.205 [0.557, 8.723]	2.8 [-2.6, 8.2]	0.339 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEU_SSIE: Incidence of AESI unusual feeling/sensation by specific medical condition
SAF-S

	CR845		Placebo					
AESI unusual feeling/sensation	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
E: Presence of specific medical conditions								0.996
No	194	7 (3.6) [1.5, 7.3]	199	4 (2.0) [0.6, 5.1]	1.795 [0.534, 6.035]	1.825 [0.526, 6.336]	1.6 [-2.2, 5.4]	0.337
Yes	41	4 (9.8) [2.7, 23.1]	37	2 (5.4) [0.7, 18.2]	1.805 [0.351, 9.287]	1.892 [0.326, 10.987]	4.4 [-9.9, 18.6]	0.678 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEU_SSIF: Incidence of AESI unusual feeling/sensation by use of concomitant itch medication
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI unusual feeling/sensation	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
F: Use of concomitant itch medication								0.932
No	148	7 (4.7) [1.9, 9.5]	151	4 (2.6) [0.7, 6.6]	1.785 [0.534, 5.972]	1.824 [0.523, 6.368]	2.1 [-2.9, 7.0]	0.340
Yes	87	4 (4.6) [1.3, 11.4]	85	2 (2.4) [0.3, 8.2]	1.954 [0.368, 10.389]	2.000 [0.357, 11.219]	2.2 [-4.4, 8.9]	0.682 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEU_SSIG: Incidence of AESI unusual feeling/sensation by region
SAF-S

	CR845		Placebo						
AESI unusual feeling/sensation	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
G: Region								0.201	
USA	145	7 (4.8) [2.0, 9.7]	133	4 (3.0) [0.8, 7.5]	1.605 [0.481, 5.360]	1.636 [0.468, 5.719]	1.8 [-3.4, 7.1]	0.438	
Asia	8	0 (0.0) [0.0, 36.9]	12	0 (0.0) [0.0, 26.5]					
Eastern Europe	54	4 (7.4) [2.1, 17.9]	60	0 (0.0) [0.0, 6.0]	9.982 + [0.550, 181.216]	10.782 + [0.567, 205.085]	7.4 [-1.3, 16.2]	0.047	*
Western Europe/European origin	28	0 (0.0) [0.0, 12.3]	31	2 (6.5) [0.8, 21.4]	0.221 + [0.011, 4.408]	0.207 + [0.010, 4.503]	-6.5 [-18.5, 5.6]	0.493	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEU_SSIH: Incidence of AESI unusual feeling/sensation by dialysis method
SAF-S

	CR845		Placebo					
AESI unusual feeling/sensation	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
H: Dialysis method								NE
Hemodialysis (HD)	220	11 (5.0) [2.5, 8.8]	199	6 (3.0) [1.1, 6.4]	1.658 [0.625, 4.401]	1.693 [0.614, 4.666]	2.0 [-2.2, 6.2]	0.304
Hemodiafiltration (HDF)	15	0 (0.0) [0.0, 21.8]	37	0 (0.0) [0.0, 9.5]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEUN_SSIA: Incidence of AESI unusual feeling/sensation - non-severe by age
SAF-S

AESI unusual feeling/sensation - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
A: Age		n<10 for all subgroups						NE
< 65 years	146	6 (4.1) [1.5, 8.7]	153	2 (1.3) [0.2, 4.6]				
>= 65 years	89	4 (4.5) [1.2, 11.1]	83	4 (4.8) [1.3, 11.9]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEUN_SSIB: Incidence of AESI unusual feeling/sensation - non-severe by sex
SAF-S

AESI unusual feeling/sensation - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
B: Sex		n<10 for all subgroups						NE
Male	135	5 (3.7) [1.2, 8.4]	139	3 (2.2) [0.4, 6.2]				
Female	100	5 (5.0) [1.6, 11.3]	97	3 (3.1) [0.6, 8.8]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEUN_SSIC: Incidence of AESI unusual feeling/sensation - non-severe by race
SAF-S

AESI unusual feeling/sensation - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
C: Race								0.712	
Black/African American	53	3 (5.7) [1.2, 15.7]	38	1 (2.6) [0.1, 13.8]	2.151 [0.233, 19.894]	2.220 [0.222, 22.203]	3.0 [-7.3, 13.3]	0.638	#
White	162	7 (4.3) [1.8, 8.7]	169	4 (2.4) [0.6, 5.9]	1.826 [0.545, 6.119]	1.863 [0.535, 6.488]	2.0 [-2.5, 6.4]	0.322	
Other	20	0 (0.0) [0.0, 16.8]	29	1 (3.4) [0.1, 17.8]	0.476 + [0.020, 11.131]	0.463 + [0.018, 11.958]	-3.4 [-14.3, 7.4]	1.000	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEUN_SSID: Incidence of AESI unusual feeling/sensation - non-severe by baseline WI-NRS
SAF-S

AESI unusual feeling/sensation - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)		n<10 for all subgroups						NE
>= 4 to < 7	101	4 (4.0) [1.1, 9.8]	113	3 (2.7) [0.6, 7.6]				
>= 7	134	6 (4.5) [1.7, 9.5]	123	3 (2.4) [0.5, 7.0]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEUN_SSIE: Incidence of AESI unusual feeling/sensation - non-severe by specific medical condition
SAF-S

AESI unusual feeling/sensation - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
E: Presence of specific medical conditions								0.879	
No	194	6 (3.1) [1.1, 6.6]	199	4 (2.0) [0.6, 5.1]	1.539 [0.441, 5.368]	1.556 [0.432, 5.601]	1.1 [-2.5, 4.7]	0.539	#
Yes	41	4 (9.8) [2.7, 23.1]	37	2 (5.4) [0.7, 18.2]	1.805 [0.351, 9.287]	1.892 [0.326, 10.987]	4.4 [-9.9, 18.6]	0.678	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEUN_SSIF: Incidence of AESI unusual feeling/sensation - non-severe by use of concomitant itch medication
SAF-S

AESI unusual feeling/sensation - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
F: Use of concomitant itch medication								0.818	
No	148	6 (4.1) [1.5, 8.6]	151	4 (2.6) [0.7, 6.6]	1.530 [0.441, 5.313]	1.553 [0.429, 5.619]	1.4 [-3.3, 6.2]	0.538	#
Yes	87	4 (4.6) [1.3, 11.4]	85	2 (2.4) [0.3, 8.2]	1.954 [0.368, 10.389]	2.000 [0.357, 11.219]	2.2 [-4.4, 8.9]	0.682	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEUN_SSIG: Incidence of AESI unusual feeling/sensation - non-severe by region
SAF-S

	CR845		Placebo						
AESI unusual feeling/sensation - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
G: Region								0.199	
USA	145	6 (4.1) [1.5, 8.8]	133	4 (3.0) [0.8, 7.5]	1.376 [0.397, 4.769]	1.392 [0.384, 5.045]	1.1 [-3.9, 6.2]	0.752	#
Asia	8	0 (0.0) [0.0, 36.9]	12	0 (0.0) [0.0, 26.5]					
Eastern Europe	54	4 (7.4) [2.1, 17.9]	60	0 (0.0) [0.0, 6.0]	9.982 + [0.550, 181.216]	10.782 + [0.567, 205.085]	7.4 [-1.3, 16.2]	0.047	*
Western Europe/European origin	28	0 (0.0) [0.0, 12.3]	31	2 (6.5) [0.8, 21.4]	0.221 + [0.011, 4.408]	0.207 + [0.010, 4.503]	-6.5 [-18.5, 5.6]	0.493	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AEUN_SSIH: Incidence of AESI unusual feeling/sensation - non-severe by dialysis method
SAF-S

	CR845		Placebo					
AESI unusual feeling/sensation - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
H: Dialysis method								NE
Hemodialysis (HD)	220	10 (4.5) [2.2, 8.2]	199	6 (3.0) [1.1, 6.4]	1.508 [0.558, 4.073]	1.532 [0.546, 4.294]	1.5 [-2.6, 5.6]	0.415
Hemodiafiltration (HDF)	15	0 (0.0) [0.0, 21.8]	37	0 (0.0) [0.0, 9.5]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AER_SSIA: Incidence of AESI tachycardia/palpitation by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI tachycardia/palpitation	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
A: Age		n<10 for all subgroups						NE
< 65 years	146	3 (2.1) [0.4, 5.9]	153	5 (3.3) [1.1, 7.5]				
>= 65 years	89	2 (2.2) [0.3, 7.9]	83	2 (2.4) [0.3, 8.4]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AER_SSIB: Incidence of AESI tachycardia/palpitation by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI tachycardia/palpitation	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
B: Sex		n<10 for all subgroups						NE
Male	135	3 (2.2) [0.5, 6.4]	139	3 (2.2) [0.4, 6.2]				
Female	100	2 (2.0) [0.2, 7.0]	97	4 (4.1) [1.1, 10.2]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AER_SSIC: Incidence of AESI tachycardia/palpitation by race
SAF-S

	CR845		Placebo					
AESI tachycardia/palpitation	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
C: Race		n<10 for all subgroups						NE
Black/African American	53	1 (1.9) [0.0, 10.1]	38	1 (2.6) [0.1, 13.8]				
White	162	4 (2.5) [0.7, 6.2]	169	4 (2.4) [0.6, 5.9]				
Other	20	0 (0.0) [0.0, 16.8]	29	2 (6.9) [0.8, 22.8]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AER_SSID: Incidence of AESI tachycardia/palpitation by baseline WI-NRS
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI tachycardia/palpitation	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)		n<10 for all subgroups						NE
>= 4 to < 7	101	3 (3.0) [0.6, 8.4]	113	3 (2.7) [0.6, 7.6]				
>= 7	134	2 (1.5) [0.2, 5.3]	123	4 (3.3) [0.9, 8.1]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AER_SSIE: Incidence of AESI tachycardia/palpitation by specific medical condition
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI tachycardia/palpitation	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
E: Presence of specific medical conditions		n<10 for all subgroups						NE
No	194	4 (2.1) [0.6, 5.2]	199	5 (2.5) [0.8, 5.8]				
Yes	41	1 (2.4) [0.1, 12.9]	37	2 (5.4) [0.7, 18.2]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AER_SSIF: Incidence of AESI tachycardia/palpitation by use of concomitant itch medication
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI tachycardia/palpitation	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
F: Use of concomitant itch medication		n<10 for all subgroups						NE
No	148	2 (1.4) [0.2, 4.8]	151	3 (2.0) [0.4, 5.7]				
Yes	87	3 (3.4) [0.7, 9.7]	85	4 (4.7) [1.3, 11.6]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AER_SSIG: Incidence of AESI tachycardia/palpitation by region
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI tachycardia/palpitation	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
G: Region		n<10 for all subgroups						NE
USA	145	4 (2.8) [0.8, 6.9]	133	3 (2.3) [0.5, 6.5]				
Asia	8	0 (0.0) [0.0, 36.9]	12	0 (0.0) [0.0, 26.5]				
Eastern Europe	54	1 (1.9) [0.0, 9.9]	60	1 (1.7) [0.0, 8.9]				
Western Europe/European origin	28	0 (0.0) [0.0, 12.3]	31	3 (9.7) [2.0, 25.8]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AER_SSIH: Incidence of AESI tachycardia/palpitation by dialysis method
SAF-S

	CR845		Placebo					
AESI tachycardia/palpitation	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
H: Dialysis method								NE
Hemodialysis (HD)	220	5 (2.3) [0.7, 5.2]	199	7 (3.5) [1.4, 7.1]	0.646 [0.208, 2.003]	0.638 [0.199, 2.043]	-1.2 [-5.0, 2.5]	0.446
Hemodiafiltration (HDF)	15	0 (0.0) [0.0, 21.8]	37	0 (0.0) [0.0, 9.5]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AERN_SSIA: Incidence of AESI tachycardia/palpitation - non-severe by age
SAF-S

AESI tachycardia/palpitation - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
A: Age		n<10 for all subgroups						NE
< 65 years	146	3 (2.1) [0.4, 5.9]	153	5 (3.3) [1.1, 7.5]				
>= 65 years	89	2 (2.2) [0.3, 7.9]	83	2 (2.4) [0.3, 8.4]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AERN_SSIB: Incidence of AESI tachycardia/palpitation - non-severe by sex
SAF-S

AESI tachycardia/palpitation - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
B: Sex		n<10 for all subgroups						NE
Male	135	3 (2.2) [0.5, 6.4]	139	3 (2.2) [0.4, 6.2]				
Female	100	2 (2.0) [0.2, 7.0]	97	4 (4.1) [1.1, 10.2]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AERN_SSIC: Incidence of AESI tachycardia/palpitation - non-severe by race
SAF-S

AESI tachycardia/palpitation - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
C: Race		n<10 for all subgroups						NE
Black/African American	53	1 (1.9) [0.0, 10.1]	38	1 (2.6) [0.1, 13.8]				
White	162	4 (2.5) [0.7, 6.2]	169	4 (2.4) [0.6, 5.9]				
Other	20	0 (0.0) [0.0, 16.8]	29	2 (6.9) [0.8, 22.8]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AERN_SSID: Incidence of AESI tachycardia/palpitation - non-severe by baseline WI-NRS
SAF-S

AESI tachycardia/palpitation - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)		n<10 for all subgroups						NE
>= 4 to < 7	101	3 (3.0) [0.6, 8.4]	113	3 (2.7) [0.6, 7.6]				
>= 7	134	2 (1.5) [0.2, 5.3]	123	4 (3.3) [0.9, 8.1]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AERN_SSIE: Incidence of AESI tachycardia/palpitation - non-severe by specific medical condition
SAF-S

AESI tachycardia/palpitation - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
E: Presence of specific medical conditions		n<10 for all subgroups						NE
No	194	4 (2.1) [0.6, 5.2]	199	5 (2.5) [0.8, 5.8]				
Yes	41	1 (2.4) [0.1, 12.9]	37	2 (5.4) [0.7, 18.2]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AERN_SSIF: Incidence of AESI tachycardia/palpitation - non-severe by use of concomitant itch medication
SAF-S

	CR845		Placebo					
AESI tachycardia/palpitation - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
F: Use of concomitant itch medication		n<10 for all subgroups						NE
No	148	2 (1.4) [0.2, 4.8]	151	3 (2.0) [0.4, 5.7]				
Yes	87	3 (3.4) [0.7, 9.7]	85	4 (4.7) [1.3, 11.6]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AERN_SSIG: Incidence of AESI tachycardia/palpitation - non-severe by region
SAF-S

	CR845		Placebo					
AESI tachycardia/palpitation - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
G: Region		n<10 for all subgroups						NE
USA	145	4 (2.8) [0.8, 6.9]	133	3 (2.3) [0.5, 6.5]				
Asia	8	0 (0.0) [0.0, 36.9]	12	0 (0.0) [0.0, 26.5]				
Eastern Europe	54	1 (1.9) [0.0, 9.9]	60	1 (1.7) [0.0, 8.9]				
Western Europe/European origin	28	0 (0.0) [0.0, 12.3]	31	3 (9.7) [2.0, 25.8]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Table BT2AERN_SSIH: Incidence of AESI tachycardia/palpitation - non-severe by dialysis method
SAF-S

	CR845		Placebo					
AESI tachycardia/palpitation - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
H: Dialysis method								NE
Hemodialysis (HD)	220	5 (2.3) [0.7, 5.2]	199	7 (3.5) [1.4, 7.1]	0.646 [0.208, 2.003]	0.638 [0.199, 2.043]	-1.2 [-5.0, 2.5]	0.446
Hemodiafiltration (HDF)	15	0 (0.0) [0.0, 21.8]	37	0 (0.0) [0.0, 9.5]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae, created on: 17FEB2022

Anhang 4-H-3:
Zusatzauswertungen der IPD Meta-Analyse

Table IT2WIB_IOA0: Baseline weekly WI-NRS (categorical)
ITT

		CR845		Placebo	
	Category	N	n (%)	N	n (%)
Baseline weekly WI-NRS	< 3 points	426	0 (0.0)	425	0 (0.0)
	3 - < 4 points	426	0 (0.0)	425	0 (0.0)
	4 - 6 points	426	95 (22.3)	425	122 (28.7)
	> 6 - 7 points	426	118 (27.7)	425	82 (19.3)
	> 7 points	426	213 (50.0)	425	221 (52.0)
	Missing	426	0 (0.0)	425	0 (0.0)

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients in category. WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek_i, created on: 11FEB2022

Table IT2DTB_IOA0: Baseline 5-D total score (categorical)
ITT

		CR845		Placebo	
	Category	N	n (%)	N	n (%)
Baseline 5-D total score	< 10 points	426	8 (1.9)	425	5 (1.2)
	10 - 20 points	426	341 (80.0)	425	344 (80.9)
	> 20 points	426	68 (16.0)	425	76 (17.9)
	Missing	426	9 (2.1)	425	0 (0.0)

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients in category.
Source Data: afived_i, created on: 10FEB2022

Table IT2DDB_IOA0: Baseline 5-D degree score (categorical)
ITT

		CR845		Placebo	
	Category	N	n (%)	N	n (%)
Baseline 5-D degree score	1 point	426	2 (0.5)	425	1 (0.2)
	2 - 4 points	426	391 (91.8)	425	382 (89.9)
	5 points	426	27 (6.3)	425	42 (9.9)
	Missing	426	6 (1.4)	425	0 (0.0)

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients in category.
Source Data: afived_i, created on: 10FEB2022

Table IT2DLB_IOA0: Baseline 5-D duration score (categorical)
ITT

		CR845		Placebo	
	Category	N	n (%)	N	n (%)
Baseline 5-D duration score	1 point	426	87 (20.4)	425	85 (20.0)
	2 - 4 points	426	256 (60.1)	425	253 (59.5)
	5 points	426	75 (17.6)	425	87 (20.5)
	Missing	426	8 (1.9)	425	0 (0.0)

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients in category.
Source Data: afived_i, created on: 10FEB2022

Table IT2DWB_IOA0: Baseline 5-D direction score (categorical)
ITT

		CR845		Placebo	
	Category	N	n (%)	N	n (%)
Baseline 5-D direction score	1 point	426	1 (0.2)	425	0 (0.0)
	2 - 4 points	426	372 (87.3)	425	374 (88.0)
	5 points	426	47 (11.0)	425	51 (12.0)
	Missing	426	6 (1.4)	425	0 (0.0)

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients in category.
Source Data: afived_i, created on: 10FEB2022

Table IT2DNB_IOA0: Baseline 5-D disability score (categorical)
ITT

		CR845		Placebo	
	Category	N	n (%)	N	n (%)
Baseline 5-D disability score	1 point	426	25 (5.9)	425	25 (5.9)
	2 - 4 points	426	308 (72.3)	425	294 (69.2)
	5 points	426	86 (20.2)	425	106 (24.9)
	Missing	426	7 (1.6)	425	0 (0.0)

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients in category.
Source Data: afived_i, created on: 10FEB2022

Table IT2DVB_IOA0: Baseline 5-D distribution score (categorical)
ITT

		CR845		Placebo	
	Category	N	n (%)	N	n (%)
Baseline 5-D distribution score	1 point	426	26 (6.1)	425	22 (5.2)
	2 - 4 points	426	315 (73.9)	425	339 (79.8)
	5 points	426	79 (18.5)	425	64 (15.1)
	Missing	426	6 (1.4)	425	0 (0.0)

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients in category.
Source Data: afived_i, created on: 10FEB2022

Table IT2DDC_IMH0: Change from baseline in 5-D degree score
ITT

		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
5-D degree score	Baseline	CR845	426	420 (98.6)	3.5 (0.7)	1	3.0	5	
		Placebo	425	425 (100.0)	3.5 (0.8)	1	3.0	5	
	Week 4	CR845	426	383 (89.9)	2.8 (0.8)	1	3.0	5	
		Placebo	425	390 (91.8)	3.1 (0.8)	1	3.0	5	
	Week 8	CR845	426	369 (86.6)	2.7 (0.8)	1	3.0	5	
		Placebo	425	392 (92.2)	2.9 (0.8)	1	3.0	5	
	Week 10	CR845	426	363 (85.2)	2.6 (0.8)	1	3.0	5	
		Placebo	425	384 (90.4)	2.9 (0.8)	1	3.0	5	
	Week 12	CR845	426	365 (85.7)	2.6 (0.8)	1	2.0	5	
		Placebo	425	385 (90.6)	2.8 (0.9)	1	3.0	5	
Change from baseline in 5-D degree score	Week 4	CR845	426	379 (89.0)	-0.7 (0.9)	-4	-1.0	3	-0.29 [-0.43, -0.14]
		Placebo	425	390 (91.8)	-0.4 (0.9)	-3	0.0	2	
	Week 8	CR845	426	365 (85.7)	-0.8 (1.0)	-4	-1.0	3	-0.16 [-0.30, -0.01]
		Placebo	425	392 (92.2)	-0.6 (0.9)	-4	0.0	2	
	Week 10	CR845	426	359 (84.3)	-0.9 (1.0)	-4	-1.0	3	-0.25 [-0.39, -0.10]
		Placebo	425	384 (90.4)	-0.6 (0.9)	-4	-1.0	2	
	Week 12	CR845	426	362 (85.0)	-0.9 (1.0)	-4	-1.0	3	-0.17 [-0.31, -0.03]
		Placebo	425	385 (90.6)	-0.7 (0.9)	-3	-1.0	2	

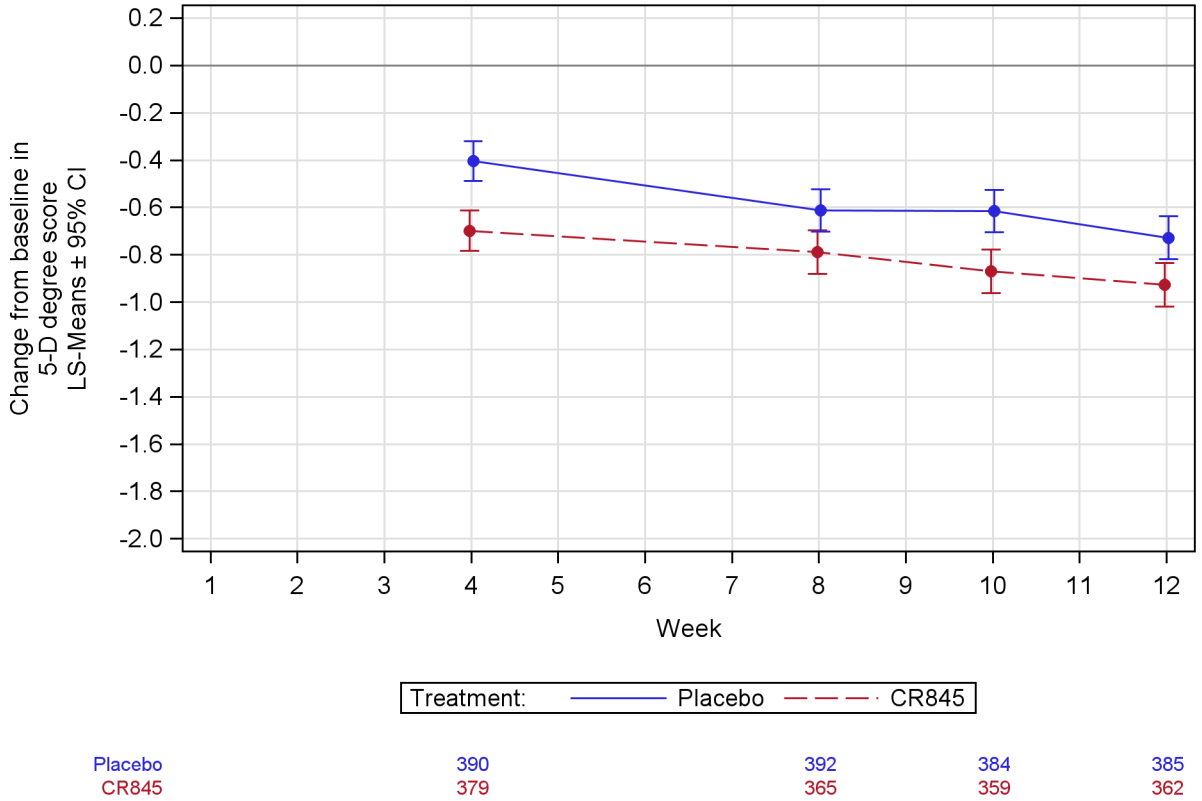
ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DDC_IMC0: Change from baseline in 5-D degree score - MMRM results
ITT

Change from baseline in 5-D degree score				Repeated measures analysis				
				Change from Baseline		Treatment Difference		
Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Week 4	CR845	426	379 (89.0)	-0.7 (0.0)	(-0.8, -0.6)	-0.3 (0.1)	(-0.4, -0.2)	<0.001 *
	Placebo	425	390 (91.8)	-0.4 (0.0)	(-0.5, -0.3)			
Week 8	CR845	426	365 (85.7)	-0.8 (0.0)	(-0.9, -0.7)	-0.2 (0.1)	(-0.3, -0.1)	0.003 *
	Placebo	425	392 (92.2)	-0.6 (0.0)	(-0.7, -0.5)			
Week 10	CR845	426	359 (84.3)	-0.9 (0.0)	(-1.0, -0.8)	-0.3 (0.1)	(-0.4, -0.1)	<0.001 *
	Placebo	425	384 (90.4)	-0.6 (0.0)	(-0.7, -0.5)			
Week 12	CR845	426	362 (85.0)	-0.9 (0.0)	(-1.0, -0.8)	-0.2 (0.1)	(-0.3, -0.1)	<0.001 *
	Placebo	425	385 (90.6)	-0.7 (0.0)	(-0.8, -0.6)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval . * = significant treatment effect.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived_i, created on: 17FEB2022

Figure IF2DDC_IMG0: Course of change from baseline in 5-D degree score
ITT



Note: ITT = Intent-to-treat Set.
Symbols present least square mean (LS-Mean), bars present 95% confidence intervals (CI).
CR845 = Difelikefalin.
Source Table: IT2DDC_IMC0
Source Data: afived_i, created on: 17FEB2022

Table IT2DLC_IMH0: Change from baseline in 5-D duration score
ITT

		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
5-D duration score	Baseline	CR845	426	418 (98.1)	2.7 (1.4)	1	2.0	5	
		Placebo	425	425 (100.0)	2.8 (1.4)	1	2.0	5	
	Week 4	CR845	426	383 (89.9)	2.0 (1.2)	1	2.0	5	
		Placebo	425	390 (91.8)	2.4 (1.4)	1	2.0	5	
	Week 8	CR845	426	369 (86.6)	1.8 (1.1)	1	1.0	5	
		Placebo	425	392 (92.2)	2.1 (1.3)	1	2.0	5	
	Week 10	CR845	426	363 (85.2)	1.8 (1.1)	1	1.0	5	
		Placebo	425	384 (90.4)	2.1 (1.3)	1	2.0	5	
	Week 12	CR845	426	365 (85.7)	1.8 (1.1)	1	1.0	5	
		Placebo	425	385 (90.6)	2.1 (1.3)	1	2.0	5	
Change from baseline in 5-D duration score	Week 4	CR845	426	377 (88.5)	-0.7 (1.3)	-4	-1.0	4	-0.21 [-0.35, -0.07]
		Placebo	425	390 (91.8)	-0.4 (1.6)	-4	0.0	4	
	Week 8	CR845	426	363 (85.2)	-0.9 (1.4)	-4	-1.0	3	-0.16 [-0.30, -0.02]
		Placebo	425	392 (92.2)	-0.7 (1.5)	-4	-0.5	4	
	Week 10	CR845	426	357 (83.8)	-0.9 (1.5)	-4	-1.0	4	-0.14 [-0.28, 0.01]
		Placebo	425	384 (90.4)	-0.7 (1.5)	-4	-1.0	4	
	Week 12	CR845	426	360 (84.5)	-1.0 (1.5)	-4	-1.0	4	-0.17 [-0.32, -0.03]
		Placebo	425	385 (90.6)	-0.7 (1.5)	-4	-1.0	4	

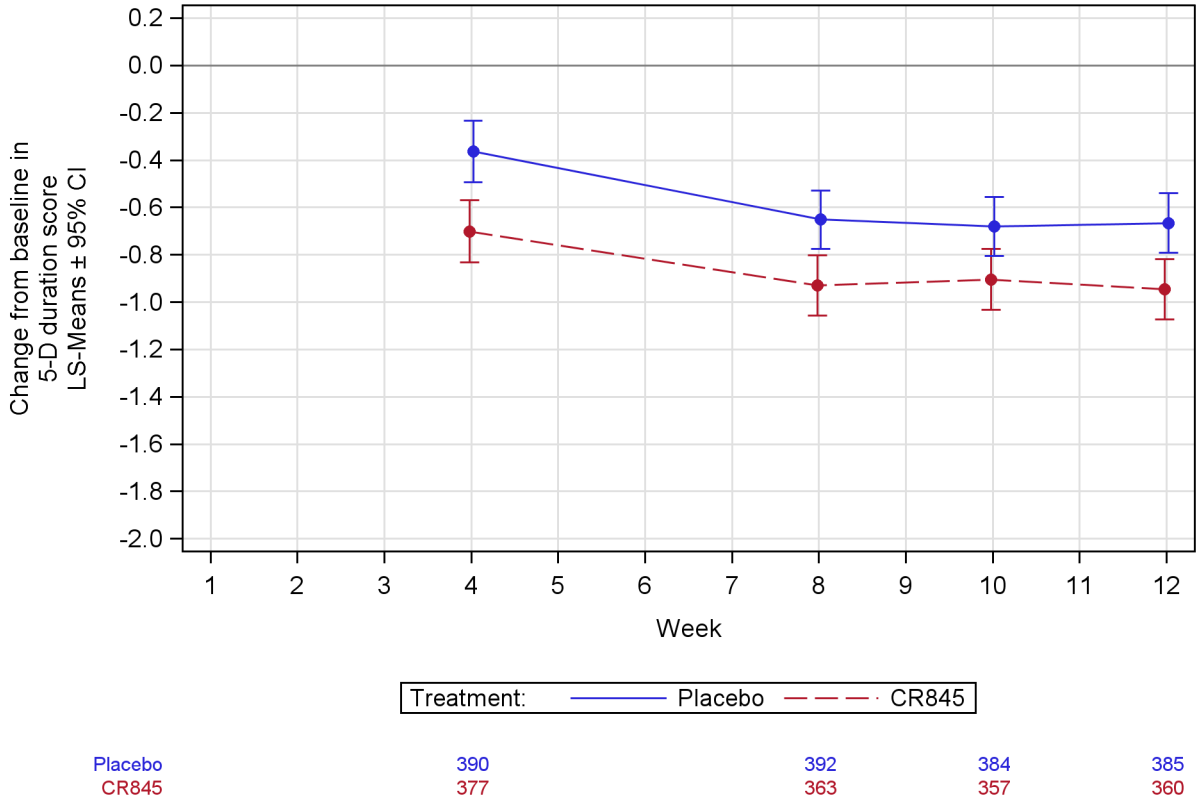
Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DLC_IMC0: Change from baseline in 5-D duration score - MMRM results
ITT

Change from baseline in 5-D duration score				Repeated measures analysis				
				Change from Baseline		Treatment Difference		
Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Week 4	CR845	426	377 (88.5)	-0.7 (0.1)	(-0.8, -0.6)	-0.3 (0.1)	(-0.5, -0.2)	<0.001 *
	Placebo	425	390 (91.8)	-0.4 (0.1)	(-0.5, -0.2)			
Week 8	CR845	426	363 (85.2)	-0.9 (0.1)	(-1.1, -0.8)	-0.3 (0.1)	(-0.4, -0.1)	<0.001 *
	Placebo	425	392 (92.2)	-0.7 (0.1)	(-0.8, -0.5)			
Week 10	CR845	426	357 (83.8)	-0.9 (0.1)	(-1.0, -0.8)	-0.2 (0.1)	(-0.4, -0.1)	0.006 *
	Placebo	425	384 (90.4)	-0.7 (0.1)	(-0.8, -0.6)			
Week 12	CR845	426	360 (84.5)	-0.9 (0.1)	(-1.1, -0.8)	-0.3 (0.1)	(-0.4, -0.1)	<0.001 *
	Placebo	425	385 (90.6)	-0.7 (0.1)	(-0.8, -0.5)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval . * = significant treatment effect.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived_i, created on: 17FEB2022

Figure IF2DLC_IMG0: Course of change from baseline in 5-D duration score
ITT



Note: ITT = Intent-to-treat Set.
Symbols present least square mean (LS-Mean), bars present 95% confidence intervals (CI).
CR845 = Difelikefalin.
Source Table: IT2DLC_IMC0
Source Data: afived_i, created on: 17FEB2022

Table IT2DWC_IMH0: Change from baseline in 5-D direction score
ITT

		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
5-D direction score	Baseline	CR845	426	420 (98.6)	3.9 (0.6)	1	4.0	5	
		Placebo	425	425 (100.0)	3.9 (0.7)	2	4.0	5	
	Week 4	CR845	426	384 (90.1)	2.7 (0.8)	1	3.0	5	
		Placebo	425	390 (91.8)	3.1 (0.9)	1	3.0	5	
	Week 8	CR845	426	368 (86.4)	2.6 (0.8)	1	3.0	5	
		Placebo	425	392 (92.2)	2.9 (0.9)	1	3.0	5	
	Week 10	CR845	426	363 (85.2)	2.5 (0.8)	1	2.0	5	
		Placebo	425	384 (90.4)	2.9 (0.9)	1	3.0	5	
	Week 12	CR845	426	364 (85.4)	2.6 (0.9)	1	2.0	5	
		Placebo	425	385 (90.6)	2.9 (1.0)	1	3.0	5	
Change from baseline in 5-D direction score	Week 4	CR845	426	380 (89.2)	-1.2 (1.0)	-4	-1.0	2	-0.44 [-0.58, -0.30]
		Placebo	425	390 (91.8)	-0.8 (1.0)	-4	-1.0	3	
	Week 8	CR845	426	364 (85.4)	-1.3 (1.0)	-4	-1.0	2	-0.34 [-0.49, -0.20]
		Placebo	425	392 (92.2)	-0.9 (1.1)	-4	-1.0	2	
	Week 10	CR845	426	359 (84.3)	-1.3 (1.0)	-4	-1.0	1	-0.40 [-0.54, -0.25]
		Placebo	425	384 (90.4)	-0.9 (1.1)	-4	-1.0	3	
	Week 12	CR845	426	361 (84.7)	-1.3 (1.0)	-4	-1.0	2	-0.31 [-0.45, -0.16]
		Placebo	425	385 (90.6)	-1.0 (1.1)	-4	-1.0	2	

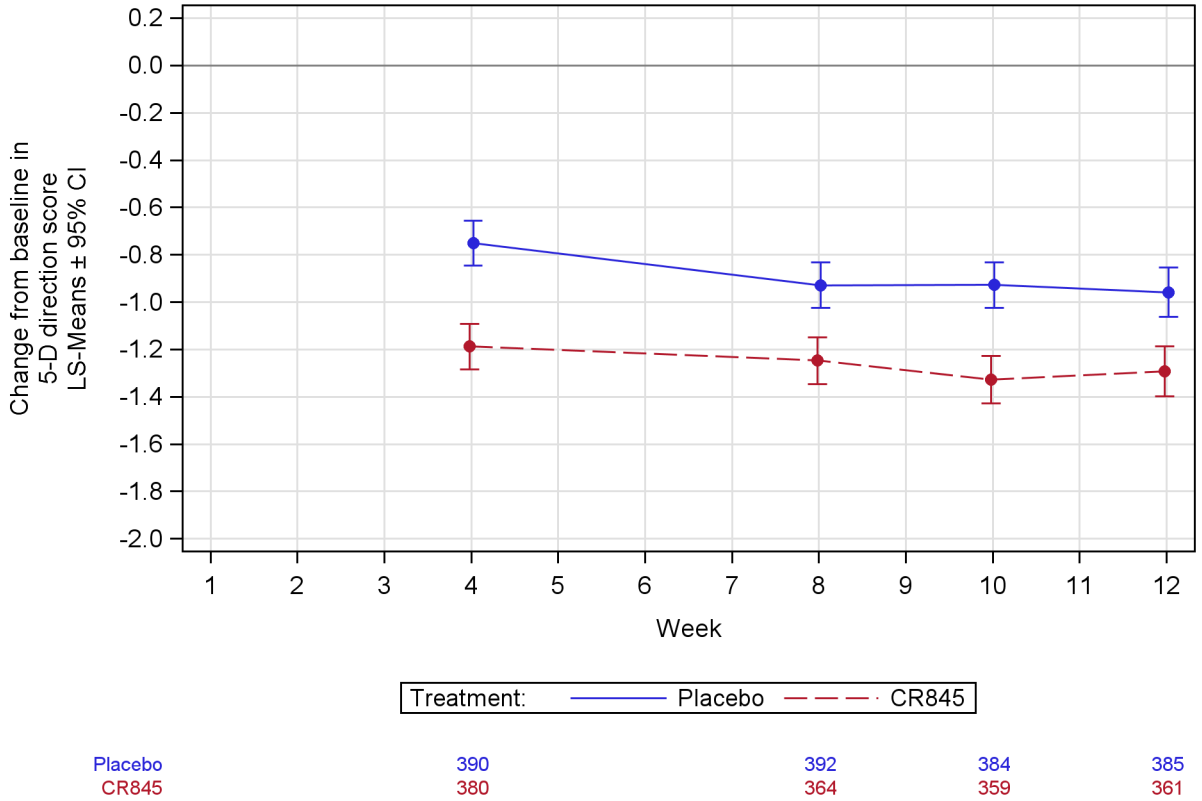
Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DWC_IMC0: Change from baseline in 5-D direction score - MMRM results
ITT

Change from baseline in 5-D direction score				Repeated measures analysis				
				Change from Baseline		Treatment Difference		
Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Week 4	CR845	426	380 (89.2)	-1.2 (0.0)	(-1.3, -1.1)	-0.4 (0.1)	(-0.6, -0.3)	<0.001 *
	Placebo	425	390 (91.8)	-0.8 (0.0)	(-0.8, -0.7)			
Week 8	CR845	426	364 (85.4)	-1.2 (0.1)	(-1.3, -1.1)	-0.3 (0.1)	(-0.4, -0.2)	<0.001 *
	Placebo	425	392 (92.2)	-0.9 (0.0)	(-1.0, -0.8)			
Week 10	CR845	426	359 (84.3)	-1.3 (0.1)	(-1.4, -1.2)	-0.4 (0.1)	(-0.5, -0.3)	<0.001 *
	Placebo	425	384 (90.4)	-0.9 (0.0)	(-1.0, -0.8)			
Week 12	CR845	426	361 (84.7)	-1.3 (0.1)	(-1.4, -1.2)	-0.3 (0.1)	(-0.5, -0.2)	<0.001 *
	Placebo	425	385 (90.6)	-1.0 (0.1)	(-1.1, -0.9)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval . * = significant treatment effect.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived_i, created on: 17FEB2022

Figure IF2DWC_IMG0: Course of change from baseline in 5-D direction score
ITT



Note: ITT = Intent-to-treat Set.
Symbols present least square mean (LS-Mean), bars present 95% confidence intervals (CI).
CR845 = Difelikefalin.
Source Table: IT2DWC_IMC0
Source Data: afived_i, created on: 17FEB2022

Table IT2DNC_IMH0: Change from baseline in 5-D disability score
ITT

		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
5-D disability score	Baseline	CR845	426	419 (98.4)	3.5 (1.1)	1	4.0	5	
		Placebo	425	425 (100.0)	3.6 (1.1)	1	4.0	5	
	Week 4	CR845	426	384 (90.1)	2.9 (1.1)	1	3.0	5	
		Placebo	425	390 (91.8)	3.1 (1.2)	1	3.0	5	
	Week 8	CR845	426	369 (86.6)	2.6 (1.2)	1	2.0	5	
		Placebo	425	392 (92.2)	2.9 (1.2)	1	3.0	5	
	Week 10	CR845	426	363 (85.2)	2.5 (1.2)	1	2.0	5	
		Placebo	425	384 (90.4)	2.7 (1.2)	1	3.0	5	
	Week 12	CR845	426	365 (85.7)	2.5 (1.2)	1	2.0	5	
		Placebo	425	385 (90.6)	2.6 (1.2)	1	3.0	5	
Change from baseline in 5-D disability score	Week 4	CR845	426	380 (89.2)	-0.6 (1.2)	-4	-1.0	3	-0.08 [-0.22, 0.06]
		Placebo	425	390 (91.8)	-0.5 (1.3)	-4	0.0	4	
	Week 8	CR845	426	365 (85.7)	-0.9 (1.3)	-4	-1.0	4	-0.10 [-0.24, 0.05]
		Placebo	425	392 (92.2)	-0.8 (1.3)	-4	-1.0	4	
	Week 10	CR845	426	359 (84.3)	-1.0 (1.3)	-4	-1.0	3	-0.12 [-0.27, 0.02]
		Placebo	425	384 (90.4)	-0.9 (1.3)	-4	-1.0	3	
	Week 12	CR845	426	362 (85.0)	-1.1 (1.4)	-4	-1.0	4	-0.06 [-0.21, 0.08]
		Placebo	425	385 (90.6)	-1.0 (1.3)	-4	-1.0	3	

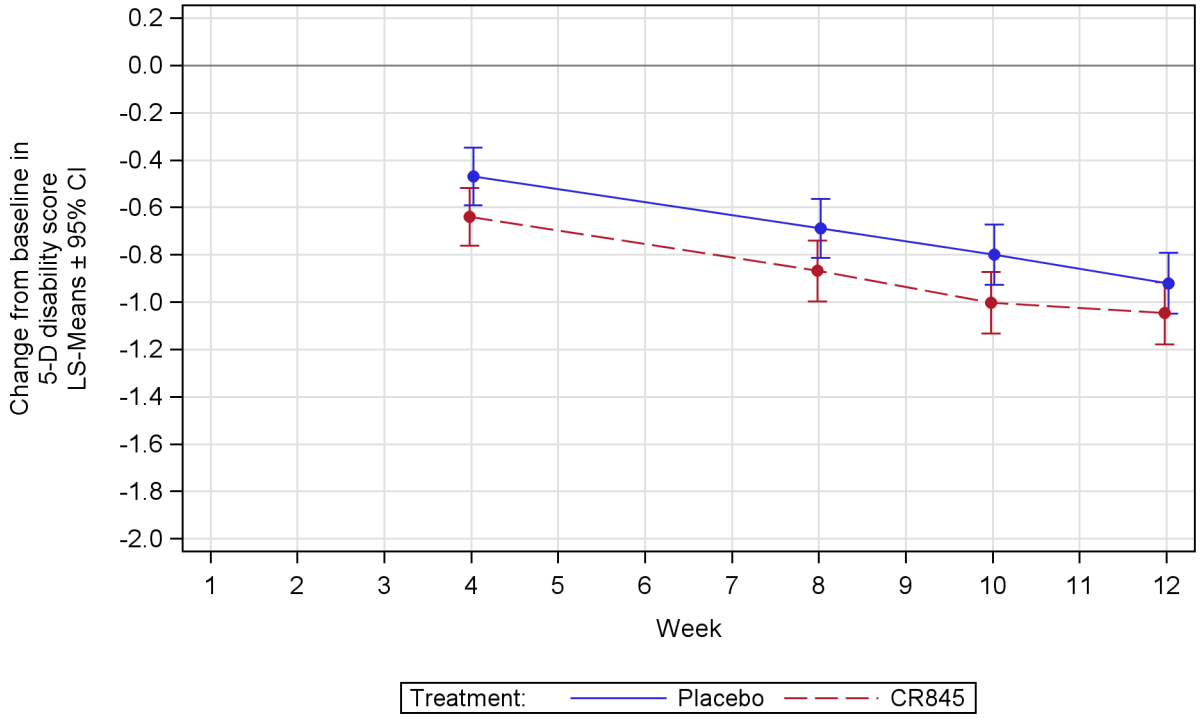
Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DNC_IMC0: Change from baseline in 5-D disability score - MMRM results
ITT

Change from baseline in 5-D disability score				Repeated measures analysis				
				Change from Baseline		Treatment Difference		
Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Week 4	CR845	426	380 (89.2)	-0.6 (0.1)	(-0.8, -0.5)	-0.2 (0.1)	(-0.3, -0.0)	0.026 *
	Placebo	425	390 (91.8)	-0.5 (0.1)	(-0.6, -0.3)			
Week 8	CR845	426	365 (85.7)	-0.9 (0.1)	(-1.0, -0.7)	-0.2 (0.1)	(-0.3, -0.0)	0.027 *
	Placebo	425	392 (92.2)	-0.7 (0.1)	(-0.8, -0.6)			
Week 10	CR845	426	359 (84.3)	-1.0 (0.1)	(-1.1, -0.9)	-0.2 (0.1)	(-0.4, -0.0)	0.014 *
	Placebo	425	384 (90.4)	-0.8 (0.1)	(-0.9, -0.7)			
Week 12	CR845	426	362 (85.0)	-1.0 (0.1)	(-1.2, -0.9)	-0.1 (0.1)	(-0.3, 0.0)	0.132
	Placebo	425	385 (90.6)	-0.9 (0.1)	(-1.0, -0.8)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval . * = significant treatment effect.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived_i, created on: 17FEB2022

Figure IF2DNC_IMG0: Course of change from baseline in 5-D disability score
ITT



Note: ITT = Intent-to-treat Set.
Symbols present least square mean (LS-Mean), bars present 95% confidence intervals (CI).
CR845 = Difelikefalin.
Source Table: IT2DNC_IMC0
Source Data: afived_i, created on: 17FEB2022

Table IT2DVC_IMH0: Change from baseline in 5-D distribution score
ITT

		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
5-D distribution score	Baseline	CR845	426	420 (98.6)	3.2 (1.2)	1	3.0	5	
		Placebo	425	425 (100.0)	3.1 (1.1)	1	3.0	5	
	Week 4	CR845	426	384 (90.1)	2.7 (1.2)	1	3.0	5	
		Placebo	425	390 (91.8)	2.9 (1.2)	1	3.0	5	
	Week 8	CR845	426	369 (86.6)	2.6 (1.2)	1	2.0	5	
		Placebo	425	392 (92.2)	2.8 (1.2)	1	3.0	5	
	Week 10	CR845	426	363 (85.2)	2.6 (1.2)	1	3.0	5	
		Placebo	425	384 (90.4)	2.8 (1.2)	1	3.0	5	
	Week 12	CR845	426	365 (85.7)	2.5 (1.2)	1	2.0	5	
		Placebo	425	385 (90.6)	2.8 (1.2)	1	3.0	5	
Change from baseline in 5-D distribution score	Week 4	CR845	426	380 (89.2)	-0.5 (1.0)	-4	0.0	3	-0.24 [-0.38, -0.10]
		Placebo	425	390 (91.8)	-0.2 (1.0)	-4	0.0	3	
	Week 8	CR845	426	365 (85.7)	-0.6 (1.2)	-4	0.0	4	-0.20 [-0.35, -0.06]
		Placebo	425	392 (92.2)	-0.3 (1.2)	-4	0.0	4	
	Week 10	CR845	426	359 (84.3)	-0.6 (1.2)	-4	0.0	3	-0.19 [-0.34, -0.05]
		Placebo	425	384 (90.4)	-0.3 (1.1)	-4	0.0	3	
	Week 12	CR845	426	362 (85.0)	-0.6 (1.2)	-4	0.0	4	-0.27 [-0.41, -0.13]
		Placebo	425	385 (90.6)	-0.3 (1.1)	-4	0.0	3	

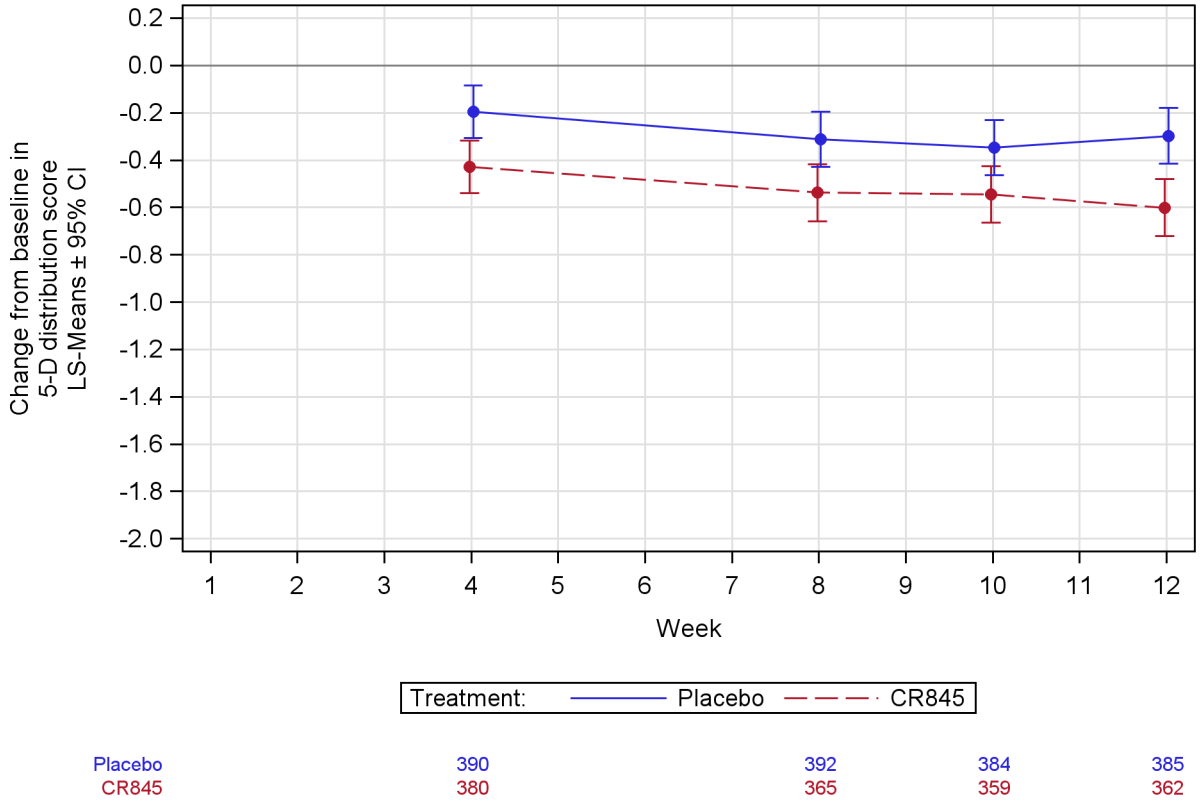
Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DVC_IMC0: Change from baseline in 5-D distribution score - MMRM results
ITT

Change from baseline in 5-D distribution score				Repeated measures analysis				
				Change from Baseline		Treatment Difference		
Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Week 4	CR845	426	380 (89.2)	-0.4 (0.1)	(-0.5, -0.3)	-0.2 (0.1)	(-0.4, -0.1)	<0.001 *
	Placebo	425	390 (91.8)	-0.2 (0.1)	(-0.3, -0.1)			
Week 8	CR845	426	365 (85.7)	-0.5 (0.1)	(-0.7, -0.4)	-0.2 (0.1)	(-0.4, -0.1)	0.003 *
	Placebo	425	392 (92.2)	-0.3 (0.1)	(-0.4, -0.2)			
Week 10	CR845	426	359 (84.3)	-0.5 (0.1)	(-0.7, -0.4)	-0.2 (0.1)	(-0.3, -0.1)	0.008 *
	Placebo	425	384 (90.4)	-0.3 (0.1)	(-0.5, -0.2)			
Week 12	CR845	426	362 (85.0)	-0.6 (0.1)	(-0.7, -0.5)	-0.3 (0.1)	(-0.5, -0.2)	<0.001 *
	Placebo	425	385 (90.6)	-0.3 (0.1)	(-0.4, -0.2)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval . * = significant treatment effect.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived_i, created on: 17FEB2022

Figure IF2DVC_IMG0: Course of change from baseline in 5-D distribution score
ITT



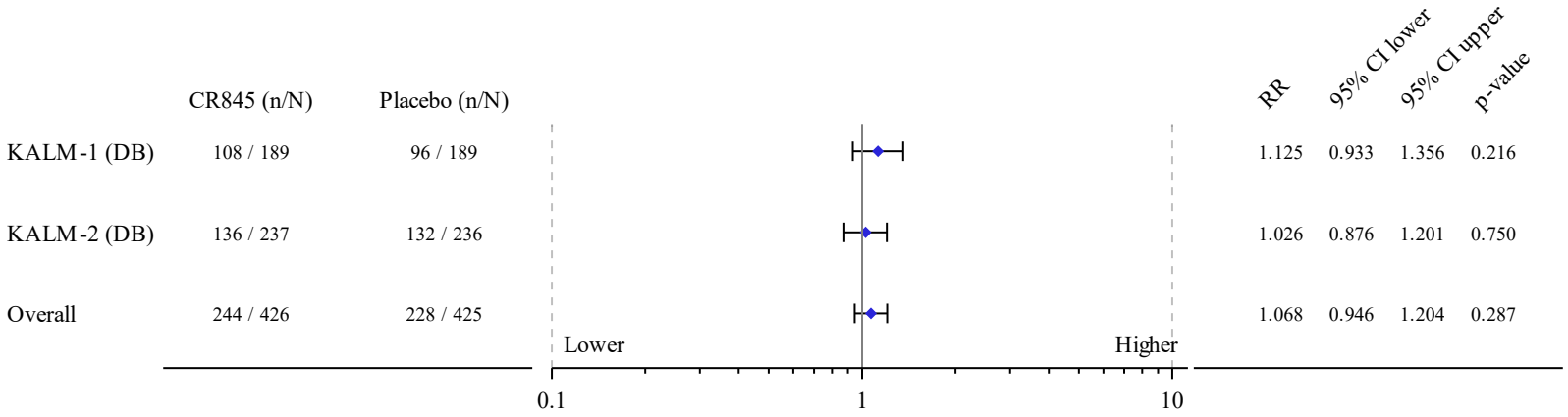
Note: ITT = Intent-to-treat Set.
Symbols present least square mean (LS-Mean), bars present 95% confidence intervals (CI).
CR845 = Difelikefalin.
Source Table: IT2DVC_IMC0
Source Data: afived_i, created on: 17FEB2022

Table IT2DDCD1_IMP0: Decrease of 5-D degree score of at least 1 point
ITT

		CR845			Placebo						
Variable	Time	N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Decrease of 5-D degree score of at least 1 point	Week 12	426	362 (85.0)	244 (57.3) [52.4, 62.0]	425	385 (90.6)	228 (53.6) [48.8, 58.5]	1.068 [0.946, 1.204]	1.158 [0.884, 1.518]	3.6 [-3.3, 10.5]	0.287

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: afived_i, created on: 10FEB2022

Figure IF2DDCD1_IMFR0: Forest plot for decrease of 5-D degree score of at least 1 point - relative risk
ITT



Test for heterogeneity - pvalue: 0.460, I-square: 0.0 %

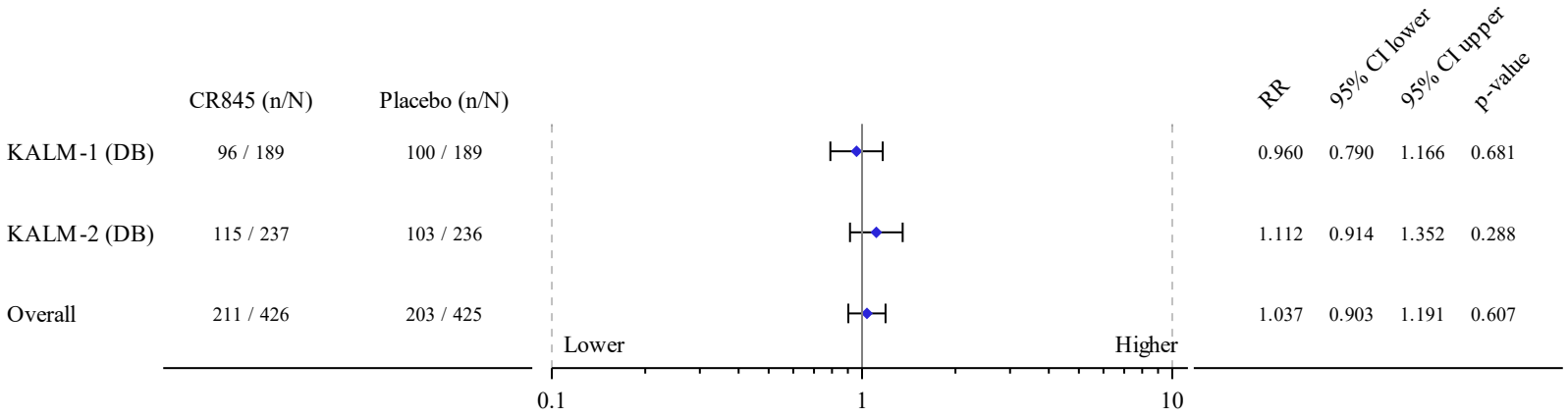
Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. RR = relative risk. CI = confidence interval.
Heterogeneity was investigated with Cochran Q test. NE = not evaluable.
Source tables: AT2DDCD1_IMP0, BT2DDCD1_IMP0, IT2DDCD1_IMP0

Table IT2DLCD1_IMP0: Decrease of 5-D duration score of at least 1 point
ITT

		CR845			Placebo						
Variable	Time	N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Decrease of 5-D duration score of at least 1 point	Week 12	426	360 (84.5)	211 (49.5) [44.7, 54.4]	425	385 (90.6)	203 (47.8) [42.9, 52.6]	1.037 [0.903, 1.191]	1.073 [0.820, 1.404]	1.8 [-5.2, 8.7]	0.607

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: afived_i, created on: 10FEB2022

Figure IF2DLCD1_IMFR0: Forest plot for decrease of 5-D duration score of at least 1 point - relative risk
ITT



Test for heterogeneity - pvalue: 0.297, I-square: 8.2 %

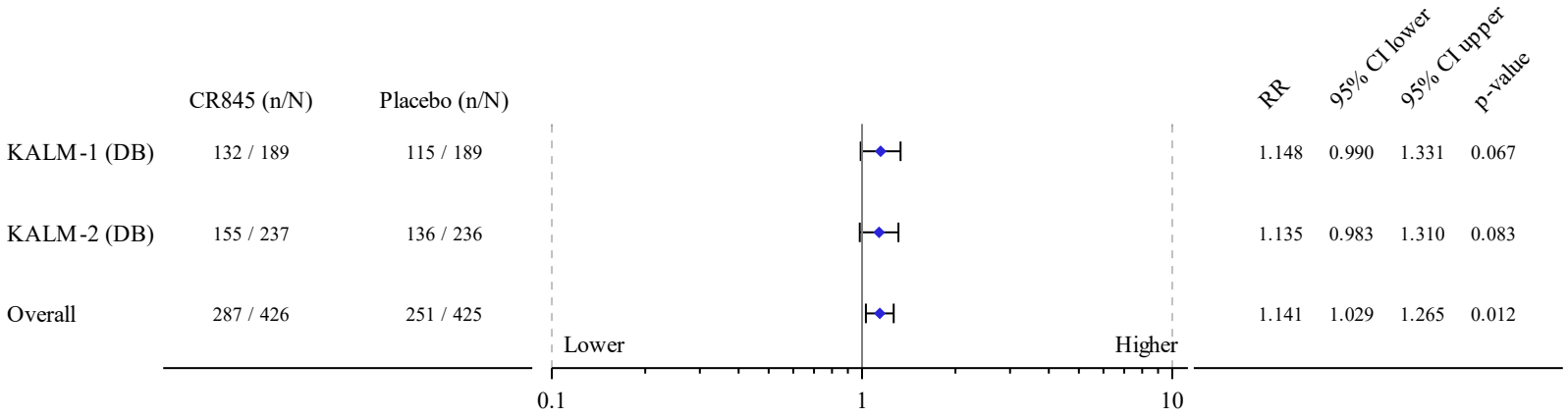
Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. RR = relative risk. CI = confidence interval.
Heterogeneity was investigated with Cochran Q test. NE = not evaluable.
Source tables: AT2DLCD1_IMP0, BT2DLCD1_IMP0, IT2DLCD1_IMP0

Table IT2DWCD1_IMP0: Decrease of 5-D direction score of at least 1 point
ITT

		CR845			Placebo						
Variable	Time	N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Decrease of 5-D direction score of at least 1 point	Week 12	426	361 (84.7)	287 (67.4) [62.7, 71.8]	425	385 (90.6)	251 (59.1) [54.2, 63.8]	1.141 [1.029, 1.265]	1.431 [1.082, 1.894]	8.3 [1.6, 15.0]	0.012 *

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: afived_i, created on: 10FEB2022

Figure IF2DWCD1_IMFR0: Forest plot for decrease of 5-D direction score of at least 1 point - relative risk
ITT



Test for heterogeneity - pvalue: 0.914, I-square: 0.0 %

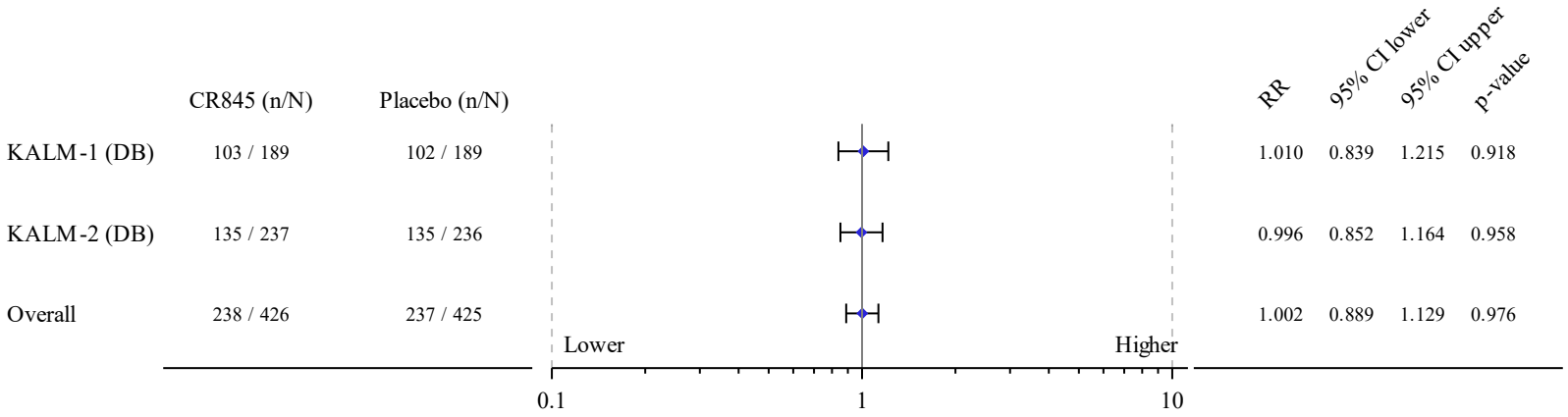
Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. RR = relative risk. CI = confidence interval.
Heterogeneity was investigated with Cochran Q test. NE = not evaluable.
Source tables: AT2DWCD1_IMP0, BT2DWCD1_IMP0, IT2DWCD1_IMP0

Table IT2DNCD1_IMP0: Decrease of 5-D disability score of at least 1 point
ITT

		CR845			Placebo						
Variable	Time	N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Decrease of 5-D disability score of at least 1 point	Week 12	426	362 (85.0)	238 (55.9) [51.0, 60.6]	425	385 (90.6)	237 (55.8) [50.9, 60.5]	1.002 [0.889, 1.129]	1.004 [0.766, 1.316]	0.1 [-6.8, 7.0]	0.976

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: afived_i, created on: 10FEB2022

Figure IF2DNCD1_IMFR0: Forest plot for decrease of 5-D disability score of at least 1 point - relative risk
ITT



Test for heterogeneity - pvalue: 0.910, I-square: 0.0 %

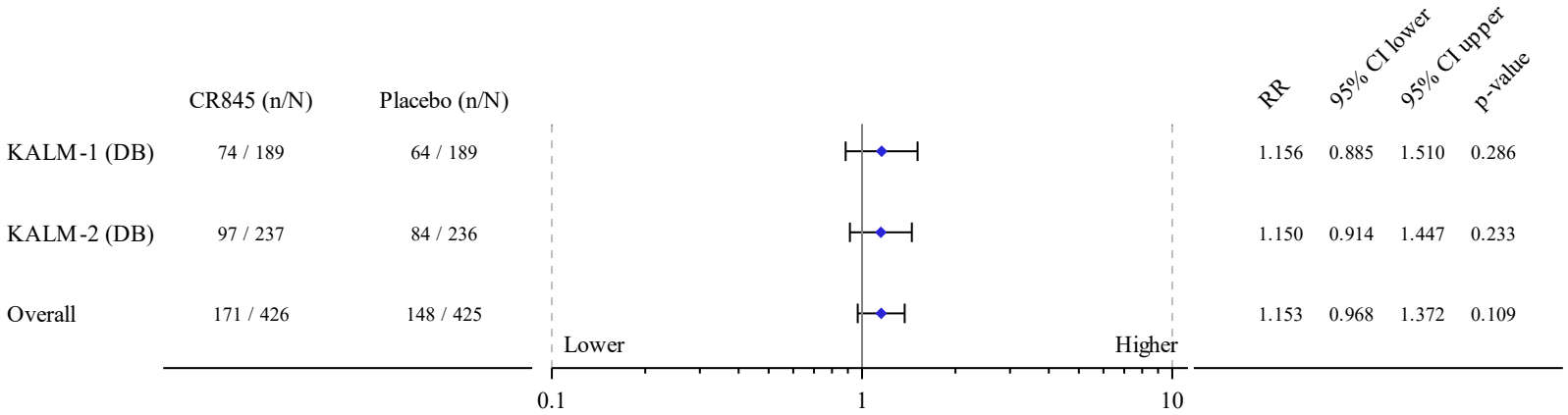
Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. RR = relative risk. CI = confidence interval.
Heterogeneity was investigated with Cochran Q test. NE = not evaluable.
Source tables: AT2DNCD1_IMP0, BT2DNCD1_IMP0, IT2DNCD1_IMP0

Table IT2DVCD1_IMP0: Decrease of 5-D distribution score of at least 1 point
ITT

		CR845			Placebo						
Variable	Time	N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Decrease of 5-D distribution score of at least 1 point	Week 12	426	362 (85.0)	171 (40.1) [35.5, 45.0]	425	385 (90.6)	148 (34.8) [30.3, 39.6]	1.153 [0.968, 1.372]	1.255 [0.950, 1.658]	5.3 [-1.4, 12.0]	0.109

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: afived_i, created on: 10FEB2022

Figure IF2DVCD1_IMFR0: Forest plot for decrease of 5-D distribution score of at least 1 point - relative risk
ITT



Test for heterogeneity - pvalue: 0.976, I-square: 0.0 %

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. RR = relative risk. CI = confidence interval.
Heterogeneity was investigated with Cochran Q test. NE = not evaluable.
Source tables: AT2DVCD1_IMP0, BT2DVCD1_IMP0, IT2DVCD1_IMP0

Table IT2STB_IOA0: Baseline Skindex-10 total score (categorical)
ITT

		CR845		Placebo	
	Category	N	n (%)	N	n (%)
Baseline Skindex-10 total score	< 15 points	426	34 (8.0)	425	40 (9.4)
	15 - 45 points	426	264 (62.0)	425	249 (58.6)
	> 45 points	426	116 (27.2)	425	126 (29.6)
	Missing	426	12 (2.8)	425	10 (2.4)

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients in category.
Source Data: askin_i, created on: 11FEB2022

Table IT2SDB_IOA0: Baseline Skindex-10 disease score (categorical)
ITT

		CR845		Placebo	
	Category	N	n (%)	N	n (%)
Baseline Skindex-10 disease score	< 3 points	426	7 (1.6)	425	2 (0.5)
	3 - 15 points	426	271 (63.6)	425	281 (66.1)
	> 15 points	426	141 (33.1)	425	138 (32.5)
	Missing	426	7 (1.6)	425	4 (0.9)

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients in category.
Source Data: askin_i, created on: 11FEB2022

Table IT2SMB_IOA0: Baseline Skindex-10 mood/emotional distress score (categorical)
ITT

		CR845		Placebo	
	Category	N	n (%)	N	n (%)
Baseline Skindex-10 mood/emotional distress score	< 3 points	426	21 (4.9)	425	25 (5.9)
	3 - 15 points	426	296 (69.5)	425	292 (68.7)
	> 15 points	426	99 (23.2)	425	103 (24.2)
	Missing	426	10 (2.3)	425	5 (1.2)

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients in category.
Source Data: askin_i, created on: 11FEB2022

Table IT2SSB_IOA0: Baseline Skindex-10 social functioning score (categorical)
ITT

		CR845		Placebo	
	Category	N	n (%)	N	n (%)
Baseline Skindex-10 social functioning score	< 4 points	426	92 (21.6)	425	83 (19.5)
	4 - 20 points	426	260 (61.0)	425	265 (62.4)
	> 20 points	426	67 (15.7)	425	71 (16.7)
	Missing	426	7 (1.6)	425	6 (1.4)

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients in category.
Source Data: askin_i, created on: 11FEB2022

Table IT2SDC_IMH0: Change from baseline in Skindex-10 disease score
ITT

		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Skindex-10 disease score	Baseline	CR845	426	419 (98.4)	13.1 (4.0)	0	14.0	18	
		Placebo	425	421 (99.1)	13.0 (4.0)	0	14.0	18	
	Week 4	CR845	426	380 (89.2)	9.4 (5.0)	0	9.0	18	
		Placebo	425	381 (89.6)	10.4 (4.8)	0	10.0	18	
	Week 8	CR845	426	367 (86.2)	8.4 (5.1)	0	8.0	18	
		Placebo	425	386 (90.8)	9.3 (4.9)	0	9.0	18	
	Week 10	CR845	426	361 (84.7)	7.6 (5.0)	0	7.0	18	
		Placebo	425	378 (88.9)	8.9 (4.9)	0	9.0	18	
	Week 12	CR845	426	361 (84.7)	7.3 (5.1)	0	6.0	18	
		Placebo	425	377 (88.7)	8.6 (5.0)	0	9.0	18	
Change from baseline in Skindex-10 disease score	Week 4	CR845	426	376 (88.3)	-3.7 (4.7)	-17	-3.0	10	-0.25 [-0.39, -0.11]
		Placebo	425	378 (88.9)	-2.5 (4.6)	-17	-2.0	12	
	Week 8	CR845	426	363 (85.2)	-4.6 (5.1)	-17	-5.0	11	-0.18 [-0.33, -0.04]
		Placebo	425	383 (90.1)	-3.7 (4.7)	-18	-3.0	9	
	Week 10	CR845	426	357 (83.8)	-5.4 (5.1)	-18	-5.0	9	-0.28 [-0.42, -0.13]
		Placebo	425	375 (88.2)	-4.1 (4.8)	-18	-3.0	8	
	Week 12	CR845	426	358 (84.0)	-5.8 (5.4)	-18	-6.0	9	-0.27 [-0.42, -0.12]
		Placebo	425	375 (88.2)	-4.4 (4.9)	-18	-4.0	12	

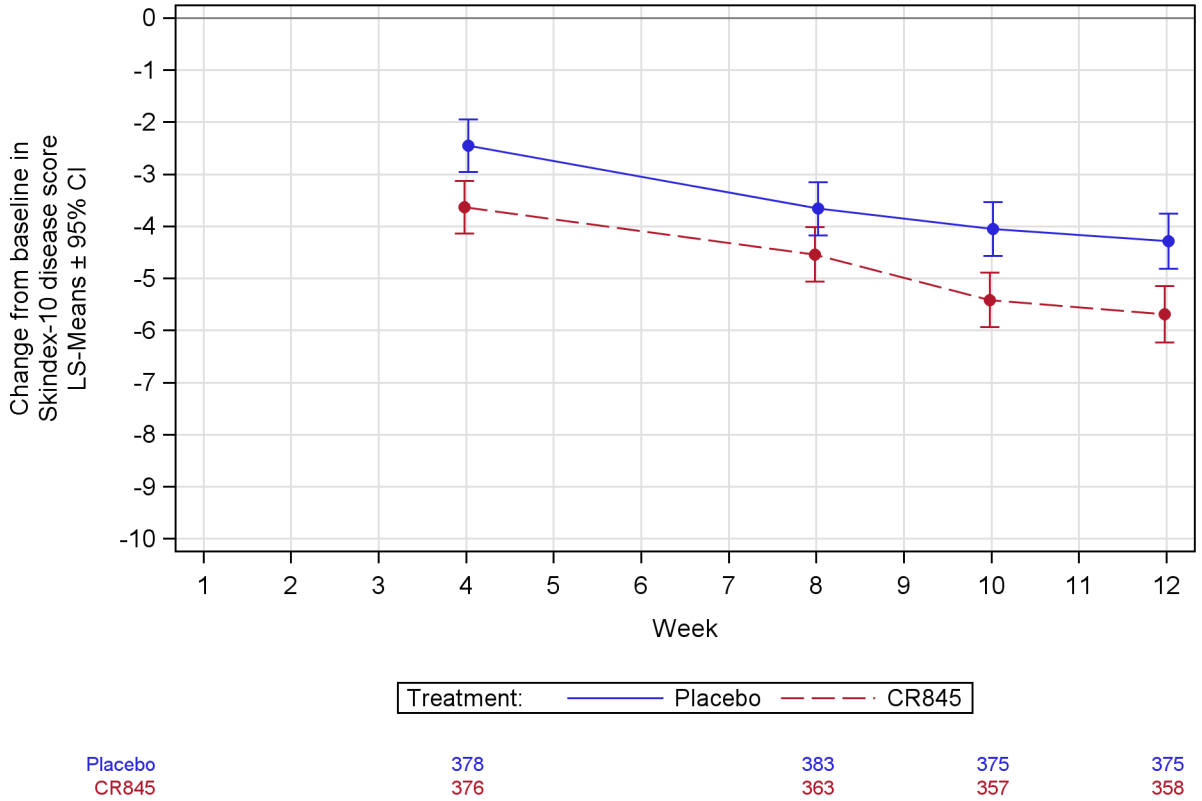
Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SDC_IMC0: Change from baseline in Skindex-10 disease score - MMRM results
ITT

Change from baseline in Skindex-10 disease score				Repeated measures analysis				
				Change from Baseline		Treatment Difference		
Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Week 4	CR845	426	376 (88.3)	-3.6 (0.3)	(-4.1, -3.1)	-1.2 (0.3)	(-1.8, -0.6)	<0.001 *
	Placebo	425	378 (88.9)	-2.5 (0.3)	(-3.0, -1.9)			
Week 8	CR845	426	363 (85.2)	-4.5 (0.3)	(-5.1, -4.0)	-0.9 (0.3)	(-1.5, -0.2)	0.007 *
	Placebo	425	383 (90.1)	-3.7 (0.3)	(-4.2, -3.1)			
Week 10	CR845	426	357 (83.8)	-5.4 (0.3)	(-5.9, -4.9)	-1.4 (0.3)	(-2.0, -0.7)	<0.001 *
	Placebo	425	375 (88.2)	-4.0 (0.3)	(-4.6, -3.5)			
Week 12	CR845	426	358 (84.0)	-5.7 (0.3)	(-6.2, -5.2)	-1.4 (0.3)	(-2.1, -0.7)	<0.001 *
	Placebo	425	375 (88.2)	-4.3 (0.3)	(-4.8, -3.8)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval . * = significant treatment effect.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin_i, created on: 17FEB2022

Figure IF2SDC_IMG0: Course of change from baseline in Skindex-10 disease score
ITT



Note: ITT = Intent-to-treat Set.
Symbols present least square mean (LS-Mean), bars present 95% confidence intervals (CI).
CR845 = Difelikefalin.
Source Table: IT2SDC_IMC0
Source Data: askin_i, created on: 17FEB2022

Table IT2SMC_IMH0: Change from baseline in Skindex-10 mood/emotional distress score
ITT

		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Skindex-10 mood/emotional distress score	Baseline	CR845	426	416 (97.7)	11.5 (4.8)	0	12.0	18	
		Placebo	425	420 (98.8)	11.4 (5.0)	0	12.0	18	
	Week 4	CR845	426	381 (89.4)	8.0 (5.3)	0	8.0	18	
		Placebo	425	385 (90.6)	8.9 (5.4)	0	9.0	18	
	Week 8	CR845	426	363 (85.2)	6.9 (5.5)	0	6.0	18	
		Placebo	425	386 (90.8)	7.7 (5.5)	0	7.5	18	
	Week 10	CR845	426	360 (84.5)	6.1 (5.4)	0	5.0	18	
		Placebo	425	380 (89.4)	7.5 (5.4)	0	7.0	18	
	Week 12	CR845	426	364 (85.4)	5.9 (5.3)	0	5.0	18	
		Placebo	425	382 (89.9)	7.0 (5.6)	0	6.0	18	
Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	426	373 (87.6)	-3.5 (5.2)	-18	-3.0	14	-0.20 [-0.34, -0.05]
		Placebo	425	380 (89.4)	-2.5 (5.1)	-17	-2.0	17	
	Week 8	CR845	426	355 (83.3)	-4.6 (5.4)	-18	-4.0	14	-0.17 [-0.32, -0.03]
		Placebo	425	382 (89.9)	-3.7 (5.1)	-18	-3.0	15	
	Week 10	CR845	426	353 (82.9)	-5.4 (5.3)	-18	-5.0	11	-0.28 [-0.43, -0.14]
		Placebo	425	376 (88.5)	-3.9 (5.4)	-18	-3.0	13	
	Week 12	CR845	426	357 (83.8)	-5.7 (5.5)	-18	-6.0	13	-0.23 [-0.38, -0.09]
		Placebo	425	378 (88.9)	-4.4 (5.5)	-18	-4.0	14	

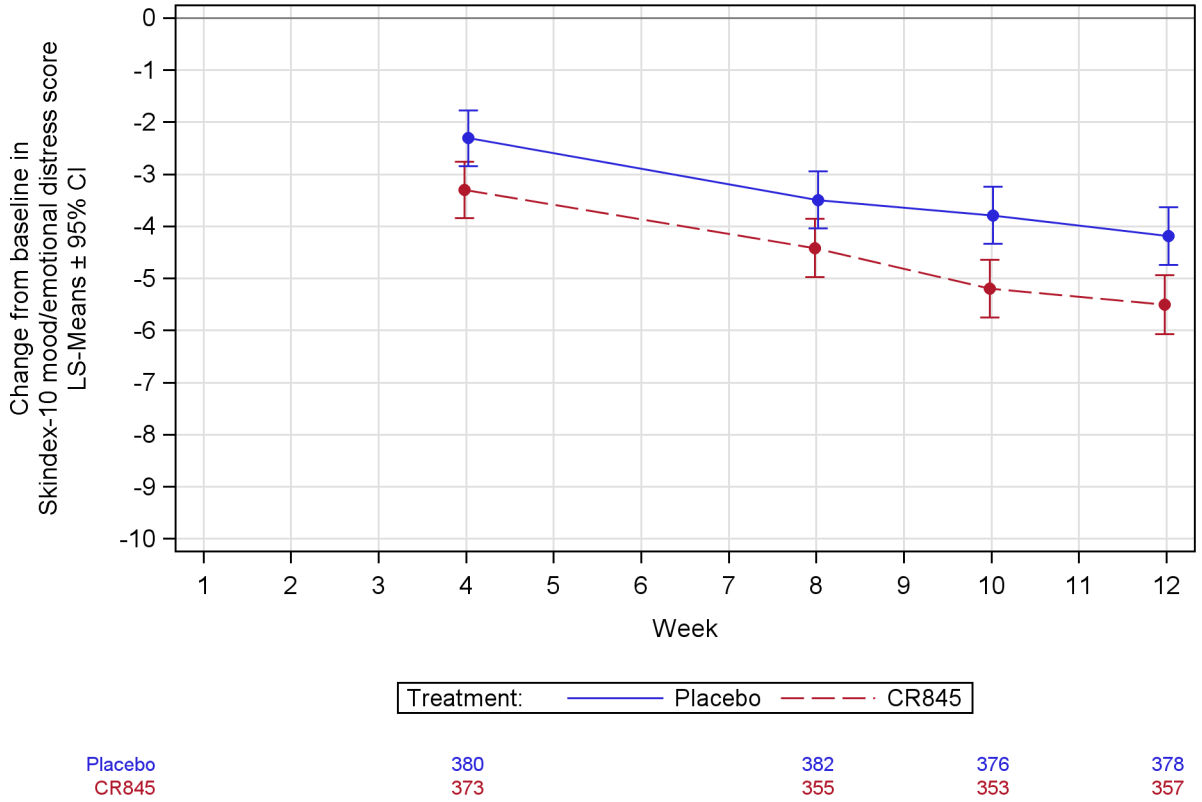
Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SMC_IMC0: Change from baseline in Skindex-10 mood/emotional distress score - MMRM results
ITT

Change from baseline in Skindex-10 mood/emotional distress score				Repeated measures analysis				
				Change from Baseline		Treatment Difference		
Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Week 4	CR845	426	373 (87.6)	-3.3 (0.3)	(-3.8, -2.8)	-1.0 (0.3)	(-1.7, -0.3)	0.003 *
	Placebo	425	380 (89.4)	-2.3 (0.3)	(-2.8, -1.8)			
Week 8	CR845	426	355 (83.3)	-4.4 (0.3)	(-5.0, -3.9)	-0.9 (0.3)	(-1.6, -0.2)	0.008 *
	Placebo	425	382 (89.9)	-3.5 (0.3)	(-4.0, -2.9)			
Week 10	CR845	426	353 (82.9)	-5.2 (0.3)	(-5.8, -4.6)	-1.4 (0.3)	(-2.1, -0.7)	<0.001 *
	Placebo	425	376 (88.5)	-3.8 (0.3)	(-4.3, -3.2)			
Week 12	CR845	426	357 (83.8)	-5.5 (0.3)	(-6.1, -4.9)	-1.3 (0.4)	(-2.0, -0.6)	<0.001 *
	Placebo	425	378 (88.9)	-4.2 (0.3)	(-4.7, -3.6)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval . * = significant treatment effect.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin_i, created on: 17FEB2022

Figure IF2SMC_IMG0: Course of change from baseline in Skindex-10 mood/emotional distress score
ITT



Placebo	380	382	376	378
CR845	373	355	353	357

Note: ITT = Intent-to-treat Set.
Symbols present least square mean (LS-Mean), bars present 95% confidence intervals (CI).
CR845 = Difelikefalin.
Source Table: IT2SMC_IMC0
Source Data: askin_i, created on: 17FEB2022

Table IT2SSC_IMH0: Change from baseline in Skindex-10 social functioning score
ITT

		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Skindex-10 social functioning score	Baseline	CR845	426	419 (98.4)	11.3 (7.8)	0	11.0	24	
		Placebo	425	419 (98.6)	11.7 (7.9)	0	12.0	24	
	Week 4	CR845	426	381 (89.4)	7.9 (7.3)	0	6.0	24	
		Placebo	425	387 (91.1)	8.6 (7.6)	0	7.0	24	
	Week 8	CR845	426	364 (85.4)	6.9 (7.1)	0	5.0	24	
		Placebo	425	389 (91.5)	7.8 (7.6)	0	6.0	24	
	Week 10	CR845	426	363 (85.2)	6.2 (7.1)	0	4.0	24	
		Placebo	425	380 (89.4)	7.4 (7.4)	0	5.0	24	
	Week 12	CR845	426	363 (85.2)	6.1 (6.9)	0	4.0	24	
		Placebo	425	382 (89.9)	7.0 (7.3)	0	4.5	24	
Change from baseline in Skindex-10 social functioning score	Week 4	CR845	426	376 (88.3)	-3.4 (6.9)	-24	-3.0	19	-0.03 [-0.17, 0.12]
		Placebo	425	383 (90.1)	-3.2 (7.3)	-24	-2.0	23	
	Week 8	CR845	426	359 (84.3)	-4.4 (7.1)	-24	-4.0	24	-0.08 [-0.22, 0.07]
		Placebo	425	385 (90.6)	-3.8 (7.4)	-24	-3.0	22	
	Week 10	CR845	426	359 (84.3)	-4.8 (7.0)	-24	-4.0	20	-0.10 [-0.25, 0.04]
		Placebo	425	375 (88.2)	-4.1 (7.7)	-24	-3.0	22	
	Week 12	CR845	426	359 (84.3)	-5.1 (7.4)	-24	-5.0	20	-0.07 [-0.21, 0.08]
		Placebo	425	378 (88.9)	-4.6 (7.6)	-24	-3.0	24	

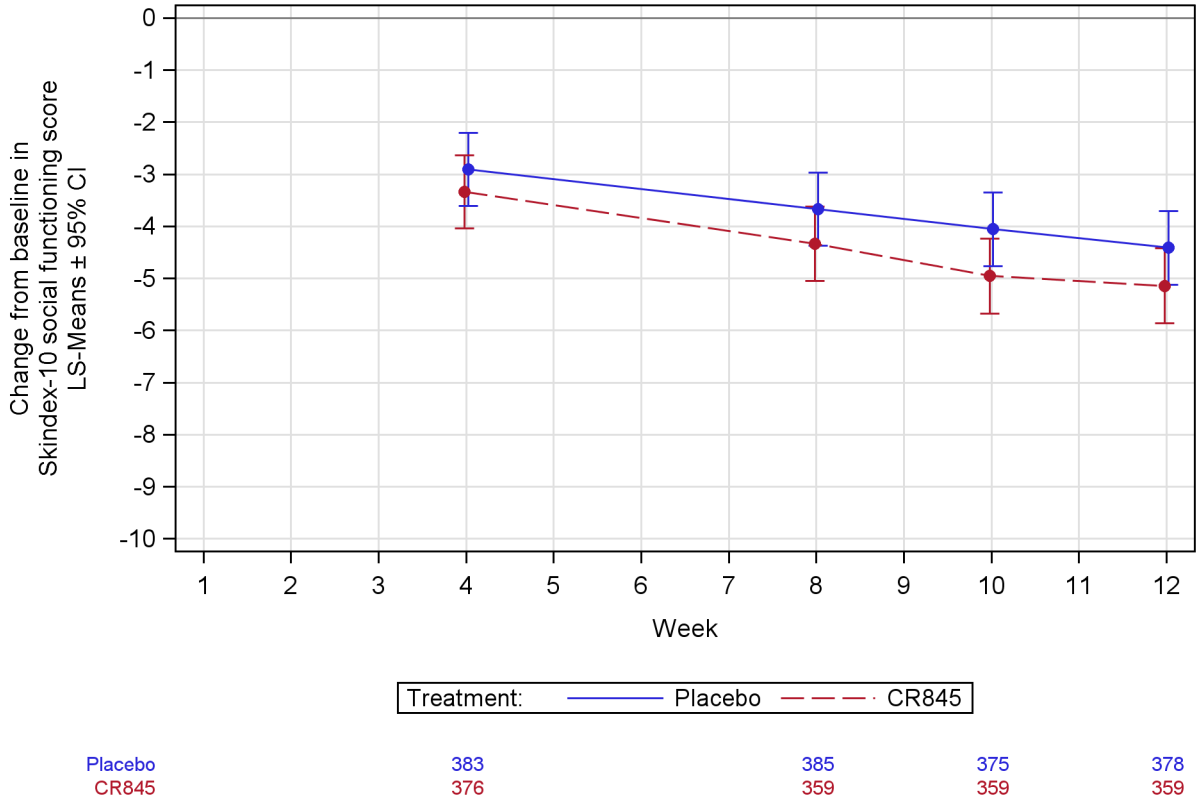
Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SSC_IMC0: Change from baseline in Skindex-10 social functioning score - MMRM results
ITT

Change from baseline in Skindex-10 social functioning score				Repeated measures analysis				
				Change from Baseline		Treatment Difference		
Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Week 4	CR845	426	376 (88.3)	-3.3 (0.4)	(-4.0, -2.6)	-0.4 (0.4)	(-1.3, 0.4)	0.326
	Placebo	425	383 (90.1)	-2.9 (0.4)	(-3.6, -2.2)			
Week 8	CR845	426	359 (84.3)	-4.3 (0.4)	(-5.0, -3.6)	-0.7 (0.4)	(-1.5, 0.2)	0.133
	Placebo	425	385 (90.6)	-3.7 (0.4)	(-4.4, -3.0)			
Week 10	CR845	426	359 (84.3)	-5.0 (0.4)	(-5.7, -4.2)	-0.9 (0.4)	(-1.8, -0.0)	0.043 *
	Placebo	425	375 (88.2)	-4.1 (0.4)	(-4.8, -3.3)			
Week 12	CR845	426	359 (84.3)	-5.1 (0.4)	(-5.9, -4.4)	-0.7 (0.4)	(-1.6, 0.1)	0.100
	Placebo	425	378 (88.9)	-4.4 (0.4)	(-5.1, -3.7)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval . * = significant treatment effect.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin_i, created on: 17FEB2022

Figure IF2SSC_IMG0: Course of change from baseline in Skindex-10 social functioning score
ITT



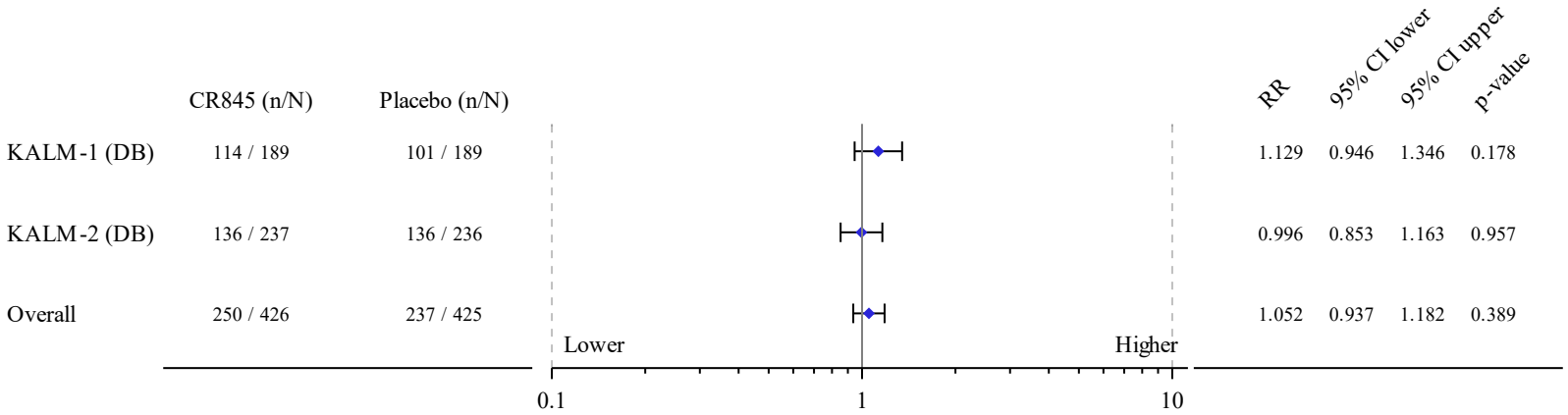
Note: ITT = Intent-to-treat Set.
Symbols present least square mean (LS-Mean), bars present 95% confidence intervals (CI).
CR845 = Difelikefalin.
Source Table: IT2SSC_IMC0
Source Data: askin_i, created on: 17FEB2022

Table IT2SDCD3_IMP0: Decrease of Skindex-10 disease score of at least 3 points
ITT

		CR845			Placebo						
Variable	Time	N	nval	n (%) [95 % CI]	N	nval	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Decrease of Skindex-10 disease score of at least 3 points	Week 12	426	358 (84.0)	250 (58.7) [53.8, 63.4]	425	375 (88.2)	237 (55.8) [50.9, 60.5]	1.052 [0.937, 1.182]	1.127 [0.859, 1.479]	2.9 [-4.0, 9.8]	0.389

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: askin_i, created on: 11FEB2022

Figure IF2SDCD3_IMFR0: Forest plot for decrease of Skindex-10 disease score of at least 3 points - relative risk
ITT



Test for heterogeneity - pvalue: 0.295, I-square: 8.7 %

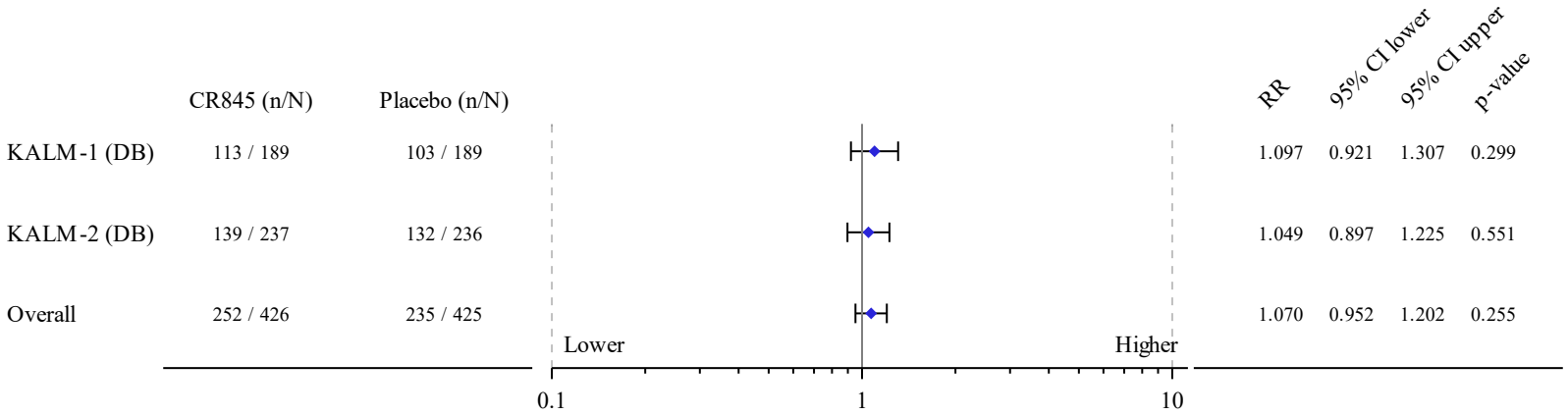
Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. RR = relative risk. CI = confidence interval.
Heterogeneity was investigated with Cochran Q test. NE = not evaluable.
Source tables: AT2SDCD3_IMP0, BT2SDCD3_IMP0, IT2SDCD3_IMP0

Table IT2SMCD3_IMP0: Decrease of Skindex-10 mood/emotional distress score of at least 3 points
ITT

		CR845			Placebo						
Variable	Time	N	nval	n (%) [95 % CI]	N	nval	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Decrease of Skindex-10 mood/emotional distress score of at least 3 points	Week 12	426	357 (83.8)	252 (59.2) [54.3, 63.9]	425	378 (88.9)	235 (55.3) [50.4, 60.1]	1.070 [0.952, 1.202]	1.171 [0.892, 1.537]	3.9 [-3.0, 10.7]	0.255

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: askin_i, created on: 11FEB2022

Figure IF2SMCD3_IMFR0: Forest plot for decrease of Skindex-10 mood/emotional distress score of at least 3 points - relative risk
ITT



Test for heterogeneity - pvalue: 0.705, I-square: 0.0 %

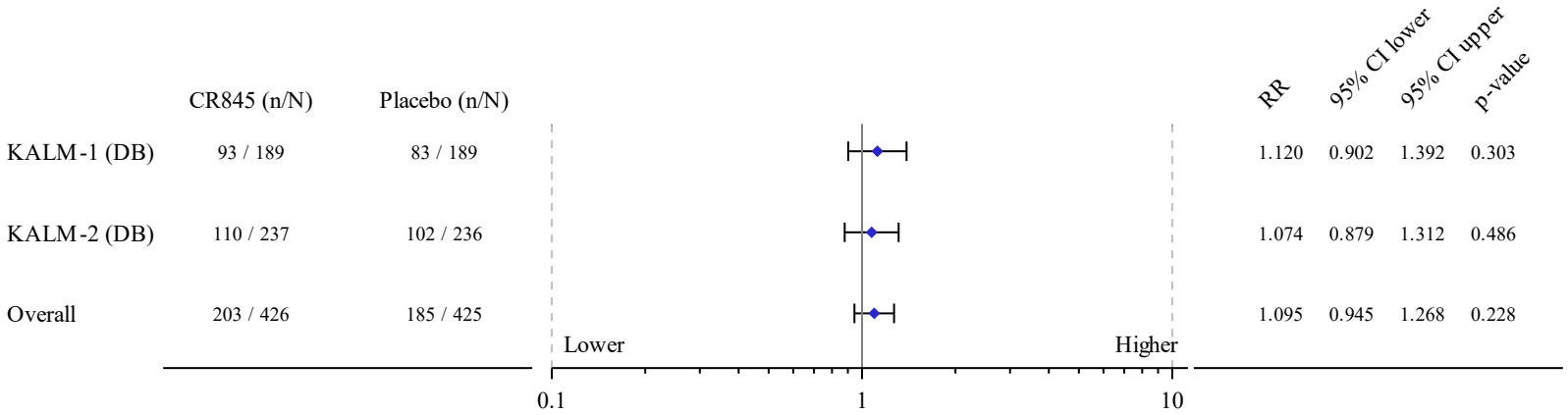
Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. RR = relative risk. CI = confidence interval.
Heterogeneity was investigated with Cochran Q test. NE = not evaluable.
Source tables: AT2SMCD3_IMP0, BT2SMCD3_IMP0, IT2SMCD3_IMP0

Table IT2SSCD4_IMP0: Decrease of Skindex-10 social functioning score of at least 4 points
ITT

		CR845			Placebo						
Variable	Time	N	nval	n (%) [95 % CI]	N	nval	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Decrease of Skindex-10 social functioning score of at least 4 points	Week 12	426	359 (84.3)	203 (47.7) [42.8, 52.5]	425	378 (88.9)	185 (43.5) [38.8, 48.4]	1.095 [0.945, 1.268]	1.181 [0.901, 1.547]	4.1 [-2.8, 11.0]	0.228

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: askin_i, created on: 11FEB2022

Figure IF2SSCD4_IMFR0: Forest plot for decrease of Skindex-10 social functioning score of at least 4 points - relative risk
ITT



Test for heterogeneity - pvalue: 0.778, I-square: 0.0 %

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. RR = relative risk. CI = confidence interval.
Heterogeneity was investigated with Cochran Q test. NE = not evaluable.
Source tables: AT2SSCD4_IMP0, BT2SSCD4_IMP0, IT2SSCD4_IMP0

Table IT2A_SMS0: TEAEs by SOC and PT
SAF-S

	CR845		Placebo					
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
SOC: Blood and lymphatic system disorders	424	9 (2.1) [1.0, 4.0]	424	11 (2.6) [1.3, 4.6]	0.818 [0.343, 1.954]	0.814 [0.334, 1.986]	-0.5 [-2.8, 1.8]	0.651
SOC: Cardiac disorders	424	31 (7.3) [5.0, 10.2]	424	27 (6.4) [4.2, 9.1]	1.148 [0.698, 1.889]	1.160 [0.680, 1.979]	0.9 [-2.7, 4.6]	0.587
SOC: Gastrointestinal disorders	424	104 (24.5) [20.5, 28.9]	424	73 (17.2) [13.7, 21.2]	1.425 [1.091, 1.861]	1.563 [1.117, 2.185]	7.3 [1.6, 13.0]	0.009 *
Constipation	424	11 (2.6) [1.3, 4.6]	424	7 (1.7) [0.7, 3.4]	1.571 [0.615, 4.015]	1.587 [0.609, 4.133]	0.9 [-1.2, 3.1]	0.341
Diarrhoea	424	37 (8.7) [6.2, 11.8]	424	20 (4.7) [2.9, 7.2]	1.850 [1.092, 3.134]	1.931 [1.101, 3.386]	4.0 [0.4, 7.6]	0.020 *
Nausea	424	21 (5.0) [3.1, 7.5]	424	19 (4.5) [2.7, 6.9]	1.105 [0.603, 2.026]	1.111 [0.588, 2.097]	0.5 [-2.6, 3.6]	0.746
Vomiting	424	25 (5.9) [3.9, 8.6]	424	20 (4.7) [2.9, 7.2]	1.250 [0.705, 2.216]	1.266 [0.692, 2.316]	1.2 [-2.1, 4.4]	0.444
SOC: General disorders and administration site conditions	424	62 (14.6) [11.4, 18.4]	424	46 (10.8) [8.1, 14.2]	1.348 [0.943, 1.926]	1.407 [0.936, 2.116]	3.8 [-0.9, 8.5]	0.100
Asthenia	424	11 (2.6) [1.3, 4.6]	424	9 (2.1) [1.0, 4.0]	1.222 [0.512, 2.919]	1.228 [0.504, 2.995]	0.5 [-1.8, 2.8]	0.651
Chest pain	424	13 (3.1) [1.6, 5.2]	424	8 (1.9) [0.8, 3.7]	1.625 [0.681, 3.880]	1.645 [0.675, 4.010]	1.2 [-1.1, 3.5]	0.270
SOC: Infections and infestations	424	91 (21.5) [17.6, 25.7]	424	82 (19.3) [15.7, 23.4]	1.110 [0.850, 1.448]	1.140 [0.816, 1.592]	2.1 [-3.5, 7.8]	0.443
Nasopharyngitis	424	9 (2.1) [1.0, 4.0]	424	15 (3.5) [2.0, 5.8]	0.600 [0.265, 1.356]	0.591 [0.256, 1.366]	-1.4 [-3.9, 1.1]	0.214
Pneumonia	424	10 (2.4) [1.1, 4.3]	424	7 (1.7) [0.7, 3.4]	1.429 [0.549, 3.718]	1.439 [0.543, 3.816]	0.7 [-1.4, 2.8]	0.463
SOC: Injury, poisoning and procedural complications	424	64 (15.1) [11.8, 18.9]	424	74 (17.5) [14.0, 21.4]	0.865 [0.637, 1.175]	0.841 [0.583, 1.212]	-2.4 [-7.6, 2.8]	0.352

Note: SAF-S = Week 12 Safety Set. Only events are displayed with an incidence of at least 10 percent in a treatment group or 10 patients with an incidence of at least 1 percent in a treatment group.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 31JAN2022

Table IT2A_SMS0: TEAEs by SOC and PT
SAF-S

	CR845		Placebo					
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Fall	424	21 (5.0) [3.1, 7.5]	424	17 (4.0) [2.4, 6.3]	1.235 [0.661, 2.308]	1.248 [0.649, 2.400]	0.9 [-2.1, 4.0]	0.507
SOC: Investigations	424	18 (4.2) [2.5, 6.6]	424	20 (4.7) [2.9, 7.2]	0.900 [0.483, 1.677]	0.896 [0.467, 1.718]	-0.5 [-3.5, 2.5]	0.740
SOC: Metabolism and nutrition disorders	424	37 (8.7) [6.2, 11.8]	424	42 (9.9) [7.2, 13.2]	0.881 [0.578, 1.342]	0.870 [0.547, 1.383]	-1.2 [-5.3, 3.0]	0.555
Hyperkalaemia	424	17 (4.0) [2.4, 6.3]	424	11 (2.6) [1.3, 4.6]	1.545 [0.733, 3.260]	1.568 [0.726, 3.389]	1.4 [-1.2, 4.1]	0.249
SOC: Musculoskeletal and connective tissue disorders	424	51 (12.0) [9.1, 15.5]	424	39 (9.2) [6.6, 12.4]	1.308 [0.881, 1.940]	1.350 [0.869, 2.097]	2.8 [-1.5, 7.2]	0.181
Back pain	424	10 (2.4) [1.1, 4.3]	424	4 (0.9) [0.3, 2.4]	2.500 [0.790, 7.909]	2.536 [0.789, 8.151]	1.4 [-0.5, 3.4]	0.106
Muscle spasms	424	11 (2.6) [1.3, 4.6]	424	8 (1.9) [0.8, 3.7]	1.375 [0.559, 3.384]	1.385 [0.551, 3.478]	0.7 [-1.5, 2.9]	0.487
Pain in extremity	424	14 (3.3) [1.8, 5.5]	424	9 (2.1) [1.0, 4.0]	1.556 [0.681, 3.555]	1.575 [0.674, 3.678]	1.2 [-1.2, 3.6]	0.291
SOC: Nervous system disorders	424	80 (18.9) [15.3, 22.9]	424	56 (13.2) [10.1, 16.8]	1.429 [1.044, 1.955]	1.528 [1.054, 2.216]	5.7 [0.5, 10.8]	0.025 *
Dizziness	424	26 (6.1) [4.0, 8.9]	424	14 (3.3) [1.8, 5.5]	1.857 [0.984, 3.507]	1.913 [0.985, 3.717]	2.8 [-0.3, 5.9]	0.052
Headache	424	17 (4.0) [2.4, 6.3]	424	10 (2.4) [1.1, 4.3]	1.700 [0.788, 3.669]	1.729 [0.782, 3.822]	1.7 [-0.9, 4.2]	0.171
Somnolence	424	17 (4.0) [2.4, 6.3]	424	9 (2.1) [1.0, 4.0]	1.889 [0.852, 4.190]	1.926 [0.849, 4.371]	1.9 [-0.7, 4.4]	0.111
SOC: Psychiatric disorders	424	33 (7.8) [5.4, 10.8]	424	21 (5.0) [3.1, 7.5]	1.571 [0.925, 2.671]	1.620 [0.921, 2.848]	2.8 [-0.7, 6.3]	0.092
SOC: Respiratory, thoracic and mediastinal disorders	424	53 (12.5) [9.5, 16.0]	424	43 (10.1) [7.4, 13.4]	1.233 [0.844, 1.801]	1.266 [0.826, 1.940]	2.4 [-2.1, 6.9]	0.279

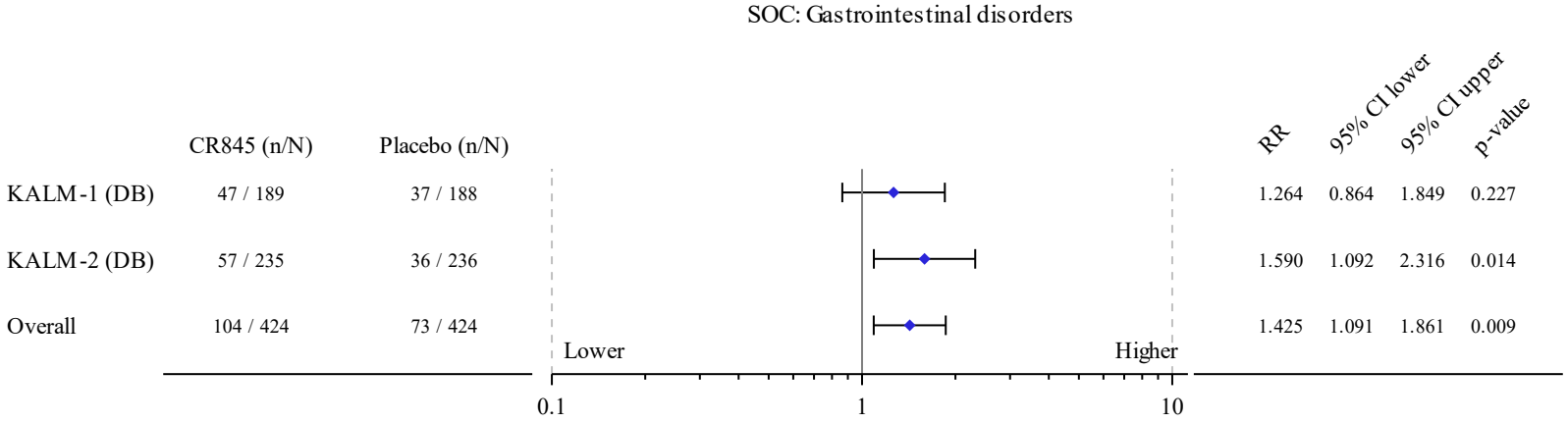
Note: SAF-S = Week 12 Safety Set. Only events are displayed with an incidence of at least 10 percent in a treatment group or 10 patients with an incidence of at least 1 percent in a treatment group.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 31JAN2022

Table IT2A_SMS0: TEAEs by SOC and PT
SAF-S

	CR845		Placebo					
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Cough	424	11 (2.6) [1.3, 4.6]	424	9 (2.1) [1.0, 4.0]	1.222 [0.512, 2.919]	1.228 [0.504, 2.995]	0.5 [-1.8, 2.8]	0.651
Dyspnoea	424	13 (3.1) [1.6, 5.2]	424	13 (3.1) [1.6, 5.2]	1.000 [0.469, 2.132]	1.000 [0.458, 2.183]	0.0 [-2.6, 2.6]	1.000
SOC: Skin and subcutaneous tissue disorders	424	16 (3.8) [2.2, 6.1]	424	21 (5.0) [3.1, 7.5]	0.762 [0.403, 1.440]	0.753 [0.387, 1.463]	-1.2 [-4.2, 1.8]	0.401
SOC: Vascular disorders	424	44 (10.4) [7.6, 13.7]	424	42 (9.9) [7.2, 13.2]	1.048 [0.702, 1.564]	1.053 [0.674, 1.645]	0.5 [-3.8, 4.8]	0.820
Hypertension	424	13 (3.1) [1.6, 5.2]	424	16 (3.8) [2.2, 6.1]	0.813 [0.396, 1.668]	0.807 [0.383, 1.698]	-0.7 [-3.4, 2.0]	0.571
Hypotension	424	18 (4.2) [2.5, 6.6]	424	14 (3.3) [1.8, 5.5]	1.286 [0.648, 2.551]	1.298 [0.637, 2.646]	0.9 [-1.9, 3.7]	0.471

Note: SAF-S = Week 12 Safety Set. Only events are displayed with an incidence of at least 10 percent in a treatment group or 10 patients with an incidence of at least 1 percent in a treatment group.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 31JAN2022

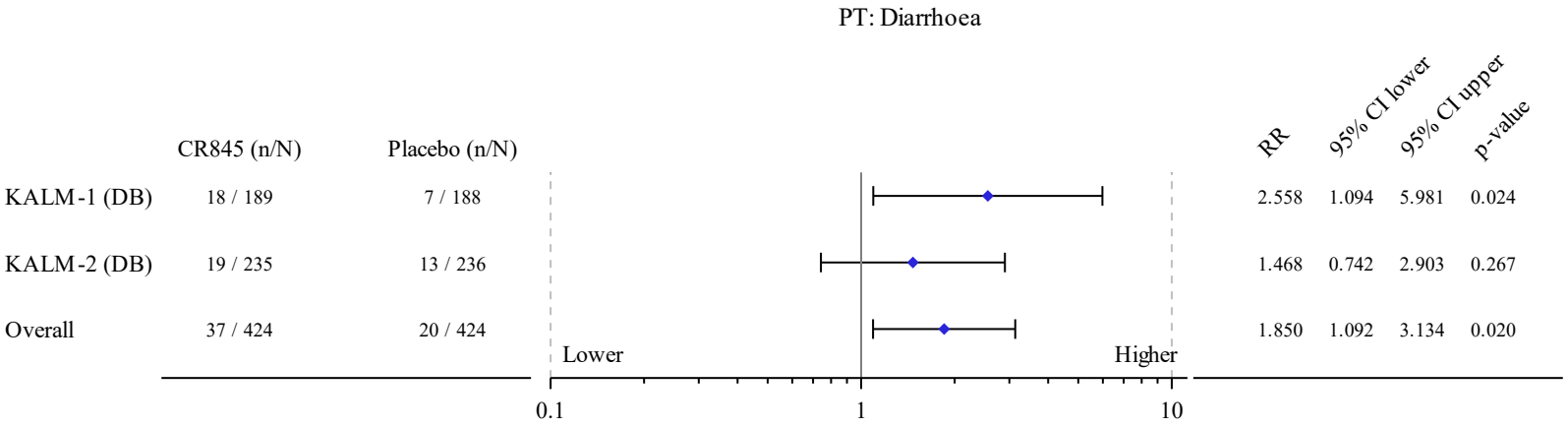
Figure IF2A_SMVR0: Forest plot for TEAEs by SOC and PT - relative risk
SAF-S



Test for heterogeneity - pvalue: 0.400, I-square: 0.0 %

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with event. RR = relative risk. CI = confidence interval. TEAE = treatment emergent adverse event. SOC = system order class. PT = preferred term.
Heterogeneity was investigated with Cochran Q test. NE = not evaluable.
Source tables: AT2A_SMS0, BT2A_SMS0, IT2A_SMS0

Figure IF2A_SMVR0: Forest plot for TEAEs by SOC and PT - relative risk
SAF-S

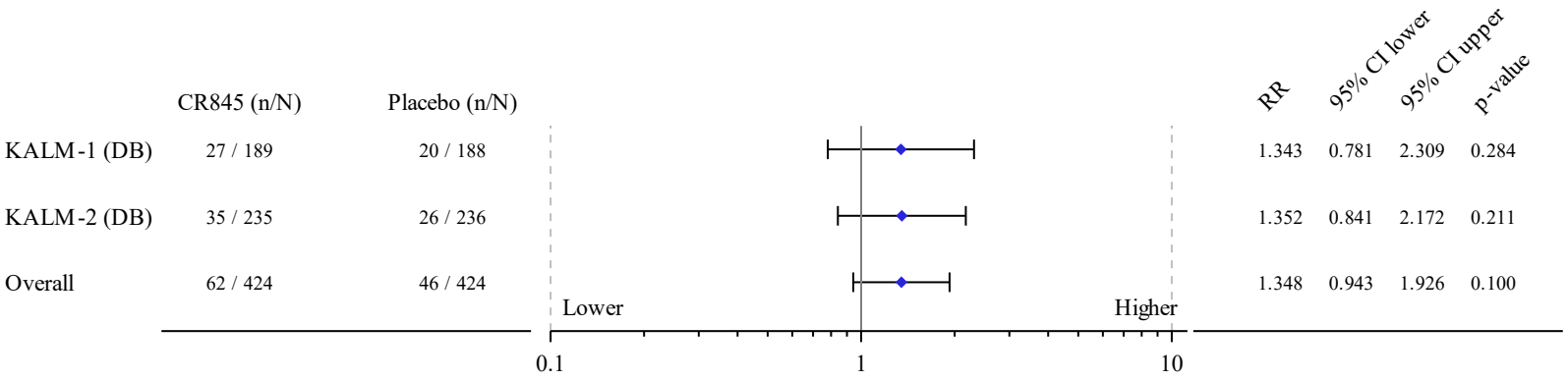


Test for heterogeneity - pvalue: 0.318, I-square: 0.0 %

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with event. RR = relative risk. CI = confidence interval. TEAE = treatment emergent adverse event. SOC = system order class. PT = preferred term.
Heterogeneity was investigated with Cochran Q test. NE = not evaluable.
Source tables: AT2A_SMS0, BT2A_SMS0, IT2A_SMS0

Figure IF2A_SMVR0: Forest plot for TEAEs by SOC and PT - relative risk
SAF-S

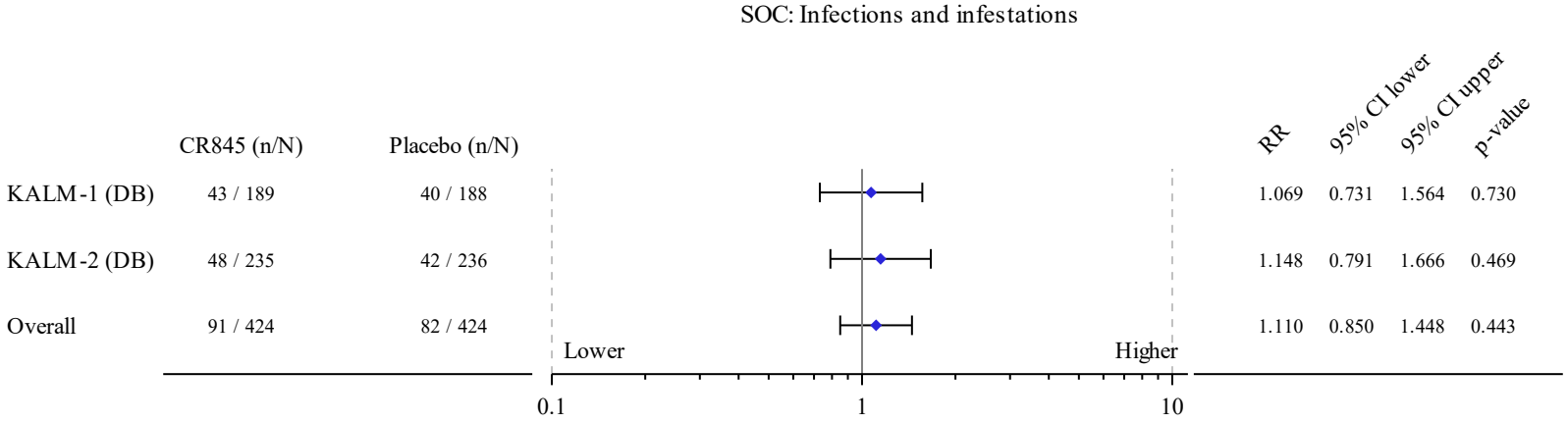
SOC: General disorders and administration site conditions



Test for heterogeneity - pvalue: 0.985, I-square: 0.0 %

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with event. RR = relative risk. CI = confidence interval. TEAE = treatment emergent adverse event. SOC = system order class. PT = preferred term.
Heterogeneity was investigated with Cochran Q test. NE = not evaluable.
Source tables: AT2A_SMS0, BT2A_SMS0, IT2A_SMS0

Figure IF2A_SMVR0: Forest plot for TEAEs by SOC and PT - relative risk
SAF-S

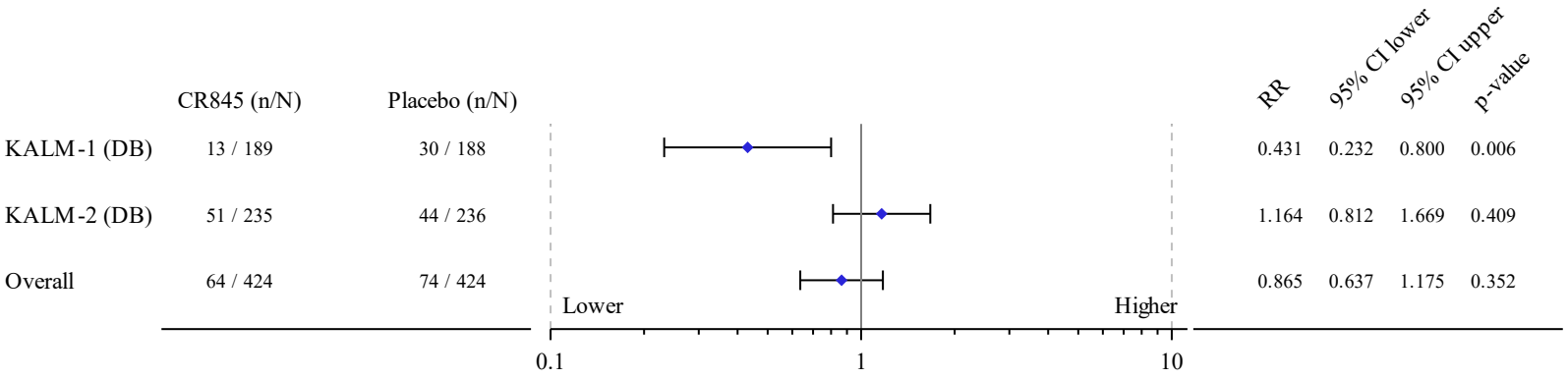


Test for heterogeneity - pvalue: 0.794, I-square: 0.0 %

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with event. RR = relative risk. CI = confidence interval. TEAE = treatment emergent adverse event. SOC = system order class. PT = preferred term.
Heterogeneity was investigated with Cochran Q test. NE = not evaluable.
Source tables: AT2A_SMS0, BT2A_SMS0, IT2A_SMS0

Figure IF2A_SMVR0: Forest plot for TEAEs by SOC and PT - relative risk
SAF-S

SOC: Injury, poisoning and procedural complications

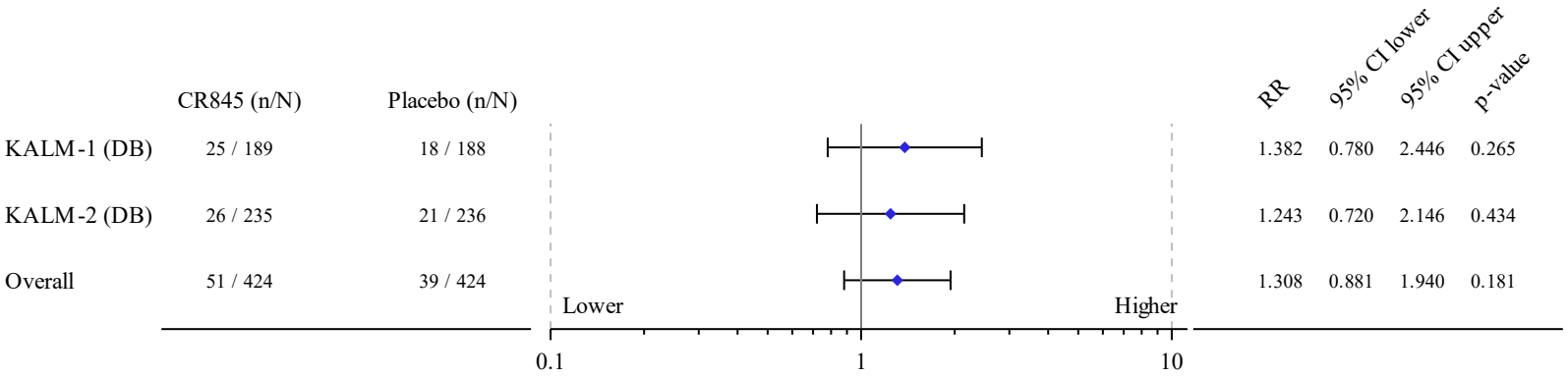


Test for heterogeneity - pvalue: 0.007, I-square: 86.5 %

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with event. RR = relative risk. CI = confidence interval. TEAE = treatment emergent adverse event. SOC = system order class. PT = preferred term.
Heterogeneity was investigated with Cochran Q test. NE = not evaluable.
Source tables: AT2A_SMS0, BT2A_SMS0, IT2A_SMS0

Figure IF2A_SMVR0: Forest plot for TEAEs by SOC and PT - relative risk
SAF-S

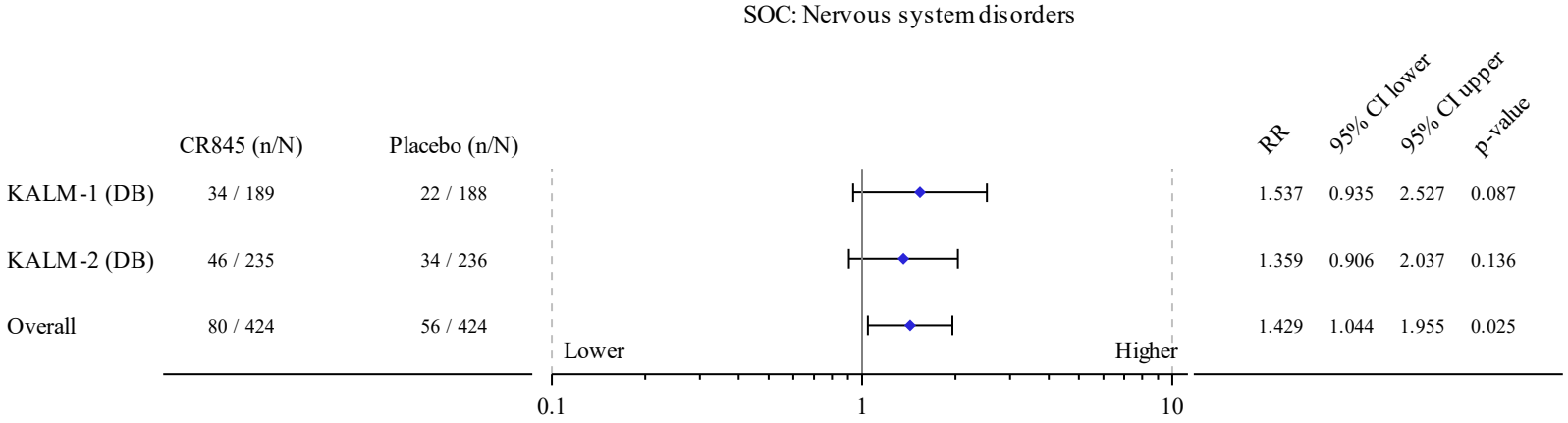
SOC: Musculoskeletal and connective tissue disorders



Test for heterogeneity - pvalue: 0.794, I-square: 0.0 %

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with event. RR = relative risk. CI = confidence interval. TEAE = treatment emergent adverse event. SOC = system order class. PT = preferred term.
Heterogeneity was investigated with Cochran Q test. NE = not evaluable.
Source tables: AT2A_SMS0, BT2A_SMS0, IT2A_SMS0

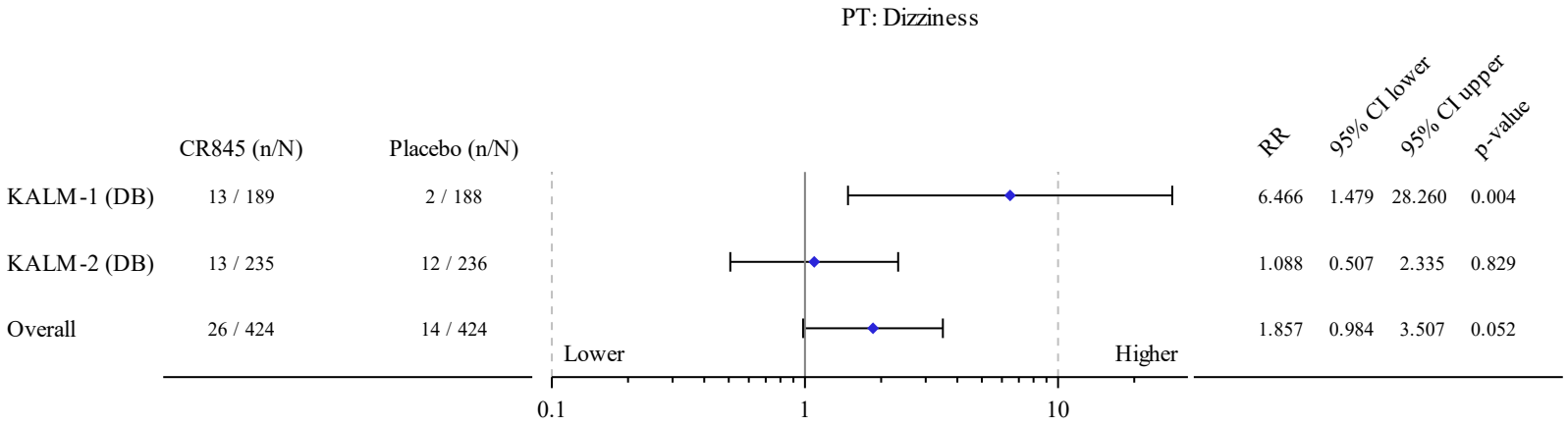
Figure IF2A_SMVR0: Forest plot for TEAEs by SOC and PT - relative risk
SAF-S



Test for heterogeneity - pvalue: 0.706, I-square: 0.0 %

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with event. RR = relative risk. CI = confidence interval. TEAE = treatment emergent adverse event. SOC = system order class. PT = preferred term.
Heterogeneity was investigated with Cochran Q test. NE = not evaluable.
Source tables: AT2A_SMS0, BT2A_SMS0, IT2A_SMS0

Figure IF2A_SMVR0: Forest plot for TEAEs by SOC and PT - relative risk
SAF-S

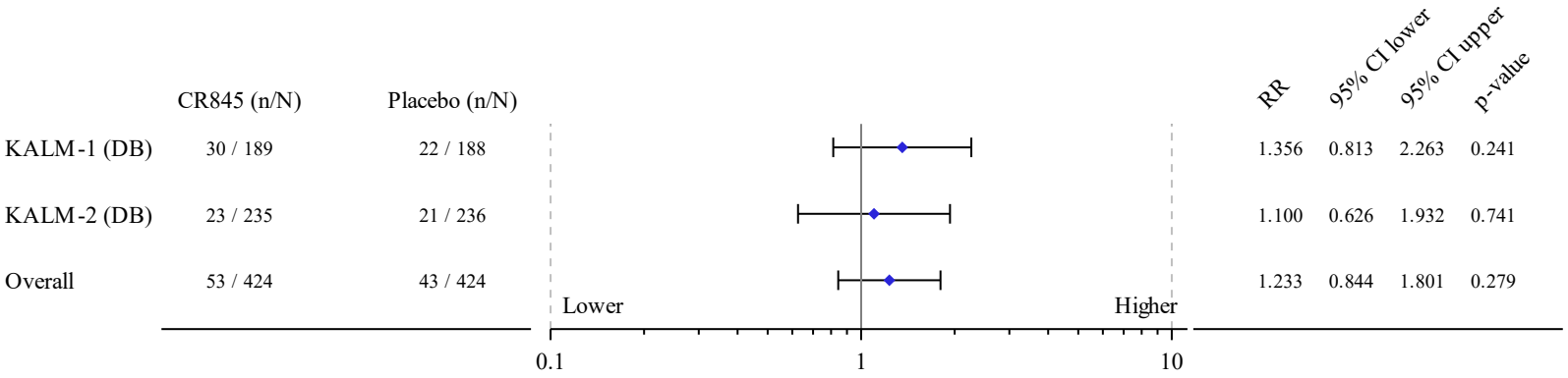


Test for heterogeneity - pvalue: 0.035, I-square: 77.4 %

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with event. RR = relative risk. CI = confidence interval. TEAE = treatment emergent adverse event. SOC = system order class. PT = preferred term.
Heterogeneity was investigated with Cochran Q test. NE = not evaluable.
Source tables: AT2A_SMS0, BT2A_SMS0, IT2A_SMS0

Figure IF2A_SMVR0: Forest plot for TEAEs by SOC and PT - relative risk
SAF-S

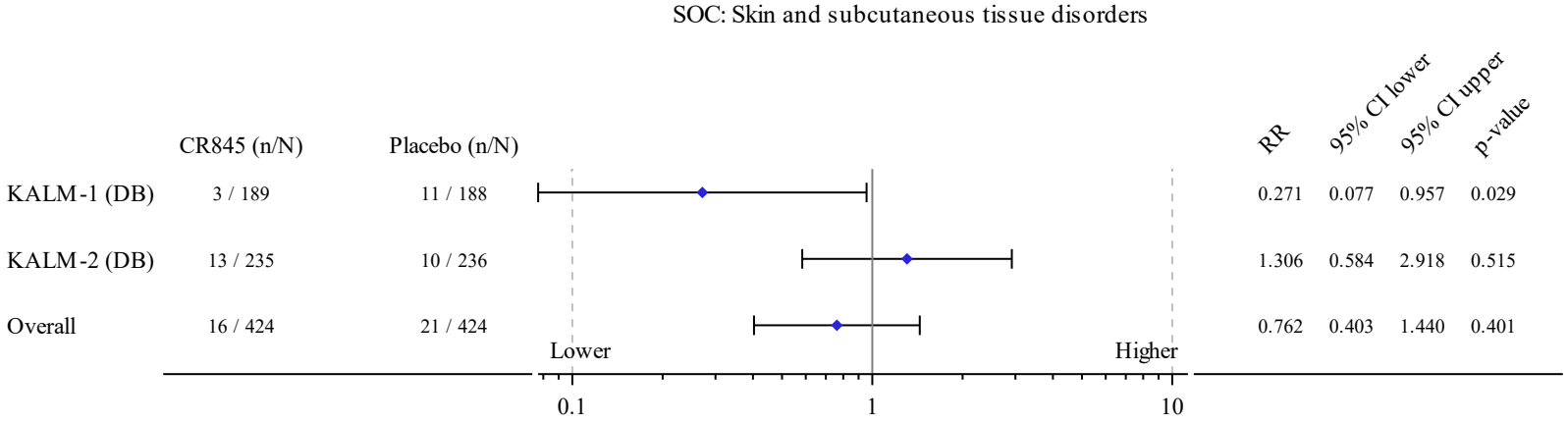
SOC: Respiratory, thoracic and mediastinal disorders



Test for heterogeneity - pvalue: 0.589, I-square: 0.0 %

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with event. RR = relative risk. CI = confidence interval. TEAE = treatment emergent adverse event. SOC = system order class. PT = preferred term.
Heterogeneity was investigated with Cochran Q test. NE = not evaluable.
Source tables: AT2A_SMS0, BT2A_SMS0, IT2A_SMS0

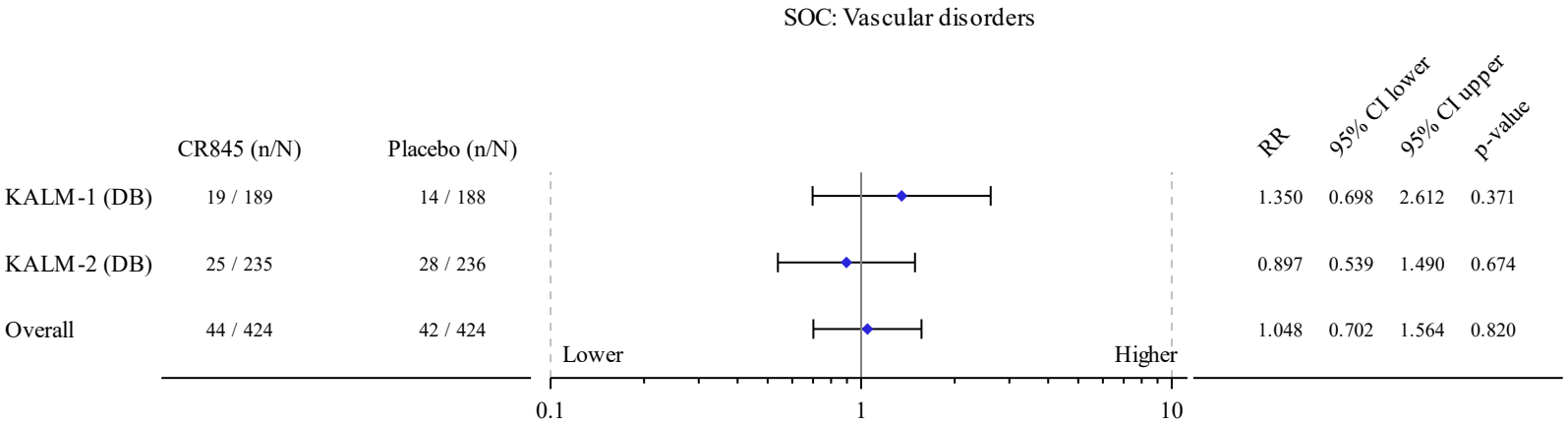
Figure IF2A_SMVR0: Forest plot for TEAEs by SOC and PT - relative risk
SAF-S



Test for heterogeneity - pvalue: 0.039, I-square: 76.4 %

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with event. RR = relative risk. CI = confidence interval. TEAE = treatment emergent adverse event. SOC = system order class. PT = preferred term.
Heterogeneity was investigated with Cochran Q test. NE = not evaluable.
Source tables: AT2A_SMS0, BT2A_SMS0, IT2A_SMS0

Figure IF2A_SMVR0: Forest plot for TEAEs by SOC and PT - relative risk
SAF-S



Test for heterogeneity - pvalue: 0.336, I-square: 0.0 %

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with event. RR = relative risk. CI = confidence interval. TEAE = treatment emergent adverse event. SOC = system order class. PT = preferred term.
Heterogeneity was investigated with Cochran Q test. NE = not evaluable.
Source tables: AT2A_SMS0, BT2A_SMS0, IT2A_SMS0

Table IT2AD_SMSD: Fatal TEAEs by SOC and PT
SAF-S

	CR845		Placebo	
Fatal TEAEs	N	n (%)	N	n (%)
SOC: Blood and lymphatic system disorders	424	1 (0.2)	424	0 (0.0)
Anaemia	424	1 (0.2)	424	0 (0.0)
SOC: Cardiac disorders	424	2 (0.5)	424	1 (0.2)
Cardiac arrest	424	1 (0.2)	424	1 (0.2)
Cardiac failure	424	1 (0.2)	424	0 (0.0)
Cardiopulmonary failure	424	1 (0.2)	424	0 (0.0)
SOC: Infections and infestations	424	2 (0.5)	424	2 (0.5)
Sepsis	424	1 (0.2)	424	0 (0.0)
Septic shock	424	0 (0.0)	424	2 (0.5)
Staphylococcal sepsis	424	1 (0.2)	424	0 (0.0)
SOC: Respiratory, thoracic and mediastinal disorders	424	0 (0.0)	424	1 (0.2)
Dyspnoea	424	0 (0.0)	424	1 (0.2)
SOC: Vascular disorders	424	0 (0.0)	424	1 (0.2)
Hypotension	424	0 (0.0)	424	1 (0.2)

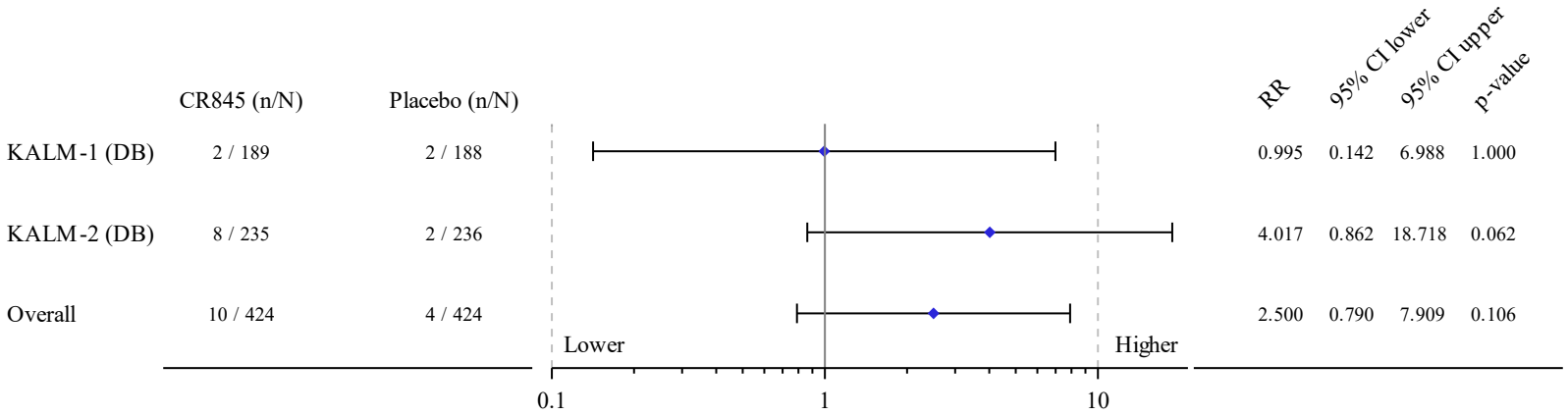
Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term.
Source Data: aae, created on: 31JAN2022

Table IT2AEGN_SMI0: Incidence of AESI gait disturbance - non-severe
SAF-S

	CR845		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
AESI gait disturbance - non-severe	424	10 (2.4) [1.1, 4.3]	424	4 (0.9) [0.3, 2.4]	2.500 [0.790, 7.909]	2.536 [0.789, 8.151]	1.4 [-0.5, 3.4]	0.106

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 31JAN2022

Figure IF2AEGN_SMFR0: Forest plot for incidence of AESI gait disturbance - non-severe - relative risk
SAF-S



Test for heterogeneity - pvalue: 0.271, I-square: 17.6 %

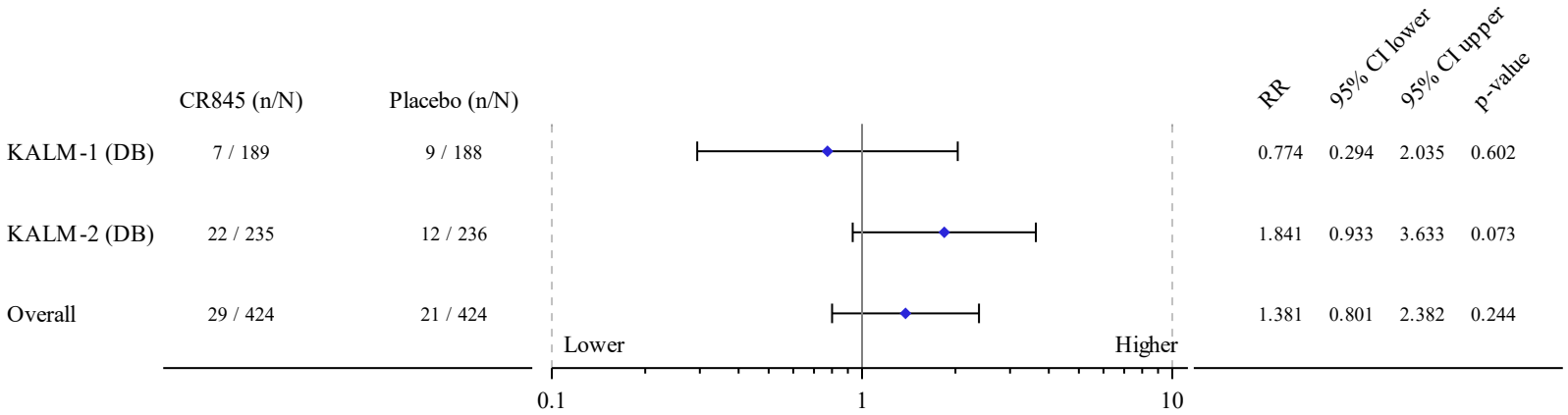
Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with event. RR = relative risk. CI = confidence interval. AESI = adverse event of special interest.
Heterogeneity was investigated with Cochran Q test. NE = not evaluable.
Source tables: AT2AEGN_SMI0, BT2AEGN_SMI0, IT2AEGN_SMI0

Table IT2AEFN_SMI0: Incidence of AESI falls/injuries - non-severe
SAF-S

	CR845		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
AESI falls/injuries - non-severe	424	29 (6.8) [4.6, 9.7]	424	21 (5.0) [3.1, 7.5]	1.381 [0.801, 2.382]	1.409 [0.790, 2.513]	1.9 [-1.5, 5.3]	0.244

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 31JAN2022

Figure IF2AEFN_SMFR0: Forest plot for incidence of AESI falls/injuries - non-severe - relative risk
SAF-S



Test for heterogeneity - pvalue: 0.151, I-square: 51.6 %

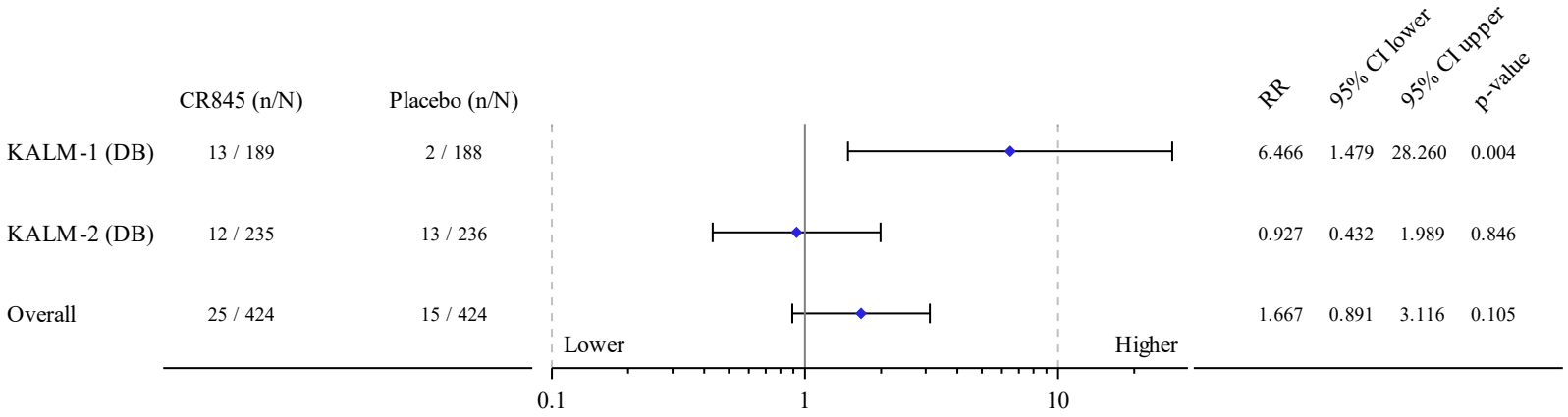
Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with event. RR = relative risk. CI = confidence interval. AESI = adverse event of special interest.
Heterogeneity was investigated with Cochran Q test. NE = not evaluable.
Source tables: AT2AEFN_SMI0, BT2AEFN_SMI0, IT2AEFN_SMI0

Table IT2AEVN_SMI0: Incidence of AESI dizziness - non-severe
SAF-S

	CR845		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
AESI dizziness - non-severe	424	25 (5.9) [3.9, 8.6]	424	15 (3.5) [2.0, 5.8]	1.667 [0.891, 3.116]	1.708 [0.888, 3.288]	2.4 [-0.7, 5.4]	0.105

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 31JAN2022

Figure IF2AEVN_SMFR0: Forest plot for incidence of AESI dizziness - non-severe - relative risk
SAF-S



Test for heterogeneity - pvalue: 0.022, I-square: 81.0 %

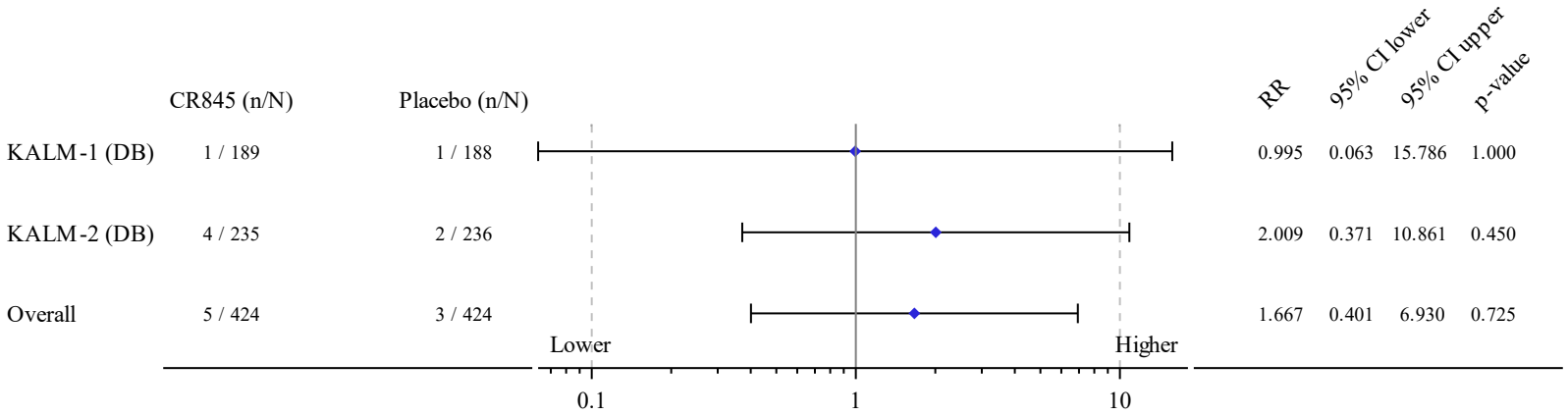
Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with event. RR = relative risk. CI = confidence interval. AESI = adverse event of special interest.
Heterogeneity was investigated with Cochran Q test. NE = not evaluable.
Source tables: AT2AEVN_SMI0, BT2AEVN_SMI0, IT2AEVN_SMI0

Table IT2AEYN_SMI0: Incidence of AESI syncope - non-severe
SAF-S

	CR845		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
AESI syncope - non-severe	424	5 (1.2) [0.4, 2.7]	424	3 (0.7) [0.1, 2.1]	1.667 [0.401, 6.930]	1.675 [0.398, 7.052]	0.5 [-1.1, 2.0]	0.725 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 31JAN2022

Figure IF2AEYN_SMFR0: Forest plot for incidence of AESI syncope - non-severe - relative risk
SAF-S



Test for heterogeneity - pvalue: 0.671, I-square: 0.0 %

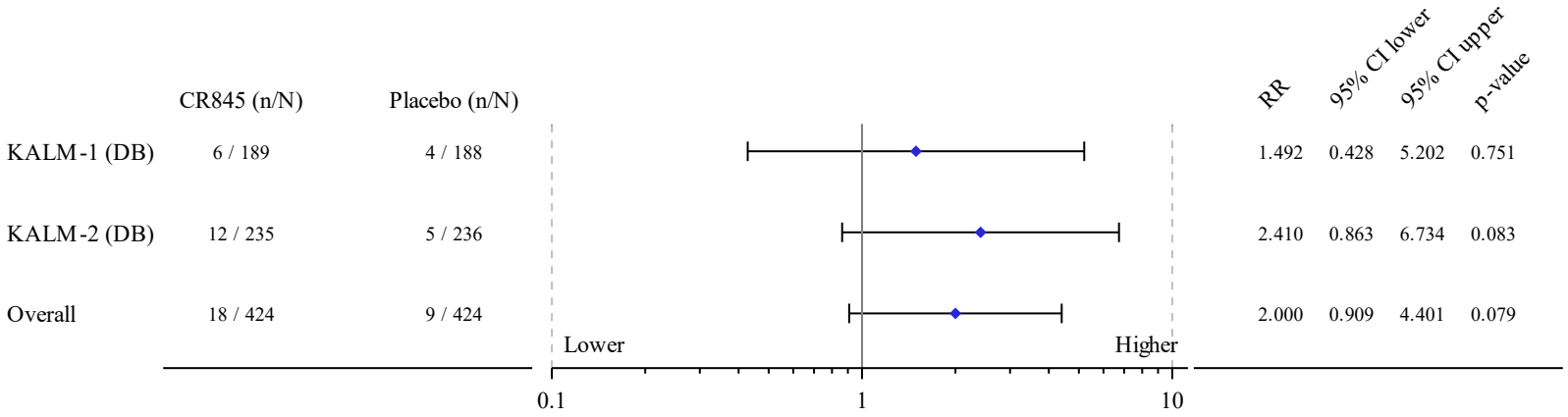
Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with event. RR = relative risk. CI = confidence interval. AESI = adverse event of special interest.
Heterogeneity was investigated with Cochran Q test. NE = not evaluable.
Source tables: AT2AEYN_SMI0, BT2AEYN_SMI0, IT2AEYN_SMI0

Table IT2AEON_SMI0: Incidence of AESI somnolence - non-severe
SAF-S

	CR845		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
AESI somnolence - non-severe	424	18 (4.2) [2.5, 6.6]	424	9 (2.1) [1.0, 4.0]	2.000 [0.909, 4.401]	2.044 [0.908, 4.604]	2.1 [-0.5, 4.7]	0.079

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 31JAN2022

Figure IF2AEON_SMFR0: Forest plot for incidence of AESI somnolence - non-severe - relative risk
SAF-S



Test for heterogeneity - pvalue: 0.561, I-square: 0.0 %

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with event. RR = relative risk. CI = confidence interval. AESI = adverse event of special interest.
Heterogeneity was investigated with Cochran Q test. NE = not evaluable.
Source tables: AT2AEON_SMI0, BT2AEON_SMI0, IT2AEON_SMI0

Table IT2AEKN_SMI0: Incidence of AESI seizures - non-severe
SAF-S

	CR845		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
AESI seizures - non-severe	424	0 (0.0) [0.0, 0.9]	424	1 (0.2) [0.0, 1.3]	0.333 + [0.014, 8.159]	0.333 + [0.014, 8.186]	-0.2 [-0.9, 0.5]	1.000 #

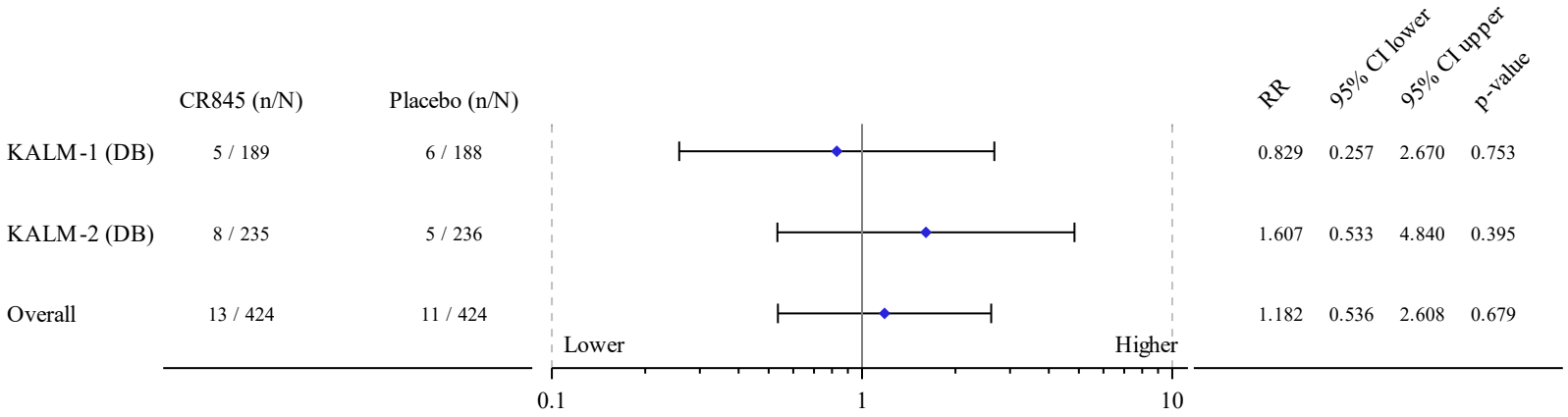
Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 31JAN2022

Table IT2AEMN_SMI0: Incidence of AESI mental status change - non-severe
SAF-S

	CR845		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
AESI mental status change - non-severe	424	13 (3.1) [1.6, 5.2]	424	11 (2.6) [1.3, 4.6]	1.182 [0.536, 2.608]	1.188 [0.526, 2.682]	0.5 [-2.0, 2.9]	0.679

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 31JAN2022

Figure IF2AEMN_SMFR0: Forest plot for incidence of AESI mental status change - non-severe - relative risk
SAF-S



Test for heterogeneity - pvalue: 0.420, I-square: 0.0 %

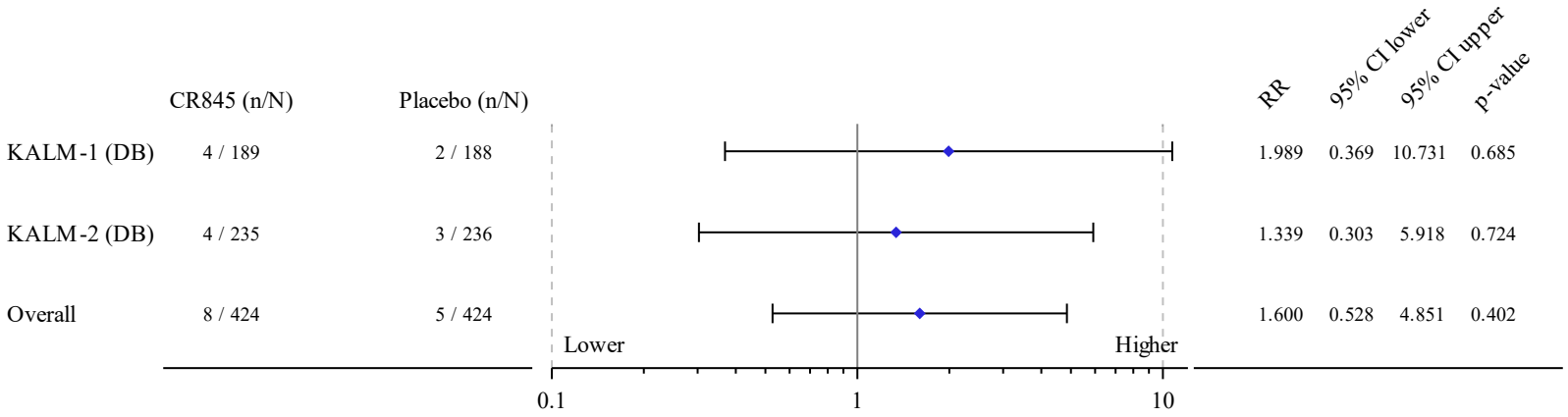
Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with event. RR = relative risk. CI = confidence interval. AESI = adverse event of special interest.
Heterogeneity was investigated with Cochran Q test. NE = not evaluable.
Source tables: AT2AEMN_SMI0, BT2AEMN_SMI0, IT2AEMN_SMI0

Table IT2AEEN_SMI0: Incidence of AESI mood change - non-severe
SAF-S

	CR845		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
AESI mood change - non-severe	424	8 (1.9) [0.8, 3.7]	424	5 (1.2) [0.4, 2.7]	1.600 [0.528, 4.851]	1.612 [0.523, 4.967]	0.7 [-1.2, 2.6]	0.402

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 31JAN2022

Figure IF2AEEN_SMFR0: Forest plot for incidence of AESI mood change - non-severe - relative risk
SAF-S



Test for heterogeneity - pvalue: 0.730, I-square: 0.0 %

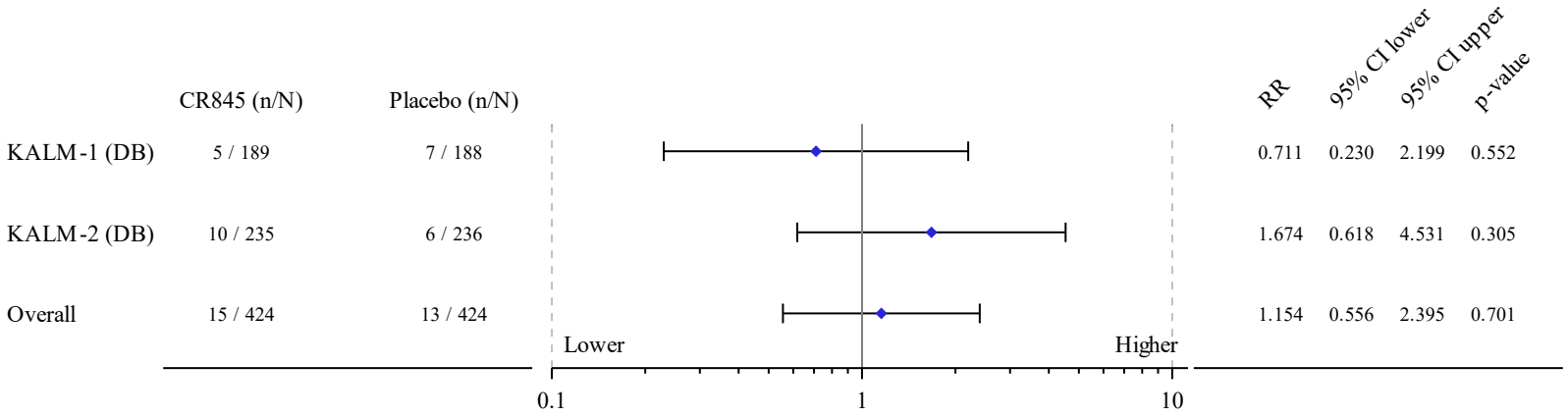
Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with event. RR = relative risk. CI = confidence interval. AESI = adverse event of special interest.
Heterogeneity was investigated with Cochran Q test. NE = not evaluable.
Source tables: AT2AEEN_SMI0, BT2AEEN_SMI0, IT2AEEN_SMI0

Table IT2AEUN_SMI0: Incidence of AESI unusual feeling/sensation - non-severe
SAF-S

	CR845		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
AESI unusual feeling/sensation - non-severe	424	15 (3.5) [2.0, 5.8]	424	13 (3.1) [1.6, 5.2]	1.154 [0.556, 2.395]	1.159 [0.545, 2.467]	0.5 [-2.2, 3.1]	0.701

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 31JAN2022

Figure IF2AEUN_SMFR0: Forest plot for incidence of AESI unusual feeling/sensation - non-severe - relative risk
SAF-S



Test for heterogeneity - pvalue: 0.265, I-square: 19.6 %

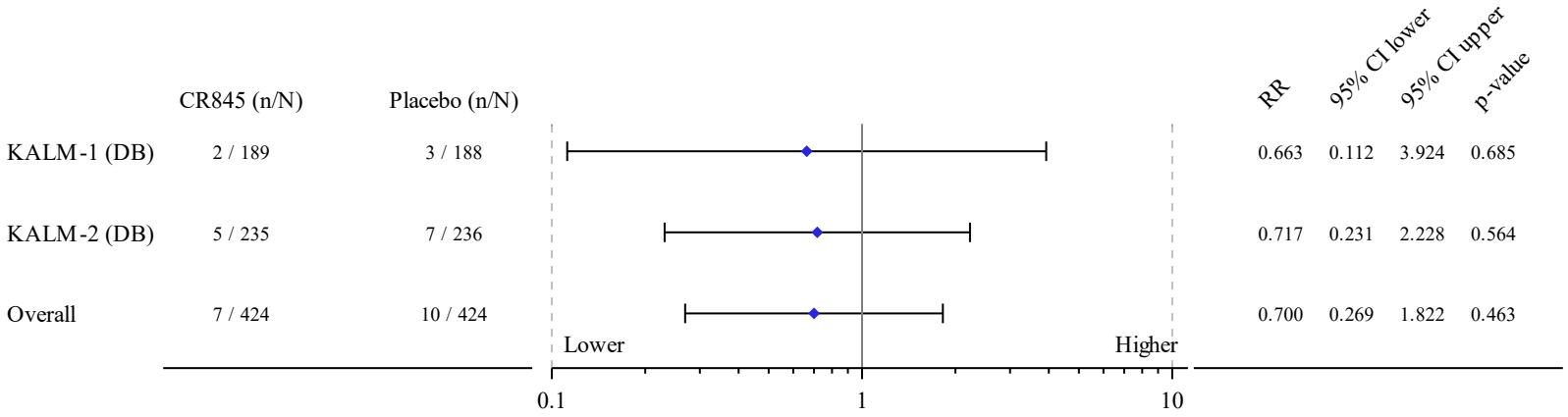
Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with event. RR = relative risk. CI = confidence interval. AESI = adverse event of special interest.
Heterogeneity was investigated with Cochran Q test. NE = not evaluable.
Source tables: AT2AEUN_SMI0, BT2AEUN_SMI0, IT2AEUN_SMI0

Table IT2AERN_SMI0: Incidence of AESI tachycardia/palpitation - non-severe
SAF-S

	CR845		Placebo					
	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
AESI tachycardia/palpitation - non-severe	424	7 (1.7) [0.7, 3.4]	424	10 (2.4) [1.1, 4.3]	0.700 [0.269, 1.822]	0.695 [0.262, 1.843]	-0.7 [-2.8, 1.4]	0.463

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae, created on: 31JAN2022

Figure IF2AERN_SMFR0: Forest plot for incidence of AESI tachycardia/palpitation - non-severe - relative risk
SAF-S



Test for heterogeneity - pvalue: 0.942, I-square: 0.0 %

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with event. RR = relative risk. CI = confidence interval. AESI = adverse event of special interest.
Heterogeneity was investigated with Cochran Q test. NE = not evaluable.
Source tables: AT2AERN_SMI0, BT2AERN_SMI0, IT2AERN_SMI0

Table IT2WIC_ISHA: Change from baseline in weekly WI-NRS by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
< 65 years	Weekly WI-NRS	Baseline	CR845	282	282 (100.0)	7.17 (1.41)	4.3	7.00	10.0	
			Placebo	290	290 (100.0)	7.20 (1.48)	4.1	7.20	10.0	
		Week 1	CR845	282	275 (97.5)	6.38 (1.82)	1.6	6.29	10.0	
			Placebo	290	280 (96.6)	6.74 (1.75)	1.3	6.86	10.0	
		Week 2	CR845	282	267 (94.7)	5.70 (2.11)	0.0	5.71	10.0	
			Placebo	290	278 (95.9)	6.31 (1.97)	1.1	6.43	10.0	
		Week 3	CR845	282	265 (94.0)	5.28 (2.29)	0.0	5.29	10.0	
			Placebo	290	273 (94.1)	6.07 (2.12)	1.0	6.00	10.0	
		Week 4	CR845	282	260 (92.2)	4.91 (2.41)	0.0	5.00	10.0	
			Placebo	290	273 (94.1)	5.86 (2.28)	1.0	5.83	10.0	
		Week 5	CR845	282	259 (91.8)	4.74 (2.45)	0.0	4.86	10.0	
			Placebo	290	272 (93.8)	5.63 (2.35)	0.3	5.57	10.0	
		Week 6	CR845	282	254 (90.1)	4.51 (2.44)	0.0	4.57	10.0	
			Placebo	290	272 (93.8)	5.51 (2.48)	0.0	5.57	10.0	
		Week 7	CR845	282	251 (89.0)	4.41 (2.48)	0.0	4.57	10.0	
			Placebo	290	268 (92.4)	5.39 (2.49)	0.0	5.43	10.0	
		Week 8	CR845	282	249 (88.3)	4.38 (2.44)	0.0	4.43	10.0	
			Placebo	290	268 (92.4)	5.29 (2.51)	0.0	5.43	10.0	
		Week 9	CR845	282	249 (88.3)	4.23 (2.46)	0.0	4.00	10.0	
			Placebo	290	269 (92.8)	5.16 (2.52)	0.0	5.00	10.0	
		Week 10	CR845	282	250 (88.7)	4.09 (2.54)	0.0	3.86	10.0	
			Placebo	290	268 (92.4)	5.19 (2.55)	0.0	5.14	10.0	
		Week 11	CR845	282	241 (85.5)	4.02 (2.58)	0.0	3.67	9.9	
			Placebo	290	264 (91.0)	5.10 (2.57)	0.0	5.00	10.0	
		Week 12	CR845	282	234 (83.0)	3.90 (2.57)	0.0	3.29	10.0	
			Placebo	290	253 (87.2)	5.04 (2.58)	0.0	5.00	10.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	282	275 (97.5)	-0.78 (1.26)	-7.8	-0.62	2.4	-0.24 [-0.40, -0.07]
			Placebo	290	280 (96.6)	-0.49 (1.19)	-4.8	-0.28	2.9	
		Week 2	CR845	282	267 (94.7)	-1.45 (1.73)	-8.9	-1.05	2.0	-0.33 [-0.50, -0.17]
			Placebo	290	278 (95.9)	-0.91 (1.50)	-5.4	-0.63	2.8	
		Week 3	CR845	282	265 (94.0)	-1.89 (1.93)	-8.1	-1.43	2.1	-0.39 [-0.56, -0.22]
			Placebo	290	273 (94.1)	-1.17 (1.75)	-6.1	-0.98	3.1	
		Week 4	CR845	282	260 (92.2)	-2.24 (2.13)	-9.3	-1.86	1.5	-0.42 [-0.60, -0.25]
			Placebo	290	273 (94.1)	-1.37 (1.98)	-7.4	-1.00	3.2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIC_ISHA: Change from baseline in weekly WI-NRS by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 5	CR845	282	259 (91.8)	-2.42 (2.26)	-10.0	-2.04	2.9	-0.38 [-0.55, -0.21]
			Placebo	290	272 (93.8)	-1.59 (2.06)	-7.8	-1.22	3.5	
		Week 6	CR845	282	254 (90.1)	-2.66 (2.33)	-9.9	-2.33	3.8	-0.43 [-0.60, -0.25]
			Placebo	290	272 (93.8)	-1.70 (2.18)	-9.0	-1.43	3.1	
		Week 7	CR845	282	251 (89.0)	-2.73 (2.37)	-10.0	-2.27	1.7	-0.40 [-0.57, -0.23]
			Placebo	290	268 (92.4)	-1.81 (2.26)	-9.0	-1.48	3.3	
		Week 8	CR845	282	249 (88.3)	-2.78 (2.31)	-8.8	-2.58	1.9	-0.37 [-0.55, -0.20]
			Placebo	290	268 (92.4)	-1.92 (2.29)	-9.0	-1.42	3.5	
		Week 9	CR845	282	249 (88.3)	-2.93 (2.33)	-10.0	-2.73	2.0	-0.38 [-0.56, -0.21]
			Placebo	290	269 (92.8)	-2.04 (2.30)	-9.0	-1.57	3.5	
		Week 10	CR845	282	250 (88.7)	-3.07 (2.45)	-10.0	-3.00	3.0	-0.45 [-0.62, -0.27]
			Placebo	290	268 (92.4)	-2.00 (2.33)	-9.0	-1.61	3.5	
		Week 11	CR845	282	241 (85.5)	-3.12 (2.47)	-10.0	-3.00	3.0	-0.44 [-0.62, -0.27]
			Placebo	290	264 (91.0)	-2.06 (2.32)	-9.0	-1.71	3.6	
		Week 12	CR845	282	234 (83.0)	-3.24 (2.50)	-10.0	-3.21	2.0	-0.45 [-0.63, -0.27]
			Placebo	290	253 (87.2)	-2.16 (2.34)	-9.0	-1.84	3.6	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIC_ISHA: Change from baseline in weekly WI-NRS by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 65 years	Weekly WI-NRS	Baseline	CR845	144	144 (100.0)	7.18 (1.38)	4.2	7.23	10.0	
			Placebo	135	135 (100.0)	7.12 (1.47)	4.1	7.00	10.0	
		Week 1	CR845	144	139 (96.5)	6.18 (1.96)	0.9	6.57	10.0	
			Placebo	135	133 (98.5)	6.45 (1.81)	0.0	6.57	10.0	
		Week 2	CR845	144	137 (95.1)	5.57 (2.31)	0.0	6.14	10.0	
			Placebo	135	132 (97.8)	5.88 (2.12)	0.0	6.00	9.9	
		Week 3	CR845	144	134 (93.1)	5.18 (2.60)	0.0	5.93	10.0	
			Placebo	135	130 (96.3)	5.72 (2.15)	0.0	5.71	10.0	
		Week 4	CR845	144	130 (90.3)	4.92 (2.56)	0.0	5.36	10.0	
			Placebo	135	130 (96.3)	5.46 (2.17)	0.0	5.64	9.9	
		Week 5	CR845	144	129 (89.6)	4.80 (2.58)	0.0	5.14	10.0	
			Placebo	135	130 (96.3)	5.15 (2.25)	0.0	5.00	9.9	
		Week 6	CR845	144	128 (88.9)	4.66 (2.56)	0.0	4.79	10.0	
			Placebo	135	128 (94.8)	5.08 (2.30)	0.0	5.00	10.0	
		Week 7	CR845	144	128 (88.9)	4.53 (2.63)	0.0	4.57	10.0	
			Placebo	135	129 (95.6)	5.13 (2.27)	0.0	5.00	10.0	
		Week 8	CR845	144	127 (88.2)	4.53 (2.62)	0.0	4.43	10.0	
			Placebo	135	126 (93.3)	5.08 (2.32)	0.0	5.00	10.0	
		Week 9	CR845	144	123 (85.4)	4.45 (2.66)	0.0	4.57	10.0	
			Placebo	135	127 (94.1)	5.01 (2.40)	0.0	4.86	10.0	
		Week 10	CR845	144	122 (84.7)	4.42 (2.62)	0.0	4.43	10.0	
			Placebo	135	125 (92.6)	4.79 (2.43)	0.0	4.71	10.0	
		Week 11	CR845	144	118 (81.9)	4.30 (2.62)	0.0	4.20	10.0	
			Placebo	135	123 (91.1)	4.86 (2.32)	0.0	4.86	10.0	
		Week 12	CR845	144	114 (79.2)	4.29 (2.63)	0.0	4.07	10.0	
			Placebo	135	119 (88.1)	4.65 (2.49)	0.0	4.50	10.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	144	139 (96.5)	-1.01 (1.41)	-5.6	-0.79	2.1	-0.27 [-0.51, -0.03]
			Placebo	135	133 (98.5)	-0.65 (1.27)	-6.3	-0.48	2.8	
		Week 2	CR845	144	137 (95.1)	-1.59 (1.88)	-10.0	-1.17	1.7	-0.19 [-0.43, 0.05]
			Placebo	135	132 (97.8)	-1.23 (1.82)	-8.7	-1.00	3.5	
		Week 3	CR845	144	134 (93.1)	-1.97 (2.17)	-10.0	-1.79	1.8	-0.31 [-0.56, -0.07]
			Placebo	135	130 (96.3)	-1.35 (1.78)	-7.4	-1.13	3.3	
		Week 4	CR845	144	130 (90.3)	-2.27 (2.20)	-10.0	-1.99	2.0	-0.31 [-0.55, -0.06]
			Placebo	135	130 (96.3)	-1.63 (2.00)	-8.6	-1.29	3.5	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIC_ISHA: Change from baseline in weekly WI-NRS by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 5	CR845	144	129 (89.6)	-2.39 (2.26)	-10.0	-2.11	1.8	-0.21 [-0.45, 0.03]
			Placebo	135	130 (96.3)	-1.93 (2.12)	-8.7	-1.56	3.4	
		Week 6	CR845	144	128 (88.9)	-2.53 (2.31)	-10.0	-2.08	1.8	-0.21 [-0.46, 0.03]
			Placebo	135	128 (94.8)	-2.05 (2.17)	-8.3	-1.80	2.9	
		Week 7	CR845	144	128 (88.9)	-2.66 (2.43)	-10.0	-2.30	1.9	-0.30 [-0.54, -0.05]
			Placebo	135	129 (95.6)	-1.99 (2.07)	-7.8	-1.68	2.8	
		Week 8	CR845	144	127 (88.2)	-2.64 (2.39)	-10.0	-2.54	2.1	-0.26 [-0.51, -0.01]
			Placebo	135	126 (93.3)	-2.05 (2.15)	-7.5	-1.70	3.2	
		Week 9	CR845	144	123 (85.4)	-2.72 (2.41)	-10.0	-2.63	1.6	-0.25 [-0.50, 0.00]
			Placebo	135	127 (94.1)	-2.14 (2.27)	-8.1	-1.83	2.8	
		Week 10	CR845	144	122 (84.7)	-2.76 (2.37)	-10.0	-2.31	2.8	-0.19 [-0.44, 0.06]
			Placebo	135	125 (92.6)	-2.30 (2.31)	-9.0	-2.00	2.8	
		Week 11	CR845	144	118 (81.9)	-2.90 (2.40)	-10.0	-2.77	1.8	-0.29 [-0.54, -0.04]
			Placebo	135	123 (91.1)	-2.23 (2.25)	-7.2	-2.00	2.8	
		Week 12	CR845	144	114 (79.2)	-2.94 (2.51)	-10.0	-2.54	3.0	-0.22 [-0.48, 0.04]
			Placebo	135	119 (88.1)	-2.40 (2.37)	-8.7	-2.17	2.8	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIC_ISHB: Change from baseline in weekly WI-NRS by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Male	Weekly WI-NRS	Baseline	CR845	249	249 (100.0)	7.11 (1.44)	4.2	7.00	10.0	
			Placebo	258	258 (100.0)	7.07 (1.46)	4.1	7.00	10.0	
		Week 1	CR845	249	241 (96.8)	6.33 (1.84)	1.6	6.29	10.0	
			Placebo	258	252 (97.7)	6.55 (1.72)	0.0	6.71	10.0	
		Week 2	CR845	249	235 (94.4)	5.69 (2.12)	0.1	5.71	10.0	
			Placebo	258	250 (96.9)	6.07 (2.01)	0.0	6.14	10.0	
		Week 3	CR845	249	231 (92.8)	5.38 (2.31)	0.0	5.83	10.0	
			Placebo	258	244 (94.6)	5.94 (2.13)	0.0	6.00	10.0	
		Week 4	CR845	249	227 (91.2)	5.04 (2.38)	0.0	5.40	10.0	
			Placebo	258	247 (95.7)	5.69 (2.24)	0.0	5.71	10.0	
		Week 5	CR845	249	225 (90.4)	4.93 (2.43)	0.0	5.00	10.0	
			Placebo	258	244 (94.6)	5.48 (2.35)	0.0	5.57	10.0	
		Week 6	CR845	249	223 (89.6)	4.75 (2.42)	0.0	4.86	10.0	
			Placebo	258	241 (93.4)	5.45 (2.38)	0.0	5.43	10.0	
		Week 7	CR845	249	220 (88.4)	4.70 (2.52)	0.0	4.86	10.0	
			Placebo	258	241 (93.4)	5.38 (2.37)	0.0	5.43	10.0	
		Week 8	CR845	249	219 (88.0)	4.74 (2.48)	0.0	4.71	10.0	
			Placebo	258	241 (93.4)	5.28 (2.38)	0.0	5.14	10.0	
		Week 9	CR845	249	213 (85.5)	4.61 (2.49)	0.0	4.43	10.0	
			Placebo	258	240 (93.0)	5.15 (2.41)	0.0	5.00	10.0	
		Week 10	CR845	249	215 (86.3)	4.43 (2.62)	0.0	4.43	10.0	
			Placebo	258	239 (92.6)	5.06 (2.39)	0.0	5.00	10.0	
		Week 11	CR845	249	206 (82.7)	4.39 (2.59)	0.0	4.14	10.0	
			Placebo	258	236 (91.5)	5.00 (2.39)	0.0	4.86	10.0	
		Week 12	CR845	249	200 (80.3)	4.33 (2.58)	0.0	4.07	10.0	
			Placebo	258	227 (88.0)	4.99 (2.42)	0.0	4.86	10.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	249	241 (96.8)	-0.80 (1.28)	-7.8	-0.57	2.1	-0.20 [-0.38, -0.02]
			Placebo	258	252 (97.7)	-0.55 (1.21)	-6.3	-0.34	2.8	
		Week 2	CR845	249	235 (94.4)	-1.41 (1.65)	-7.3	-1.09	1.7	-0.25 [-0.43, -0.07]
			Placebo	258	250 (96.9)	-1.01 (1.62)	-6.5	-0.71	2.8	
		Week 3	CR845	249	231 (92.8)	-1.73 (1.82)	-7.6	-1.39	2.1	-0.34 [-0.52, -0.16]
			Placebo	258	244 (94.6)	-1.13 (1.73)	-7.1	-0.94	2.8	
		Week 4	CR845	249	227 (91.2)	-2.07 (1.94)	-8.1	-1.84	1.5	-0.35 [-0.53, -0.17]
			Placebo	258	247 (95.7)	-1.39 (1.98)	-8.0	-1.07	3.1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIC_ISHB: Change from baseline in weekly WI-NRS by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 5	CR845	249	225 (90.4)	-2.19 (2.04)	-8.6	-2.00	2.0	-0.28 [-0.46, -0.10]
			Placebo	258	244 (94.6)	-1.61 (2.09)	-8.7	-1.25	3.5	
		Week 6	CR845	249	223 (89.6)	-2.37 (2.10)	-8.9	-2.11	1.7	-0.35 [-0.53, -0.17]
			Placebo	258	241 (93.4)	-1.64 (2.10)	-9.0	-1.46	3.1	
		Week 7	CR845	249	220 (88.4)	-2.41 (2.21)	-8.9	-2.09	1.7	-0.33 [-0.52, -0.15]
			Placebo	258	241 (93.4)	-1.69 (2.14)	-9.0	-1.43	3.3	
		Week 8	CR845	249	219 (88.0)	-2.37 (2.18)	-8.9	-2.02	1.9	-0.26 [-0.45, -0.08]
			Placebo	258	241 (93.4)	-1.80 (2.15)	-9.0	-1.48	3.3	
		Week 9	CR845	249	213 (85.5)	-2.52 (2.19)	-8.9	-2.54	2.0	-0.26 [-0.45, -0.08]
			Placebo	258	240 (93.0)	-1.95 (2.17)	-9.0	-1.63	3.5	
		Week 10	CR845	249	215 (86.3)	-2.69 (2.35)	-8.9	-2.50	3.0	-0.30 [-0.48, -0.11]
			Placebo	258	239 (92.6)	-2.01 (2.17)	-9.0	-1.71	3.5	
		Week 11	CR845	249	206 (82.7)	-2.71 (2.33)	-8.3	-2.56	3.0	-0.30 [-0.48, -0.11]
			Placebo	258	236 (91.5)	-2.05 (2.19)	-9.0	-1.93	3.6	
		Week 12	CR845	249	200 (80.3)	-2.77 (2.37)	-8.3	-2.64	3.0	-0.30 [-0.50, -0.11]
			Placebo	258	227 (88.0)	-2.08 (2.20)	-9.0	-1.90	3.6	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIC_ISHB: Change from baseline in weekly WI-NRS by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Female	Weekly WI-NRS	Baseline	CR845	177	177 (100.0)	7.25 (1.34)	4.3	7.20	10.0	
			Placebo	167	167 (100.0)	7.33 (1.48)	4.1	7.38	10.0	
		Week 1	CR845	177	173 (97.7)	6.30 (1.90)	0.9	6.43	10.0	
			Placebo	167	161 (96.4)	6.80 (1.85)	1.3	7.00	10.0	
		Week 2	CR845	177	169 (95.5)	5.62 (2.27)	0.0	6.14	10.0	
			Placebo	167	160 (95.8)	6.32 (2.04)	0.3	6.57	10.0	
		Week 3	CR845	177	168 (94.9)	5.06 (2.49)	0.0	5.21	10.0	
			Placebo	167	159 (95.2)	5.98 (2.14)	1.3	6.00	10.0	
		Week 4	CR845	177	163 (92.1)	4.74 (2.55)	0.0	5.00	10.0	
			Placebo	167	156 (93.4)	5.80 (2.28)	0.4	5.76	10.0	
		Week 5	CR845	177	163 (92.1)	4.52 (2.55)	0.0	4.86	9.6	
			Placebo	167	158 (94.6)	5.47 (2.29)	0.3	5.36	10.0	
		Week 6	CR845	177	159 (89.8)	4.29 (2.53)	0.0	4.43	10.0	
			Placebo	167	159 (95.2)	5.27 (2.50)	0.1	5.43	10.0	
		Week 7	CR845	177	159 (89.8)	4.11 (2.51)	0.0	4.14	10.0	
			Placebo	167	156 (93.4)	5.18 (2.49)	0.0	5.14	10.0	
		Week 8	CR845	177	157 (88.7)	3.99 (2.47)	0.0	4.00	9.6	
			Placebo	167	153 (91.6)	5.13 (2.56)	0.0	5.29	10.0	
		Week 9	CR845	177	159 (89.8)	3.90 (2.52)	0.0	3.86	9.4	
			Placebo	167	156 (93.4)	5.05 (2.60)	0.0	5.21	10.0	
		Week 10	CR845	177	157 (88.7)	3.88 (2.48)	0.0	3.71	9.9	
			Placebo	167	154 (92.2)	5.07 (2.70)	0.0	5.00	10.0	
		Week 11	CR845	177	153 (86.4)	3.73 (2.55)	0.0	3.29	9.3	
			Placebo	167	151 (90.4)	5.06 (2.65)	0.0	5.00	10.0	
		Week 12	CR845	177	148 (83.6)	3.62 (2.55)	0.0	3.15	9.0	
			Placebo	167	145 (86.8)	4.80 (2.74)	0.0	4.57	10.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	177	173 (97.7)	-0.95 (1.35)	-5.6	-0.71	2.4	-0.31 [-0.53, -0.10]
			Placebo	167	161 (96.4)	-0.54 (1.23)	-3.9	-0.43	2.9	
		Week 2	CR845	177	169 (95.5)	-1.62 (1.94)	-10.0	-1.14	2.0	-0.33 [-0.55, -0.12]
			Placebo	167	160 (95.8)	-1.03 (1.61)	-8.7	-0.79	3.5	
		Week 3	CR845	177	168 (94.9)	-2.16 (2.23)	-10.0	-1.82	1.7	-0.39 [-0.61, -0.17]
			Placebo	167	159 (95.2)	-1.37 (1.79)	-7.4	-1.10	3.3	
		Week 4	CR845	177	163 (92.1)	-2.50 (2.41)	-10.0	-2.04	2.0	-0.43 [-0.65, -0.20]
			Placebo	167	156 (93.4)	-1.55 (2.01)	-8.6	-1.17	3.5	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIC_ISHB: Change from baseline in weekly WI-NRS by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 5	CR845	177	163 (92.1)	-2.71 (2.51)	-10.0	-2.25	2.9	-0.38 [-0.60, -0.16]
			Placebo	167	158 (94.6)	-1.85 (2.06)	-7.7	-1.50	3.4	
		Week 6	CR845	177	159 (89.8)	-2.96 (2.56)	-10.0	-2.75	3.8	-0.36 [-0.59, -0.14]
			Placebo	167	159 (95.2)	-2.08 (2.28)	-8.3	-1.93	3.0	
		Week 7	CR845	177	159 (89.8)	-3.12 (2.56)	-10.0	-2.64	1.9	-0.40 [-0.63, -0.18]
			Placebo	167	156 (93.4)	-2.15 (2.26)	-8.5	-1.76	2.7	
		Week 8	CR845	177	157 (88.7)	-3.23 (2.45)	-10.0	-2.86	2.1	-0.42 [-0.65, -0.20]
			Placebo	167	153 (91.6)	-2.21 (2.36)	-8.5	-1.71	3.5	
		Week 9	CR845	177	159 (89.8)	-3.32 (2.49)	-10.0	-2.96	1.6	-0.42 [-0.65, -0.20]
			Placebo	167	156 (93.4)	-2.27 (2.45)	-8.4	-1.84	3.1	
		Week 10	CR845	177	157 (88.7)	-3.35 (2.48)	-10.0	-3.13	1.9	-0.44 [-0.67, -0.22]
			Placebo	167	154 (92.2)	-2.24 (2.54)	-9.0	-1.74	3.1	
		Week 11	CR845	177	153 (86.4)	-3.50 (2.53)	-10.0	-3.45	1.8	-0.51 [-0.74, -0.28]
			Placebo	167	151 (90.4)	-2.22 (2.45)	-8.5	-2.00	2.9	
		Week 12	CR845	177	148 (83.6)	-3.64 (2.60)	-10.0	-3.55	1.4	-0.45 [-0.68, -0.22]
			Placebo	167	145 (86.8)	-2.48 (2.55)	-8.7	-2.17	2.7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIC_ISHC: Change from baseline in weekly WI-NRS by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Black/African American	Weekly WI-NRS	Baseline	CR845	135	135 (100.0)	7.15 (1.34)	4.3	7.13	10.0	
			Placebo	114	114 (100.0)	7.34 (1.52)	4.3	7.50	10.0	
		Week 1	CR845	135	132 (97.8)	6.26 (1.79)	1.4	6.43	10.0	
			Placebo	114	108 (94.7)	6.77 (1.83)	2.0	6.93	10.0	
		Week 2	CR845	135	126 (93.3)	5.76 (2.03)	0.0	6.00	10.0	
			Placebo	114	105 (92.1)	6.33 (1.96)	1.0	6.43	10.0	
		Week 3	CR845	135	124 (91.9)	5.28 (2.25)	0.0	5.71	10.0	
			Placebo	114	107 (93.9)	6.04 (2.04)	1.0	6.00	10.0	
		Week 4	CR845	135	121 (89.6)	4.98 (2.42)	0.0	5.29	10.0	
			Placebo	114	106 (93.0)	5.83 (2.22)	1.0	5.57	10.0	
		Week 5	CR845	135	120 (88.9)	4.93 (2.41)	0.0	5.07	10.0	
			Placebo	114	107 (93.9)	5.65 (2.31)	0.3	5.71	10.0	
		Week 6	CR845	135	115 (85.2)	4.62 (2.41)	0.0	4.71	10.0	
			Placebo	114	107 (93.9)	5.50 (2.41)	0.0	5.29	10.0	
		Week 7	CR845	135	115 (85.2)	4.46 (2.45)	0.0	4.57	10.0	
			Placebo	114	106 (93.0)	5.39 (2.42)	0.0	5.38	10.0	
		Week 8	CR845	135	116 (85.9)	4.44 (2.44)	0.0	4.43	10.0	
			Placebo	114	105 (92.1)	5.31 (2.50)	0.0	5.43	10.0	
		Week 9	CR845	135	115 (85.2)	4.20 (2.44)	0.0	4.14	10.0	
			Placebo	114	108 (94.7)	5.20 (2.45)	0.0	5.00	10.0	
		Week 10	CR845	135	115 (85.2)	3.95 (2.40)	0.0	3.71	10.0	
			Placebo	114	108 (94.7)	5.16 (2.51)	0.0	5.00	10.0	
		Week 11	CR845	135	106 (78.5)	3.95 (2.50)	0.0	3.57	10.0	
			Placebo	114	105 (92.1)	5.11 (2.44)	0.0	5.00	10.0	
		Week 12	CR845	135	104 (77.0)	3.75 (2.49)	0.0	3.24	9.7	
			Placebo	114	102 (89.5)	5.01 (2.48)	0.0	4.86	10.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	135	132 (97.8)	-0.90 (1.47)	-7.8	-0.70	2.1	-0.22 [-0.47, 0.04]
			Placebo	114	108 (94.7)	-0.61 (1.10)	-3.5	-0.48	2.3	
		Week 2	CR845	135	126 (93.3)	-1.37 (1.83)	-10.0	-1.05	1.6	-0.21 [-0.47, 0.05]
			Placebo	114	105 (92.1)	-1.03 (1.47)	-5.6	-0.88	2.2	
		Week 3	CR845	135	124 (91.9)	-1.83 (2.02)	-10.0	-1.52	2.1	-0.28 [-0.54, -0.02]
			Placebo	114	107 (93.9)	-1.30 (1.72)	-7.1	-1.02	2.6	
		Week 4	CR845	135	121 (89.6)	-2.12 (2.26)	-10.0	-1.82	2.0	-0.28 [-0.54, -0.02]
			Placebo	114	106 (93.0)	-1.52 (2.02)	-8.0	-1.25	2.6	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIC_ISHC: Change from baseline in weekly WI-NRS by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 5	CR845	135	120 (88.9)	-2.21 (2.27)	-10.0	-1.89	2.0	-0.24 [-0.51, 0.02]
			Placebo	114	107 (93.9)	-1.67 (2.15)	-8.1	-1.34	2.8	
		Week 6	CR845	135	115 (85.2)	-2.54 (2.32)	-10.0	-2.11	1.8	-0.29 [-0.56, -0.03]
			Placebo	114	107 (93.9)	-1.87 (2.26)	-9.0	-1.52	2.3	
		Week 7	CR845	135	115 (85.2)	-2.70 (2.36)	-10.0	-2.27	1.9	-0.31 [-0.57, -0.04]
			Placebo	114	106 (93.0)	-1.98 (2.31)	-9.0	-1.54	2.3	
		Week 8	CR845	135	116 (85.9)	-2.74 (2.40)	-10.0	-2.55	2.1	-0.27 [-0.53, -0.00]
			Placebo	114	105 (92.1)	-2.09 (2.39)	-9.0	-1.48	2.1	
		Week 9	CR845	135	115 (85.2)	-2.97 (2.38)	-10.0	-2.86	1.6	-0.34 [-0.60, -0.07]
			Placebo	114	108 (94.7)	-2.17 (2.34)	-9.0	-1.54	2.2	
		Week 10	CR845	135	115 (85.2)	-3.24 (2.36)	-10.0	-3.30	1.9	-0.43 [-0.70, -0.17]
			Placebo	114	108 (94.7)	-2.22 (2.39)	-9.0	-1.70	2.3	
		Week 11	CR845	135	106 (78.5)	-3.26 (2.42)	-10.0	-3.35	1.8	-0.45 [-0.73, -0.18]
			Placebo	114	105 (92.1)	-2.19 (2.32)	-9.0	-1.98	2.6	
		Week 12	CR845	135	104 (77.0)	-3.45 (2.47)	-10.0	-3.42	1.4	-0.48 [-0.75, -0.20]
			Placebo	114	102 (89.5)	-2.30 (2.35)	-9.0	-1.86	3.6	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIC_ISHC: Change from baseline in weekly WI-NRS by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
White	Weekly WI-NRS	Baseline	CR845	255	255 (100.0)	7.20 (1.44)	4.2	7.13	10.0	
			Placebo	262	262 (100.0)	7.10 (1.46)	4.1	7.00	10.0	
		Week 1	CR845	255	246 (96.5)	6.34 (1.90)	0.9	6.43	10.0	
			Placebo	262	257 (98.1)	6.56 (1.71)	0.0	6.57	10.0	
		Week 2	CR845	255	244 (95.7)	5.63 (2.23)	0.0	5.71	10.0	
			Placebo	262	257 (98.1)	6.06 (2.03)	0.0	6.14	10.0	
		Week 3	CR845	255	243 (95.3)	5.23 (2.45)	0.0	5.29	10.0	
			Placebo	262	249 (95.0)	5.89 (2.17)	0.0	6.00	10.0	
		Week 4	CR845	255	237 (92.9)	4.90 (2.48)	0.0	5.14	10.0	
			Placebo	262	249 (95.0)	5.64 (2.27)	0.0	5.86	10.0	
		Week 5	CR845	255	236 (92.5)	4.67 (2.53)	0.0	4.86	10.0	
			Placebo	262	247 (94.3)	5.37 (2.35)	0.0	5.43	10.0	
		Week 6	CR845	255	235 (92.2)	4.54 (2.51)	0.0	4.57	10.0	
			Placebo	262	246 (93.9)	5.33 (2.43)	0.0	5.43	10.0	
		Week 7	CR845	255	232 (91.0)	4.43 (2.56)	0.0	4.43	10.0	
			Placebo	262	245 (93.5)	5.27 (2.40)	0.0	5.29	10.0	
		Week 8	CR845	255	228 (89.4)	4.42 (2.53)	0.0	4.43	10.0	
			Placebo	262	242 (92.4)	5.22 (2.43)	0.0	5.29	10.0	
		Week 9	CR845	255	228 (89.4)	4.34 (2.59)	0.0	4.21	10.0	
			Placebo	262	242 (92.4)	5.13 (2.49)	0.0	5.14	10.0	
		Week 10	CR845	255	226 (88.6)	4.32 (2.64)	0.0	4.00	10.0	
			Placebo	262	240 (91.6)	5.05 (2.51)	0.0	5.00	10.0	
		Week 11	CR845	255	223 (87.5)	4.18 (2.64)	0.0	3.86	10.0	
			Placebo	262	238 (90.8)	5.03 (2.49)	0.0	5.00	10.0	
		Week 12	CR845	255	214 (83.9)	4.13 (2.64)	0.0	3.80	10.0	
			Placebo	262	229 (87.4)	4.95 (2.57)	0.0	4.86	10.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	255	246 (96.5)	-0.86 (1.23)	-5.6	-0.65	2.4	-0.25 [-0.42, -0.07]
			Placebo	262	257 (98.1)	-0.55 (1.26)	-6.3	-0.38	2.9	
		Week 2	CR845	255	244 (95.7)	-1.56 (1.74)	-8.9	-1.21	2.0	-0.29 [-0.47, -0.12]
			Placebo	262	257 (98.1)	-1.06 (1.70)	-8.7	-0.71	3.5	
		Week 3	CR845	255	243 (95.3)	-1.98 (2.01)	-7.9	-1.70	2.0	-0.40 [-0.57, -0.22]
			Placebo	262	249 (95.0)	-1.22 (1.83)	-7.4	-1.00	3.3	
		Week 4	CR845	255	237 (92.9)	-2.33 (2.13)	-9.3	-1.98	1.4	-0.41 [-0.59, -0.23]
			Placebo	262	249 (95.0)	-1.47 (2.05)	-8.6	-1.09	3.5	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIC_ISHC: Change from baseline in weekly WI-NRS by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 5	CR845	255	236 (92.5)	-2.54 (2.30)	-10.0	-2.17	2.9	-0.36 [-0.54, -0.18]
			Placebo	262	247 (94.3)	-1.75 (2.14)	-8.7	-1.38	3.5	
		Week 6	CR845	255	235 (92.2)	-2.67 (2.35)	-9.9	-2.57	3.8	-0.39 [-0.57, -0.21]
			Placebo	262	246 (93.9)	-1.77 (2.20)	-8.3	-1.57	3.1	
		Week 7	CR845	255	232 (91.0)	-2.75 (2.41)	-10.0	-2.37	1.7	-0.40 [-0.59, -0.22]
			Placebo	262	245 (93.5)	-1.82 (2.18)	-7.8	-1.57	3.3	
		Week 8	CR845	255	228 (89.4)	-2.75 (2.32)	-8.3	-2.62	1.9	-0.39 [-0.57, -0.21]
			Placebo	262	242 (92.4)	-1.87 (2.24)	-7.6	-1.52	3.5	
		Week 9	CR845	255	228 (89.4)	-2.83 (2.36)	-10.0	-2.71	2.0	-0.37 [-0.55, -0.19]
			Placebo	262	242 (92.4)	-1.97 (2.30)	-8.1	-1.63	3.5	
		Week 10	CR845	255	226 (88.6)	-2.86 (2.45)	-10.0	-2.81	3.0	-0.36 [-0.54, -0.18]
			Placebo	262	240 (91.6)	-2.00 (2.34)	-9.0	-1.68	3.5	
		Week 11	CR845	255	223 (87.5)	-2.98 (2.47)	-10.0	-2.95	3.0	-0.39 [-0.58, -0.21]
			Placebo	262	238 (90.8)	-2.03 (2.33)	-7.9	-1.71	3.6	
		Week 12	CR845	255	214 (83.9)	-3.05 (2.55)	-10.0	-2.94	3.0	-0.38 [-0.57, -0.19]
			Placebo	262	229 (87.4)	-2.12 (2.38)	-8.7	-1.88	3.6	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIC_ISHC: Change from baseline in weekly WI-NRS by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Other	Weekly WI-NRS	Baseline	CR845	35	35 (100.0)	7.04 (1.34)	4.8	7.00	10.0	
			Placebo	47	47 (100.0)	7.10 (1.44)	4.4	7.13	10.0	
		Week 1	CR845	35	35 (100.0)	6.36 (1.97)	2.7	6.29	10.0	
			Placebo	47	46 (97.9)	6.73 (1.94)	2.4	6.79	10.0	
		Week 2	CR845	35	33 (94.3)	5.54 (2.44)	1.3	5.43	10.0	
			Placebo	47	46 (97.9)	6.31 (2.10)	2.0	6.50	10.0	
		Week 3	CR845	35	31 (88.6)	5.28 (2.62)	0.0	5.43	10.0	
			Placebo	47	45 (95.7)	5.97 (2.11)	2.0	5.71	10.0	
		Week 4	CR845	35	31 (88.6)	4.78 (2.53)	0.0	4.71	10.0	
			Placebo	47	46 (97.9)	5.78 (2.18)	1.7	5.71	10.0	
		Week 5	CR845	35	31 (88.6)	4.80 (2.51)	0.0	5.00	10.0	
			Placebo	47	46 (97.9)	5.48 (2.19)	1.3	5.14	10.0	
		Week 6	CR845	35	31 (88.6)	4.54 (2.60)	0.0	4.57	9.1	
			Placebo	47	45 (95.7)	5.16 (2.40)	1.0	5.00	10.0	
		Week 7	CR845	35	31 (88.6)	4.60 (2.70)	0.0	4.71	10.0	
			Placebo	47	44 (93.6)	5.17 (2.52)	1.0	5.07	10.0	
		Week 8	CR845	35	31 (88.6)	4.45 (2.64)	0.0	4.14	9.0	
			Placebo	47	45 (95.7)	4.90 (2.44)	1.0	4.57	10.0	
		Week 9	CR845	35	28 (80.0)	4.43 (2.44)	0.0	4.51	9.0	
			Placebo	47	44 (93.6)	4.65 (2.44)	0.7	4.21	10.0	
		Week 10	CR845	35	30 (85.7)	4.29 (2.73)	0.0	4.41	8.5	
			Placebo	47	43 (91.5)	4.74 (2.53)	0.5	4.57	10.0	
		Week 11	CR845	35	29 (82.9)	4.17 (2.66)	0.3	4.00	9.0	
			Placebo	47	42 (89.4)	4.66 (2.60)	0.6	4.21	10.0	
		Week 12	CR845	35	29 (82.9)	4.26 (2.61)	0.0	4.29	9.0	
			Placebo	47	39 (83.0)	4.33 (2.60)	0.7	3.71	10.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	35	35 (100.0)	-0.68 (1.31)	-4.1	-0.17	0.9	-0.25 [-0.69, 0.19]
			Placebo	47	46 (97.9)	-0.36 (1.26)	-4.8	-0.15	2.8	
		Week 2	CR845	35	33 (94.3)	-1.48 (1.92)	-5.9	-0.88	1.1	-0.41 [-0.86, 0.04]
			Placebo	47	46 (97.9)	-0.78 (1.49)	-5.0	-0.47	2.8	
		Week 3	CR845	35	31 (88.6)	-1.68 (2.08)	-8.1	-1.00	1.0	-0.32 [-0.78, 0.14]
			Placebo	47	45 (95.7)	-1.12 (1.43)	-5.3	-1.30	2.5	
		Week 4	CR845	35	31 (88.6)	-2.18 (2.02)	-8.1	-1.67	0.9	-0.49 [-0.96, -0.03]
			Placebo	47	46 (97.9)	-1.31 (1.57)	-5.0	-1.14	2.1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIC_ISHC: Change from baseline in weekly WI-NRS by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 5	CR845	35	31 (88.6)	-2.17 (1.95)	-8.1	-1.75	0.9	-0.33 [-0.78, 0.13]
			Placebo	47	46 (97.9)	-1.61 (1.55)	-5.2	-1.41	1.9	
		Week 6	CR845	35	31 (88.6)	-2.49 (2.17)	-8.1	-2.04	0.8	-0.27 [-0.73, 0.19]
			Placebo	47	45 (95.7)	-1.95 (1.92)	-6.8	-1.64	1.9	
		Week 7	CR845	35	31 (88.6)	-2.43 (2.34)	-8.1	-1.75	0.9	-0.24 [-0.70, 0.22]
			Placebo	47	44 (93.6)	-1.91 (2.08)	-6.7	-1.76	1.9	
		Week 8	CR845	35	31 (88.6)	-2.58 (2.24)	-8.1	-2.33	0.0	-0.18 [-0.64, 0.28]
			Placebo	47	45 (95.7)	-2.20 (1.96)	-6.6	-1.86	1.6	
		Week 9	CR845	35	28 (80.0)	-2.61 (2.26)	-8.1	-2.30	0.0	-0.07 [-0.54, 0.41]
			Placebo	47	44 (93.6)	-2.47 (2.07)	-7.4	-2.19	1.1	
		Week 10	CR845	35	30 (85.7)	-2.74 (2.45)	-8.4	-2.13	0.5	-0.15 [-0.61, 0.32]
			Placebo	47	43 (91.5)	-2.41 (2.08)	-7.6	-2.20	1.8	
		Week 11	CR845	35	29 (82.9)	-2.82 (2.35)	-8.0	-2.25	0.0	-0.17 [-0.64, 0.31]
			Placebo	47	42 (89.4)	-2.46 (2.03)	-6.6	-2.26	1.8	
		Week 12	CR845	35	29 (82.9)	-2.70 (2.27)	-7.7	-2.04	0.3	0.06 [-0.42, 0.54]
			Placebo	47	39 (83.0)	-2.83 (2.16)	-7.5	-2.86	1.8	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIC_ISHD: Change from baseline in weekly WI-NRS by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 4 to < 7	Weekly WI-NRS	Baseline	CR845	185	185 (100.0)	5.89 (0.70)	4.2	6.00	6.9	
			Placebo	193	193 (100.0)	5.81 (0.68)	4.1	5.88	6.9	
		Week 1	CR845	185	180 (97.3)	5.00 (1.46)	0.9	5.00	8.9	
			Placebo	193	186 (96.4)	5.45 (1.43)	0.0	5.43	8.6	
		Week 2	CR845	185	178 (96.2)	4.41 (1.74)	0.0	4.57	8.4	
			Placebo	193	185 (95.9)	5.04 (1.64)	0.0	5.14	8.9	
		Week 3	CR845	185	176 (95.1)	4.00 (1.90)	0.0	4.00	8.7	
			Placebo	193	183 (94.8)	4.86 (1.80)	0.0	4.86	9.1	
		Week 4	CR845	185	172 (93.0)	3.75 (1.89)	0.0	3.71	8.0	
			Placebo	193	183 (94.8)	4.73 (1.83)	0.0	4.86	9.3	
		Week 5	CR845	185	172 (93.0)	3.71 (1.99)	0.0	3.71	8.4	
			Placebo	193	182 (94.3)	4.51 (1.85)	0.0	4.71	9.4	
		Week 6	CR845	185	167 (90.3)	3.58 (1.97)	0.0	3.71	9.0	
			Placebo	193	181 (93.8)	4.39 (1.92)	0.0	4.29	9.0	
		Week 7	CR845	185	168 (90.8)	3.52 (2.04)	0.0	3.57	8.4	
			Placebo	193	181 (93.8)	4.42 (1.99)	0.0	4.57	9.0	
		Week 8	CR845	185	166 (89.7)	3.46 (2.02)	0.0	3.21	8.6	
			Placebo	193	179 (92.7)	4.36 (2.05)	0.0	4.43	9.6	
		Week 9	CR845	185	164 (88.6)	3.32 (1.99)	0.0	3.00	8.7	
			Placebo	193	179 (92.7)	4.27 (2.04)	0.0	4.43	8.9	
		Week 10	CR845	185	163 (88.1)	3.28 (2.05)	0.0	3.00	9.3	
			Placebo	193	180 (93.3)	4.20 (2.09)	0.0	4.14	9.4	
		Week 11	CR845	185	159 (85.9)	3.15 (1.99)	0.0	3.00	9.7	
			Placebo	193	178 (92.2)	4.12 (2.13)	0.0	4.14	9.3	
		Week 12	CR845	185	151 (81.6)	3.08 (1.99)	0.0	2.75	8.2	
			Placebo	193	171 (88.6)	4.04 (2.11)	0.0	4.00	9.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	185	180 (97.3)	-0.89 (1.31)	-4.9	-0.71	2.4	-0.40 [-0.60, -0.19]
			Placebo	193	186 (96.4)	-0.37 (1.30)	-6.3	-0.28	2.9	
		Week 2	CR845	185	178 (96.2)	-1.46 (1.58)	-5.4	-1.22	1.7	-0.43 [-0.64, -0.22]
			Placebo	193	185 (95.9)	-0.78 (1.59)	-6.3	-0.63	3.5	
		Week 3	CR845	185	176 (95.1)	-1.87 (1.76)	-5.8	-1.86	2.0	-0.52 [-0.73, -0.31]
			Placebo	193	183 (94.8)	-0.95 (1.76)	-6.3	-0.88	3.3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIC_ISHD: Change from baseline in weekly WI-NRS by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 4	CR845	185	172 (93.0)	-2.11 (1.81)	-6.3	-2.03	1.5	-0.56 [-0.78, -0.35]
			Placebo	193	183 (94.8)	-1.08 (1.84)	-6.3	-1.00	3.5	
		Week 5	CR845	185	172 (93.0)	-2.18 (1.91)	-6.3	-2.22	2.9	-0.46 [-0.67, -0.25]
			Placebo	193	182 (94.3)	-1.31 (1.88)	-6.3	-1.18	3.5	
		Week 6	CR845	185	167 (90.3)	-2.30 (1.91)	-6.5	-2.38	3.8	-0.45 [-0.67, -0.24]
			Placebo	193	181 (93.8)	-1.42 (1.95)	-6.6	-1.48	3.1	
		Week 7	CR845	185	168 (90.8)	-2.37 (1.96)	-6.3	-2.29	1.7	-0.49 [-0.70, -0.28]
			Placebo	193	181 (93.8)	-1.40 (1.99)	-6.9	-1.25	3.3	
		Week 8	CR845	185	166 (89.7)	-2.43 (1.95)	-6.9	-2.40	1.9	-0.49 [-0.70, -0.27]
			Placebo	193	179 (92.7)	-1.46 (2.05)	-6.9	-1.20	3.5	
		Week 9	CR845	185	164 (88.6)	-2.57 (1.92)	-6.3	-2.73	2.0	-0.51 [-0.72, -0.29]
			Placebo	193	179 (92.7)	-1.55 (2.05)	-6.9	-1.38	3.5	
		Week 10	CR845	185	163 (88.1)	-2.61 (1.96)	-6.3	-2.80	3.0	-0.49 [-0.70, -0.27]
			Placebo	193	180 (93.3)	-1.62 (2.10)	-6.9	-1.49	3.5	
		Week 11	CR845	185	159 (85.9)	-2.72 (1.95)	-6.3	-2.96	3.0	-0.50 [-0.71, -0.28]
			Placebo	193	178 (92.2)	-1.69 (2.16)	-6.9	-1.48	3.6	
		Week 12	CR845	185	151 (81.6)	-2.78 (2.02)	-6.3	-3.04	3.0	-0.47 [-0.70, -0.25]
			Placebo	193	171 (88.6)	-1.79 (2.15)	-6.9	-1.69	3.6	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIC_ISHD: Change from baseline in weekly WI-NRS by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 7	Weekly WI-NRS	Baseline	CR845	241	241 (100.0)	8.16 (0.91)	7.0	8.00	10.0	
			Placebo	232	232 (100.0)	8.31 (0.87)	7.0	8.13	10.0	
		Week 1	CR845	241	234 (97.1)	7.33 (1.47)	1.9	7.41	10.0	
			Placebo	232	227 (97.8)	7.62 (1.40)	3.0	7.71	10.0	
		Week 2	CR845	241	226 (93.8)	6.64 (1.98)	0.0	7.00	10.0	
			Placebo	232	225 (97.0)	7.10 (1.83)	0.3	7.33	10.0	
		Week 3	CR845	241	223 (92.5)	6.23 (2.28)	0.0	6.71	10.0	
			Placebo	232	220 (94.8)	6.87 (1.96)	1.0	7.00	10.0	
		Week 4	CR845	241	218 (90.5)	5.83 (2.46)	0.0	6.31	10.0	
			Placebo	232	220 (94.8)	6.56 (2.24)	0.1	7.00	10.0	
		Week 5	CR845	241	216 (89.6)	5.60 (2.52)	0.0	6.00	10.0	
			Placebo	232	220 (94.8)	6.27 (2.37)	0.0	6.57	10.0	
		Week 6	CR845	241	215 (89.2)	5.32 (2.57)	0.0	5.71	10.0	
			Placebo	232	219 (94.4)	6.18 (2.51)	0.0	6.57	10.0	
		Week 7	CR845	241	211 (87.6)	5.20 (2.63)	0.0	5.83	10.0	
			Placebo	232	216 (93.1)	6.05 (2.50)	0.0	6.43	10.0	
		Week 8	CR845	241	210 (87.1)	5.20 (2.58)	0.0	5.36	10.0	
			Placebo	232	215 (92.7)	5.94 (2.53)	0.0	6.00	10.0	
		Week 9	CR845	241	208 (86.3)	5.08 (2.63)	0.0	5.29	10.0	
			Placebo	232	217 (93.5)	5.81 (2.60)	0.0	6.00	10.0	
		Week 10	CR845	241	209 (86.7)	4.92 (2.71)	0.0	5.00	10.0	
			Placebo	232	213 (91.8)	5.79 (2.62)	0.0	6.00	10.0	
		Week 11	CR845	241	200 (83.0)	4.87 (2.76)	0.0	4.93	10.0	
			Placebo	232	209 (90.1)	5.80 (2.53)	0.0	6.00	10.0	
		Week 12	CR845	241	197 (81.7)	4.75 (2.77)	0.0	5.00	10.0	
			Placebo	232	201 (86.6)	5.66 (2.66)	0.0	5.86	10.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	241	234 (97.1)	-0.84 (1.32)	-7.8	-0.59	2.1	-0.12 [-0.30, 0.06]
			Placebo	232	227 (97.8)	-0.69 (1.13)	-4.8	-0.43	2.8	
		Week 2	CR845	241	226 (93.8)	-1.53 (1.92)	-10.0	-1.00	2.0	-0.18 [-0.36, 0.01]
			Placebo	232	225 (97.0)	-1.21 (1.61)	-8.7	-0.86	2.8	
		Week 3	CR845	241	223 (92.5)	-1.95 (2.20)	-10.0	-1.34	2.1	-0.25 [-0.44, -0.07]
			Placebo	232	220 (94.8)	-1.45 (1.73)	-7.4	-1.15	2.5	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIC_ISHD: Change from baseline in weekly WI-NRS by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 4	CR845	241	218 (90.5)	-2.36 (2.39)	-10.0	-1.80	2.0	-0.27 [-0.46, -0.08]
			Placebo	232	220 (94.8)	-1.76 (2.06)	-8.6	-1.29	2.0	
		Week 5	CR845	241	216 (89.6)	-2.59 (2.49)	-10.0	-2.00	1.8	-0.24 [-0.43, -0.05]
			Placebo	232	220 (94.8)	-2.03 (2.19)	-8.7	-1.59	2.0	
		Week 6	CR845	241	215 (89.2)	-2.86 (2.57)	-10.0	-2.14	1.8	-0.30 [-0.49, -0.11]
			Placebo	232	219 (94.4)	-2.13 (2.31)	-9.0	-1.63	2.0	
		Week 7	CR845	241	211 (87.6)	-2.98 (2.65)	-10.0	-2.25	1.9	-0.29 [-0.48, -0.10]
			Placebo	232	216 (93.1)	-2.27 (2.28)	-9.0	-1.91	2.0	
		Week 8	CR845	241	210 (87.1)	-2.97 (2.58)	-10.0	-2.63	2.1	-0.24 [-0.43, -0.05]
			Placebo	232	215 (92.7)	-2.38 (2.32)	-9.0	-2.13	2.0	
		Week 9	CR845	241	208 (86.3)	-3.09 (2.63)	-10.0	-2.71	1.6	-0.23 [-0.42, -0.04]
			Placebo	232	217 (93.5)	-2.51 (2.39)	-9.0	-2.00	2.0	
		Week 10	CR845	241	209 (86.7)	-3.24 (2.70)	-10.0	-3.13	1.9	-0.29 [-0.48, -0.10]
			Placebo	232	213 (91.8)	-2.50 (2.43)	-9.0	-2.00	2.5	
		Week 11	CR845	241	200 (83.0)	-3.31 (2.75)	-10.0	-3.00	2.1	-0.33 [-0.52, -0.13]
			Placebo	232	209 (90.1)	-2.47 (2.35)	-9.0	-2.14	2.5	
		Week 12	CR845	241	197 (81.7)	-3.42 (2.79)	-10.0	-3.00	2.0	-0.30 [-0.50, -0.11]
			Placebo	232	201 (86.6)	-2.62 (2.45)	-9.0	-2.21	2.5	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIC_ISHE: Change from baseline in weekly WI-NRS by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	Weekly WI-NRS	Baseline	CR845	359	359 (100.0)	7.11 (1.42)	4.2	7.00	10.0	
			Placebo	360	360 (100.0)	7.10 (1.47)	4.1	7.13	10.0	
		Week 1	CR845	359	351 (97.8)	6.26 (1.90)	0.9	6.29	10.0	
			Placebo	360	348 (96.7)	6.54 (1.78)	0.0	6.57	10.0	
		Week 2	CR845	359	343 (95.5)	5.64 (2.17)	0.0	5.86	10.0	
			Placebo	360	346 (96.1)	6.09 (2.03)	0.0	6.29	10.0	
		Week 3	CR845	359	336 (93.6)	5.22 (2.37)	0.0	5.36	10.0	
			Placebo	360	340 (94.4)	5.88 (2.12)	0.0	5.86	10.0	
		Week 4	CR845	359	328 (91.4)	4.90 (2.43)	0.0	5.14	10.0	
			Placebo	360	341 (94.7)	5.63 (2.24)	0.0	5.71	10.0	
		Week 5	CR845	359	326 (90.8)	4.76 (2.43)	0.0	4.86	10.0	
			Placebo	360	340 (94.4)	5.40 (2.30)	0.0	5.31	10.0	
		Week 6	CR845	359	323 (90.0)	4.55 (2.42)	0.0	4.57	10.0	
			Placebo	360	339 (94.2)	5.32 (2.43)	0.0	5.29	10.0	
		Week 7	CR845	359	319 (88.9)	4.45 (2.49)	0.0	4.57	10.0	
			Placebo	360	334 (92.8)	5.24 (2.42)	0.0	5.21	10.0	
		Week 8	CR845	359	316 (88.0)	4.40 (2.49)	0.0	4.43	10.0	
			Placebo	360	332 (92.2)	5.16 (2.45)	0.0	5.14	10.0	
		Week 9	CR845	359	314 (87.5)	4.27 (2.50)	0.0	4.14	10.0	
			Placebo	360	333 (92.5)	5.06 (2.49)	0.0	5.00	10.0	
		Week 10	CR845	359	313 (87.2)	4.21 (2.55)	0.0	4.00	10.0	
			Placebo	360	330 (91.7)	5.00 (2.55)	0.0	5.00	10.0	
		Week 11	CR845	359	304 (84.7)	4.12 (2.58)	0.0	3.86	10.0	
			Placebo	360	327 (90.8)	4.98 (2.52)	0.0	4.86	10.0	
		Week 12	CR845	359	293 (81.6)	4.03 (2.59)	0.0	3.57	10.0	
			Placebo	360	316 (87.8)	4.83 (2.57)	0.0	4.71	10.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	359	351 (97.8)	-0.86 (1.31)	-7.8	-0.63	2.4	-0.22 [-0.37, -0.07]
			Placebo	360	348 (96.7)	-0.58 (1.24)	-6.3	-0.38	2.9	
		Week 2	CR845	359	343 (95.5)	-1.46 (1.70)	-8.9	-1.09	2.0	-0.26 [-0.41, -0.11]
			Placebo	360	346 (96.1)	-1.03 (1.64)	-8.7	-0.72	3.5	
		Week 3	CR845	359	336 (93.6)	-1.87 (1.95)	-8.1	-1.43	2.1	-0.34 [-0.49, -0.19]
			Placebo	360	340 (94.4)	-1.24 (1.77)	-7.4	-1.01	3.3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIC_ISHE: Change from baseline in weekly WI-NRS by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 4	CR845	359	328 (91.4)	-2.20 (2.09)	-9.3	-1.86	2.0	-0.36 [-0.51, -0.20]
			Placebo	360	341 (94.7)	-1.47 (2.00)	-8.6	-1.14	3.5	
		Week 5	CR845	359	326 (90.8)	-2.35 (2.17)	-10.0	-2.03	2.9	-0.31 [-0.46, -0.16]
			Placebo	360	340 (94.4)	-1.69 (2.07)	-8.7	-1.38	3.5	
		Week 6	CR845	359	323 (90.0)	-2.56 (2.23)	-9.9	-2.20	3.8	-0.35 [-0.50, -0.20]
			Placebo	360	339 (94.2)	-1.79 (2.18)	-9.0	-1.54	3.1	
		Week 7	CR845	359	319 (88.9)	-2.65 (2.32)	-10.0	-2.25	1.9	-0.35 [-0.51, -0.20]
			Placebo	360	334 (92.8)	-1.85 (2.20)	-9.0	-1.66	3.3	
		Week 8	CR845	359	316 (88.0)	-2.70 (2.28)	-8.9	-2.52	2.1	-0.33 [-0.48, -0.17]
			Placebo	360	332 (92.2)	-1.95 (2.25)	-9.0	-1.55	3.5	
		Week 9	CR845	359	314 (87.5)	-2.82 (2.30)	-10.0	-2.71	2.0	-0.34 [-0.49, -0.18]
			Placebo	360	333 (92.5)	-2.05 (2.30)	-9.0	-1.63	3.5	
		Week 10	CR845	359	313 (87.2)	-2.89 (2.36)	-10.0	-2.93	3.0	-0.34 [-0.50, -0.19]
			Placebo	360	330 (91.7)	-2.08 (2.36)	-9.0	-1.71	3.5	
		Week 11	CR845	359	304 (84.7)	-2.97 (2.40)	-10.0	-2.85	3.0	-0.37 [-0.53, -0.21]
			Placebo	360	327 (90.8)	-2.10 (2.33)	-9.0	-1.93	3.6	
		Week 12	CR845	359	293 (81.6)	-3.07 (2.48)	-10.0	-2.96	3.0	-0.34 [-0.50, -0.18]
			Placebo	360	316 (87.8)	-2.24 (2.39)	-9.0	-1.87	3.6	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIC_ISHE: Change from baseline in weekly WI-NRS by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	Weekly WI-NRS	Baseline	CR845	67	67 (100.0)	7.48 (1.22)	5.0	7.63	10.0	
			Placebo	65	65 (100.0)	7.57 (1.44)	4.3	7.63	10.0	
		Week 1	CR845	67	63 (94.0)	6.61 (1.61)	3.0	6.86	10.0	
			Placebo	65	65 (100.0)	7.20 (1.66)	2.3	7.29	10.0	
		Week 2	CR845	67	61 (91.0)	5.76 (2.27)	0.0	6.00	10.0	
			Placebo	65	64 (98.5)	6.62 (1.94)	1.5	6.86	10.0	
		Week 3	CR845	67	63 (94.0)	5.36 (2.50)	0.0	6.00	10.0	
			Placebo	65	63 (96.9)	6.40 (2.14)	1.6	6.57	10.0	
		Week 4	CR845	67	62 (92.5)	4.99 (2.62)	0.0	5.36	10.0	
			Placebo	65	62 (95.4)	6.28 (2.25)	1.2	6.43	10.0	
		Week 5	CR845	67	62 (92.5)	4.78 (2.76)	0.0	5.07	10.0	
			Placebo	65	62 (95.4)	5.87 (2.41)	1.0	5.86	10.0	
		Week 6	CR845	67	59 (88.1)	4.59 (2.79)	0.0	4.43	10.0	
			Placebo	65	61 (93.8)	5.67 (2.43)	1.0	5.86	10.0	
		Week 7	CR845	67	60 (89.6)	4.47 (2.73)	0.0	4.86	10.0	
			Placebo	65	63 (96.9)	5.64 (2.43)	0.6	5.71	10.0	
		Week 8	CR845	67	60 (89.6)	4.59 (2.59)	0.0	4.50	10.0	
			Placebo	65	62 (95.4)	5.57 (2.46)	1.0	5.55	10.0	
		Week 9	CR845	67	58 (86.6)	4.45 (2.65)	0.0	4.43	10.0	
			Placebo	65	63 (96.9)	5.39 (2.43)	0.3	5.17	10.0	
		Week 10	CR845	67	59 (88.1)	4.16 (2.69)	0.0	4.57	10.0	
			Placebo	65	63 (96.9)	5.38 (2.31)	0.5	5.29	10.0	
		Week 11	CR845	67	55 (82.1)	4.05 (2.70)	0.0	3.86	10.0	
			Placebo	65	60 (92.3)	5.30 (2.32)	0.6	5.14	10.0	
		Week 12	CR845	67	55 (82.1)	4.00 (2.61)	0.0	3.71	9.0	
			Placebo	65	56 (86.2)	5.37 (2.44)	0.7	5.24	10.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	67	63 (94.0)	-0.86 (1.32)	-5.4	-0.71	1.3	-0.41 [-0.76, -0.06]
			Placebo	65	65 (100.0)	-0.37 (1.07)	-3.4	-0.14	1.4	
		Week 2	CR845	67	61 (91.0)	-1.73 (2.17)	-10.0	-1.17	1.3	-0.42 [-0.78, -0.07]
			Placebo	65	64 (98.5)	-0.94 (1.47)	-5.6	-0.67	1.5	
		Week 3	CR845	67	63 (94.0)	-2.17 (2.33)	-10.0	-1.77	1.6	-0.49 [-0.85, -0.14]
			Placebo	65	63 (96.9)	-1.16 (1.72)	-7.1	-0.77	1.4	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIC_ISHE: Change from baseline in weekly WI-NRS by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 4	CR845	67	62 (92.5)	-2.50 (2.47)	-10.0	-1.96	1.5	-0.53 [-0.89, -0.17]
			Placebo	65	62 (95.4)	-1.33 (1.94)	-8.0	-0.95	1.9	
		Week 5	CR845	67	62 (92.5)	-2.72 (2.67)	-10.0	-2.23	2.0	-0.40 [-0.75, -0.04]
			Placebo	65	62 (95.4)	-1.76 (2.18)	-8.1	-1.15	1.7	
		Week 6	CR845	67	59 (88.1)	-2.94 (2.75)	-10.0	-2.61	1.0	-0.40 [-0.76, -0.04]
			Placebo	65	61 (93.8)	-1.95 (2.16)	-8.1	-1.53	1.3	
		Week 7	CR845	67	60 (89.6)	-3.04 (2.72)	-10.0	-2.38	1.0	-0.43 [-0.79, -0.08]
			Placebo	65	63 (96.9)	-1.97 (2.20)	-7.0	-1.48	2.0	
		Week 8	CR845	67	60 (89.6)	-2.91 (2.59)	-10.0	-2.67	1.4	-0.38 [-0.74, -0.02]
			Placebo	65	62 (95.4)	-1.99 (2.21)	-7.3	-1.51	2.0	
		Week 9	CR845	67	58 (86.6)	-3.06 (2.62)	-10.0	-2.72	1.0	-0.34 [-0.70, 0.02]
			Placebo	65	63 (96.9)	-2.22 (2.25)	-7.4	-1.71	1.4	
		Week 10	CR845	67	59 (88.1)	-3.36 (2.71)	-10.0	-3.16	1.0	-0.49 [-0.85, -0.13]
			Placebo	65	63 (96.9)	-2.18 (2.12)	-7.6	-1.92	1.7	
		Week 11	CR845	67	55 (82.1)	-3.47 (2.63)	-10.0	-3.61	1.0	-0.54 [-0.91, -0.16]
			Placebo	65	60 (92.3)	-2.20 (2.09)	-6.6	-1.96	1.5	
		Week 12	CR845	67	55 (82.1)	-3.50 (2.61)	-10.0	-3.25	1.1	-0.53 [-0.91, -0.15]
			Placebo	65	56 (86.2)	-2.25 (2.10)	-7.5	-2.19	1.7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIC_ISHF: Change from baseline in weekly WI-NRS by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	Weekly WI-NRS	Baseline	CR845	267	267 (100.0)	7.08 (1.39)	4.2	7.00	10.0	
			Placebo	262	262 (100.0)	7.17 (1.44)	4.1	7.13	10.0	
		Week 1	CR845	267	259 (97.0)	6.31 (1.91)	0.9	6.43	10.0	
			Placebo	262	255 (97.3)	6.66 (1.75)	0.0	6.86	10.0	
		Week 2	CR845	267	254 (95.1)	5.65 (2.16)	0.0	5.71	10.0	
			Placebo	262	252 (96.2)	6.16 (2.04)	0.0	6.43	10.0	
		Week 3	CR845	267	254 (95.1)	5.26 (2.37)	0.0	5.43	10.0	
			Placebo	262	246 (93.9)	5.99 (2.11)	0.0	6.00	10.0	
		Week 4	CR845	267	250 (93.6)	4.94 (2.40)	0.0	5.14	10.0	
			Placebo	262	249 (95.0)	5.74 (2.22)	0.0	5.86	10.0	
		Week 5	CR845	267	249 (93.3)	4.77 (2.43)	0.0	5.00	10.0	
			Placebo	262	248 (94.7)	5.52 (2.32)	0.0	5.66	10.0	
		Week 6	CR845	267	247 (92.5)	4.60 (2.41)	0.0	4.71	10.0	
			Placebo	262	246 (93.9)	5.42 (2.47)	0.0	5.59	10.0	
		Week 7	CR845	267	244 (91.4)	4.46 (2.50)	0.0	4.64	10.0	
			Placebo	262	247 (94.3)	5.33 (2.40)	0.0	5.43	10.0	
		Week 8	CR845	267	245 (91.8)	4.37 (2.45)	0.0	4.43	10.0	
			Placebo	262	245 (93.5)	5.26 (2.42)	0.0	5.29	10.0	
		Week 9	CR845	267	239 (89.5)	4.29 (2.49)	0.0	4.43	10.0	
			Placebo	262	248 (94.7)	5.15 (2.46)	0.0	5.14	10.0	
		Week 10	CR845	267	237 (88.8)	4.20 (2.52)	0.0	4.00	10.0	
			Placebo	262	246 (93.9)	5.09 (2.53)	0.0	5.00	10.0	
		Week 11	CR845	267	233 (87.3)	4.09 (2.54)	0.0	3.86	10.0	
			Placebo	262	243 (92.7)	5.09 (2.48)	0.0	5.00	10.0	
		Week 12	CR845	267	224 (83.9)	3.99 (2.52)	0.0	3.71	10.0	
			Placebo	262	232 (88.5)	4.99 (2.62)	0.0	5.00	10.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	267	259 (97.0)	-0.78 (1.24)	-5.6	-0.55	2.1	-0.19 [-0.36, -0.02]
			Placebo	262	255 (97.3)	-0.54 (1.28)	-6.3	-0.36	2.9	
		Week 2	CR845	267	254 (95.1)	-1.42 (1.60)	-7.6	-1.08	2.0	-0.24 [-0.41, -0.06]
			Placebo	262	252 (96.2)	-1.03 (1.70)	-8.7	-0.77	3.5	
		Week 3	CR845	267	254 (95.1)	-1.83 (1.90)	-8.1	-1.38	2.1	-0.34 [-0.52, -0.17]
			Placebo	262	246 (93.9)	-1.19 (1.84)	-7.4	-0.96	3.3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIC_ISHF: Change from baseline in weekly WI-NRS by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 4	CR845	267	250 (93.6)	-2.15 (1.98)	-8.1	-1.86	1.4	-0.35 [-0.52, -0.17]
			Placebo	262	249 (95.0)	-1.44 (2.07)	-8.6	-1.11	3.5	
		Week 5	CR845	267	249 (93.3)	-2.32 (2.09)	-8.6	-2.09	2.9	-0.32 [-0.50, -0.14]
			Placebo	262	248 (94.7)	-1.65 (2.15)	-8.7	-1.34	3.5	
		Week 6	CR845	267	247 (92.5)	-2.50 (2.17)	-8.6	-2.20	3.8	-0.33 [-0.51, -0.15]
			Placebo	262	246 (93.9)	-1.75 (2.32)	-9.0	-1.50	3.1	
		Week 7	CR845	267	244 (91.4)	-2.62 (2.27)	-8.6	-2.29	1.7	-0.34 [-0.52, -0.17]
			Placebo	262	247 (94.3)	-1.84 (2.25)	-9.0	-1.50	3.3	
		Week 8	CR845	267	245 (91.8)	-2.70 (2.21)	-8.8	-2.58	1.9	-0.34 [-0.52, -0.16]
			Placebo	262	245 (93.5)	-1.94 (2.28)	-9.0	-1.54	3.3	
		Week 9	CR845	267	239 (89.5)	-2.78 (2.22)	-9.0	-2.71	2.0	-0.33 [-0.51, -0.15]
			Placebo	262	248 (94.7)	-2.03 (2.34)	-9.0	-1.59	3.5	
		Week 10	CR845	267	237 (88.8)	-2.87 (2.28)	-9.0	-2.95	3.0	-0.33 [-0.51, -0.15]
			Placebo	262	246 (93.9)	-2.09 (2.45)	-9.0	-1.61	3.5	
		Week 11	CR845	267	233 (87.3)	-2.98 (2.33)	-9.0	-2.96	3.0	-0.37 [-0.55, -0.19]
			Placebo	262	243 (92.7)	-2.10 (2.36)	-9.0	-1.93	3.6	
		Week 12	CR845	267	224 (83.9)	-3.08 (2.39)	-9.0	-3.00	3.0	-0.37 [-0.55, -0.18]
			Placebo	262	232 (88.5)	-2.18 (2.51)	-9.0	-1.85	3.6	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIC_ISHF: Change from baseline in weekly WI-NRS by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	Weekly WI-NRS	Baseline	CR845	159	159 (100.0)	7.32 (1.40)	4.3	7.38	10.0	
			Placebo	163	163 (100.0)	7.18 (1.54)	4.1	7.13	10.0	
		Week 1	CR845	159	155 (97.5)	6.32 (1.80)	1.9	6.43	10.0	
			Placebo	163	158 (96.9)	6.63 (1.82)	2.1	6.57	10.0	
		Week 2	CR845	159	150 (94.3)	5.67 (2.22)	0.0	6.00	10.0	
			Placebo	163	158 (96.9)	6.19 (2.00)	1.0	6.00	10.0	
		Week 3	CR845	159	145 (91.2)	5.22 (2.44)	0.0	5.71	10.0	
			Placebo	163	157 (96.3)	5.90 (2.17)	1.0	5.71	10.0	
		Week 4	CR845	159	140 (88.1)	4.86 (2.55)	0.0	5.21	9.7	
			Placebo	163	154 (94.5)	5.71 (2.31)	1.0	5.57	10.0	
		Week 5	CR845	159	139 (87.4)	4.75 (2.60)	0.0	4.86	10.0	
			Placebo	163	154 (94.5)	5.39 (2.34)	0.3	5.00	10.0	
		Week 6	CR845	159	135 (84.9)	4.48 (2.60)	0.0	4.57	9.6	
			Placebo	163	154 (94.5)	5.31 (2.37)	0.1	5.14	10.0	
		Week 7	CR845	159	135 (84.9)	4.43 (2.59)	0.0	4.43	9.4	
			Placebo	163	150 (92.0)	5.25 (2.46)	0.4	5.14	10.0	
		Week 8	CR845	159	131 (82.4)	4.55 (2.59)	0.0	4.29	9.6	
			Placebo	163	149 (91.4)	5.17 (2.51)	0.1	5.14	10.0	
		Week 9	CR845	159	133 (83.6)	4.32 (2.60)	0.0	4.00	9.3	
			Placebo	163	148 (90.8)	5.05 (2.52)	0.3	4.71	10.0	
		Week 10	CR845	159	135 (84.9)	4.20 (2.66)	0.0	4.00	9.6	
			Placebo	163	147 (90.2)	5.02 (2.50)	0.1	4.71	10.0	
		Week 11	CR845	159	126 (79.2)	4.15 (2.69)	0.0	3.69	9.8	
			Placebo	163	144 (88.3)	4.92 (2.53)	0.0	4.64	10.0	
		Week 12	CR845	159	124 (78.0)	4.10 (2.72)	0.0	3.50	9.7	
			Placebo	163	140 (85.9)	4.80 (2.43)	0.0	4.43	10.0	
	Change from baseline in weekly WI-NRS	Week 1	CR845	159	155 (97.5)	-1.00 (1.43)	-7.8	-0.86	2.4	-0.34 [-0.57, -0.12]
			Placebo	163	158 (96.9)	-0.55 (1.12)	-4.7	-0.38	2.6	
		Week 2	CR845	159	150 (94.3)	-1.64 (2.05)	-10.0	-1.17	1.7	-0.36 [-0.59, -0.14]
			Placebo	163	158 (96.9)	-1.00 (1.48)	-5.4	-0.71	2.6	
		Week 3	CR845	159	145 (91.2)	-2.05 (2.19)	-10.0	-1.71	1.8	-0.40 [-0.63, -0.18]
			Placebo	163	157 (96.3)	-1.28 (1.63)	-5.4	-1.00	3.1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIC_ISHF: Change from baseline in weekly WI-NRS by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
	Change from baseline in weekly WI-NRS	Week 4	CR845	159	140 (88.1)	-2.44 (2.43)	-10.0	-1.99	2.0	-0.45 [-0.68, -0.22]
			Placebo	163	154 (94.5)	-1.47 (1.85)	-7.1	-1.10	3.1	
		Week 5	CR845	159	139 (87.4)	-2.56 (2.54)	-10.0	-2.14	2.0	-0.34 [-0.57, -0.11]
			Placebo	163	154 (94.5)	-1.79 (1.97)	-7.8	-1.40	3.4	
		Week 6	CR845	159	135 (84.9)	-2.83 (2.58)	-10.0	-2.39	1.8	-0.41 [-0.65, -0.18]
			Placebo	163	154 (94.5)	-1.90 (1.93)	-7.1	-1.73	2.5	
		Week 7	CR845	159	135 (84.9)	-2.87 (2.59)	-10.0	-2.27	1.9	-0.41 [-0.64, -0.17]
			Placebo	163	150 (92.0)	-1.92 (2.11)	-6.8	-1.75	2.3	
		Week 8	CR845	159	131 (82.4)	-2.78 (2.56)	-10.0	-2.32	2.1	-0.33 [-0.57, -0.10]
			Placebo	163	149 (91.4)	-1.99 (2.20)	-7.3	-1.57	3.5	
		Week 9	CR845	159	133 (83.6)	-2.99 (2.58)	-10.0	-2.71	1.6	-0.35 [-0.59, -0.12]
			Placebo	163	148 (90.8)	-2.15 (2.20)	-7.4	-1.83	3.1	
		Week 10	CR845	159	135 (84.9)	-3.13 (2.66)	-10.0	-2.93	2.8	-0.43 [-0.66, -0.19]
			Placebo	163	147 (90.2)	-2.11 (2.11)	-7.9	-1.88	3.1	
		Week 11	CR845	159	126 (79.2)	-3.18 (2.64)	-10.0	-3.05	1.8	-0.44 [-0.68, -0.19]
			Placebo	163	144 (88.3)	-2.14 (2.17)	-7.3	-1.96	2.8	
		Week 12	CR845	159	124 (78.0)	-3.25 (2.70)	-10.0	-3.12	1.4	-0.39 [-0.63, -0.14]
			Placebo	163	140 (85.9)	-2.33 (2.06)	-7.5	-2.00	2.6	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
WI-NRS = worst itching intensity numerical rating scale.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIC_ISCA: Change from baseline in weekly WI-NRS - MMRM results by age
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
A: Age									0.909
< 65 years	Week 1	CR845	282	275 (97.5)	-0.78 (0.09)	(-0.96, -0.61)	-0.31 (0.10)	(-0.51, -0.10)	0.003 *
		Placebo	290	280 (96.6)	-0.48 (0.09)	(-0.66, -0.30)			
>= 65 years	Week 1	CR845	144	139 (96.5)	-0.89 (0.13)	(-1.16, -0.63)	-0.34 (0.16)	(-0.66, -0.02)	0.038 *
		Placebo	135	133 (98.5)	-0.55 (0.13)	(-0.82, -0.29)			
< 65 years	Week 2	CR845	282	267 (94.7)	-1.46 (0.11)	(-1.68, -1.24)	-0.58 (0.14)	(-0.85, -0.32)	<0.001 *
		Placebo	290	278 (95.9)	-0.88 (0.11)	(-1.10, -0.66)			
>= 65 years	Week 2	CR845	144	137 (95.1)	-1.47 (0.17)	(-1.81, -1.14)	-0.34 (0.22)	(-0.78, 0.10)	0.128
		Placebo	135	132 (97.8)	-1.13 (0.17)	(-1.47, -0.80)			
< 65 years	Week 3	CR845	282	265 (94.0)	-1.90 (0.12)	(-2.14, -1.66)	-0.73 (0.16)	(-1.04, -0.43)	<0.001 *
		Placebo	290	273 (94.1)	-1.17 (0.12)	(-1.41, -0.93)			
>= 65 years	Week 3	CR845	144	134 (93.1)	-1.82 (0.19)	(-2.19, -1.46)	-0.56 (0.25)	(-1.04, -0.08)	0.023 *
		Placebo	135	130 (96.3)	-1.26 (0.19)	(-1.63, -0.89)			
< 65 years	Week 4	CR845	282	260 (92.2)	-2.26 (0.14)	(-2.53, -2.00)	-0.89 (0.17)	(-1.23, -0.54)	<0.001 *
		Placebo	290	273 (94.1)	-1.38 (0.13)	(-1.64, -1.11)			
>= 65 years	Week 4	CR845	144	130 (90.3)	-2.13 (0.19)	(-2.51, -1.76)	-0.61 (0.25)	(-1.11, -0.11)	0.017 *
		Placebo	135	130 (96.3)	-1.52 (0.19)	(-1.90, -1.14)			
< 65 years	Week 5	CR845	282	259 (91.8)	-2.42 (0.14)	(-2.70, -2.14)	-0.84 (0.18)	(-1.20, -0.48)	<0.001 *
		Placebo	290	272 (93.8)	-1.58 (0.14)	(-1.86, -1.31)			
>= 65 years	Week 5	CR845	144	129 (89.6)	-2.33 (0.20)	(-2.73, -1.94)	-0.52 (0.27)	(-1.04, 0.01)	0.053
		Placebo	135	130 (96.3)	-1.82 (0.20)	(-2.21, -1.42)			
< 65 years	Week 6	CR845	282	254 (90.1)	-2.69 (0.15)	(-2.98, -2.41)	-1.00 (0.19)	(-1.37, -0.62)	<0.001 *
		Placebo	290	272 (93.8)	-1.70 (0.15)	(-1.98, -1.41)			
>= 65 years	Week 6	CR845	144	128 (88.9)	-2.49 (0.20)	(-2.89, -2.09)	-0.56 (0.27)	(-1.09, -0.02)	0.041 *
		Placebo	135	128 (94.8)	-1.93 (0.20)	(-2.33, -1.53)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIC_ISCA: Change from baseline in weekly WI-NRS - MMRM results by age
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
< 65 years	Week 7	CR845	282	251 (89.0)	-2.75 (0.15)	(-3.04, -2.45)	-0.94 (0.19)	(-1.32, -0.56)	<0.001 *
		Placebo	290	268 (92.4)	-1.80 (0.15)	(-2.09, -1.52)			
>= 65 years	Week 7	CR845	144	128 (88.9)	-2.62 (0.21)	(-3.03, -2.22)	-0.74 (0.27)	(-1.28, -0.20)	0.007 *
		Placebo	135	129 (95.6)	-1.88 (0.21)	(-2.28, -1.47)			
< 65 years	Week 8	CR845	282	249 (88.3)	-2.81 (0.15)	(-3.11, -2.52)	-0.87 (0.20)	(-1.26, -0.48)	<0.001 *
		Placebo	290	268 (92.4)	-1.95 (0.15)	(-2.24, -1.65)			
>= 65 years	Week 8	CR845	144	127 (88.2)	-2.61 (0.21)	(-3.02, -2.20)	-0.67 (0.28)	(-1.22, -0.13)	0.016 *
		Placebo	135	126 (93.3)	-1.94 (0.21)	(-2.34, -1.53)			
< 65 years	Week 9	CR845	282	249 (88.3)	-2.95 (0.15)	(-3.25, -2.65)	-0.89 (0.20)	(-1.27, -0.50)	<0.001 *
		Placebo	290	269 (92.8)	-2.07 (0.15)	(-2.36, -1.77)			
>= 65 years	Week 9	CR845	144	123 (85.4)	-2.63 (0.21)	(-3.05, -2.21)	-0.59 (0.29)	(-1.15, -0.02)	0.042 *
		Placebo	135	127 (94.1)	-2.05 (0.21)	(-2.47, -1.62)			
< 65 years	Week 10	CR845	282	250 (88.7)	-3.06 (0.15)	(-3.37, -2.76)	-1.03 (0.20)	(-1.43, -0.63)	<0.001 *
		Placebo	290	268 (92.4)	-2.04 (0.15)	(-2.34, -1.74)			
>= 65 years	Week 10	CR845	144	122 (84.7)	-2.73 (0.22)	(-3.16, -2.31)	-0.51 (0.29)	(-1.08, 0.06)	0.081
		Placebo	135	125 (92.6)	-2.23 (0.22)	(-2.65, -1.80)			
< 65 years	Week 11	CR845	282	241 (85.5)	-3.16 (0.16)	(-3.46, -2.85)	-1.08 (0.20)	(-1.48, -0.68)	<0.001 *
		Placebo	290	264 (91.0)	-2.08 (0.15)	(-2.38, -1.78)			
>= 65 years	Week 11	CR845	144	118 (81.9)	-2.72 (0.22)	(-3.15, -2.29)	-0.56 (0.29)	(-1.13, 0.01)	0.055
		Placebo	135	123 (91.1)	-2.16 (0.22)	(-2.59, -1.74)			
< 65 years	Week 12	CR845	282	234 (83.0)	-3.22 (0.16)	(-3.53, -2.91)	-1.07 (0.21)	(-1.47, -0.66)	<0.001 *
		Placebo	290	253 (87.2)	-2.15 (0.15)	(-2.46, -1.85)			
>= 65 years	Week 12	CR845	144	114 (79.2)	-2.81 (0.23)	(-3.25, -2.37)	-0.43 (0.30)	(-1.02, 0.17)	0.157
		Placebo	135	119 (88.1)	-2.38 (0.22)	(-2.82, -1.94)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIC_ISCB: Change from baseline in weekly WI-NRS - MMRM results by sex
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
B: Sex									0.213
Male	Week 1	CR845	249	241 (96.8)	-0.68 (0.10)	(-0.88, -0.49)	-0.24 (0.11)	(-0.46, -0.03)	0.028 *
		Placebo	258	252 (97.7)	-0.44 (0.10)	(-0.63, -0.25)			
Female	Week 1	CR845	177	173 (97.7)	-0.98 (0.11)	(-1.21, -0.76)	-0.41 (0.14)	(-0.69, -0.14)	0.004 *
		Placebo	167	161 (96.4)	-0.57 (0.12)	(-0.81, -0.33)			
Male	Week 2	CR845	249	235 (94.4)	-1.32 (0.12)	(-1.56, -1.08)	-0.43 (0.15)	(-0.72, -0.14)	0.003 *
		Placebo	258	250 (96.9)	-0.89 (0.12)	(-1.12, -0.65)			
Female	Week 2	CR845	177	169 (95.5)	-1.64 (0.15)	(-1.93, -1.35)	-0.59 (0.19)	(-0.98, -0.21)	0.002 *
		Placebo	167	160 (95.8)	-1.05 (0.15)	(-1.35, -0.75)			
Male	Week 3	CR845	249	231 (92.8)	-1.64 (0.13)	(-1.90, -1.38)	-0.58 (0.16)	(-0.90, -0.26)	<0.001 *
		Placebo	258	244 (94.6)	-1.05 (0.13)	(-1.30, -0.80)			
Female	Week 3	CR845	177	168 (94.9)	-2.17 (0.16)	(-2.49, -1.85)	-0.78 (0.22)	(-1.22, -0.35)	<0.001 *
		Placebo	167	159 (95.2)	-1.39 (0.17)	(-1.73, -1.06)			
Male	Week 4	CR845	249	227 (91.2)	-1.97 (0.14)	(-2.25, -1.70)	-0.68 (0.18)	(-1.03, -0.33)	<0.001 *
		Placebo	258	247 (95.7)	-1.29 (0.14)	(-1.56, -1.03)			
Female	Week 4	CR845	177	163 (92.1)	-2.53 (0.18)	(-2.88, -2.18)	-0.94 (0.24)	(-1.42, -0.47)	<0.001 *
		Placebo	167	156 (93.4)	-1.58 (0.18)	(-1.95, -1.22)			
Male	Week 5	CR845	249	225 (90.4)	-2.12 (0.15)	(-2.41, -1.83)	-0.62 (0.19)	(-0.98, -0.25)	0.001 *
		Placebo	258	244 (94.6)	-1.50 (0.14)	(-1.78, -1.22)			
Female	Week 5	CR845	177	163 (92.1)	-2.74 (0.18)	(-3.10, -2.38)	-0.87 (0.25)	(-1.36, -0.38)	<0.001 *
		Placebo	167	158 (94.6)	-1.86 (0.19)	(-2.24, -1.49)			
Male	Week 6	CR845	249	223 (89.6)	-2.32 (0.15)	(-2.62, -2.03)	-0.78 (0.19)	(-1.16, -0.41)	<0.001 *
		Placebo	258	241 (93.4)	-1.54 (0.14)	(-1.82, -1.25)			
Female	Week 6	CR845	177	159 (89.8)	-3.01 (0.19)	(-3.39, -2.63)	-0.92 (0.26)	(-1.43, -0.40)	<0.001 *
		Placebo	167	159 (95.2)	-2.10 (0.20)	(-2.49, -1.71)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIC_ISCB: Change from baseline in weekly WI-NRS - MMRM results by sex
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Male	Week 7	CR845	249	220 (88.4)	-2.36 (0.15)	(-2.66, -2.06)	-0.77 (0.20)	(-1.16, -0.38)	<0.001 *
		Placebo	258	241 (93.4)	-1.59 (0.15)	(-1.88, -1.30)			
Female	Week 7	CR845	177	159 (89.8)	-3.15 (0.19)	(-3.53, -2.78)	-0.99 (0.26)	(-1.50, -0.47)	<0.001 *
		Placebo	167	156 (93.4)	-2.16 (0.20)	(-2.55, -1.78)			
Male	Week 8	CR845	249	219 (88.0)	-2.34 (0.16)	(-2.64, -2.03)	-0.64 (0.20)	(-1.02, -0.25)	0.001 *
		Placebo	258	241 (93.4)	-1.70 (0.15)	(-2.00, -1.41)			
Female	Week 8	CR845	177	157 (88.7)	-3.28 (0.19)	(-3.66, -2.90)	-1.00 (0.26)	(-1.53, -0.48)	<0.001 *
		Placebo	167	153 (91.6)	-2.27 (0.20)	(-2.67, -1.88)			
Male	Week 9	CR845	249	213 (85.5)	-2.43 (0.16)	(-2.74, -2.12)	-0.57 (0.20)	(-0.96, -0.18)	0.004 *
		Placebo	258	240 (93.0)	-1.86 (0.15)	(-2.15, -1.57)			
Female	Week 9	CR845	177	159 (89.8)	-3.39 (0.20)	(-3.78, -3.00)	-1.05 (0.27)	(-1.58, -0.52)	<0.001 *
		Placebo	167	156 (93.4)	-2.34 (0.20)	(-2.74, -1.94)			
Male	Week 10	CR845	249	215 (86.3)	-2.59 (0.16)	(-2.90, -2.27)	-0.66 (0.21)	(-1.06, -0.25)	0.002 *
		Placebo	258	239 (92.6)	-1.93 (0.15)	(-2.23, -1.63)			
Female	Week 10	CR845	177	157 (88.7)	-3.43 (0.20)	(-3.83, -3.04)	-1.10 (0.28)	(-1.64, -0.55)	<0.001 *
		Placebo	167	154 (92.2)	-2.34 (0.21)	(-2.75, -1.93)			
Male	Week 11	CR845	249	206 (82.7)	-2.61 (0.16)	(-2.93, -2.29)	-0.64 (0.21)	(-1.05, -0.24)	0.002 *
		Placebo	258	236 (91.5)	-1.97 (0.15)	(-2.27, -1.66)			
Female	Week 11	CR845	177	153 (86.4)	-3.54 (0.20)	(-3.93, -3.15)	-1.25 (0.27)	(-1.79, -0.72)	<0.001 *
		Placebo	167	151 (90.4)	-2.29 (0.21)	(-2.69, -1.89)			
Male	Week 12	CR845	249	200 (80.3)	-2.66 (0.17)	(-2.99, -2.34)	-0.62 (0.21)	(-1.04, -0.20)	0.004 *
		Placebo	258	227 (88.0)	-2.04 (0.16)	(-2.35, -1.73)			
Female	Week 12	CR845	177	148 (83.6)	-3.63 (0.20)	(-4.04, -3.23)	-1.15 (0.28)	(-1.70, -0.60)	<0.001 *
		Placebo	167	145 (86.8)	-2.48 (0.21)	(-2.90, -2.07)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIC_ISCC: Change from baseline in weekly WI-NRS - MMRM results by race
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
C: Race									0.948
Black/African American	Week 1	CR845	135	132 (97.8)	-0.82 (0.13)	(-1.07, -0.56)	-0.30 (0.17)	(-0.63, 0.03)	0.073
		Placebo	114	108 (94.7)	-0.52 (0.14)	(-0.79, -0.25)			
White	Week 1	CR845	255	246 (96.5)	-0.82 (0.10)	(-1.02, -0.62)	-0.30 (0.11)	(-0.52, -0.08)	0.007 *
		Placebo	262	257 (98.1)	-0.52 (0.10)	(-0.71, -0.33)			
Other	Week 1	CR845	35	35 (100.0)	-0.78 (0.30)	(-1.38, -0.19)	-0.33 (0.29)	(-0.91, 0.25)	0.260
		Placebo	47	46 (97.9)	-0.45 (0.27)	(-0.99, 0.08)			
Black/African American	Week 2	CR845	135	126 (93.3)	-1.34 (0.16)	(-1.65, -1.03)	-0.44 (0.21)	(-0.86, -0.01)	0.043 *
		Placebo	114	105 (92.1)	-0.90 (0.17)	(-1.24, -0.57)			
White	Week 2	CR845	255	244 (95.7)	-1.52 (0.12)	(-1.76, -1.27)	-0.49 (0.15)	(-0.79, -0.20)	0.001 *
		Placebo	262	257 (98.1)	-1.02 (0.12)	(-1.26, -0.78)			
Other	Week 2	CR845	35	33 (94.3)	-1.49 (0.35)	(-2.19, -0.79)	-0.62 (0.38)	(-1.38, 0.14)	0.110
		Placebo	47	46 (97.9)	-0.87 (0.31)	(-1.50, -0.25)			
Black/African American	Week 3	CR845	135	124 (91.9)	-1.78 (0.17)	(-2.13, -1.44)	-0.60 (0.24)	(-1.07, -0.12)	0.014 *
		Placebo	114	107 (93.9)	-1.19 (0.19)	(-1.56, -0.82)			
White	Week 3	CR845	255	243 (95.3)	-1.93 (0.14)	(-2.20, -1.66)	-0.72 (0.17)	(-1.05, -0.38)	<0.001 *
		Placebo	262	249 (95.0)	-1.21 (0.13)	(-1.48, -0.95)			
Other	Week 3	CR845	35	31 (88.6)	-1.71 (0.37)	(-2.45, -0.97)	-0.43 (0.41)	(-1.25, 0.38)	0.293
		Placebo	47	45 (95.7)	-1.27 (0.33)	(-1.92, -0.62)			
Black/African American	Week 4	CR845	135	121 (89.6)	-2.12 (0.20)	(-2.50, -1.73)	-0.70 (0.27)	(-1.24, -0.17)	0.011 *
		Placebo	114	106 (93.0)	-1.42 (0.21)	(-1.83, -1.00)			
White	Week 4	CR845	255	237 (92.9)	-2.26 (0.15)	(-2.55, -1.98)	-0.81 (0.19)	(-1.17, -0.45)	<0.001 *
		Placebo	262	249 (95.0)	-1.45 (0.14)	(-1.73, -1.17)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIC_ISCC: Change from baseline in weekly WI-NRS - MMRM results by race
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Other	Week 4	CR845	35	31 (88.6)	-2.19 (0.37)	(-2.93, -1.45)	-0.79 (0.42)	(-1.62, 0.03)	0.060
		Placebo	47	46 (97.9)	-1.40 (0.33)	(-2.05, -0.74)			
Black/African American	Week 5	CR845	135	120 (88.9)	-2.22 (0.20)	(-2.62, -1.82)	-0.67 (0.28)	(-1.23, -0.12)	0.018 *
		Placebo	114	107 (93.9)	-1.55 (0.22)	(-1.97, -1.12)			
White	Week 5	CR845	255	236 (92.5)	-2.48 (0.15)	(-2.78, -2.17)	-0.76 (0.20)	(-1.14, -0.37)	<0.001 *
		Placebo	262	247 (94.3)	-1.72 (0.15)	(-2.01, -1.43)			
Other	Week 5	CR845	35	31 (88.6)	-2.39 (0.37)	(-3.13, -1.64)	-0.68 (0.41)	(-1.51, 0.14)	0.104
		Placebo	47	46 (97.9)	-1.70 (0.33)	(-2.36, -1.05)			
Black/African American	Week 6	CR845	135	115 (85.2)	-2.52 (0.21)	(-2.94, -2.11)	-0.78 (0.30)	(-1.36, -0.19)	0.009 *
		Placebo	114	107 (93.9)	-1.75 (0.23)	(-2.19, -1.30)			
White	Week 6	CR845	255	235 (92.2)	-2.65 (0.16)	(-2.96, -2.35)	-0.90 (0.20)	(-1.30, -0.50)	<0.001 *
		Placebo	262	246 (93.9)	-1.76 (0.15)	(-2.06, -1.46)			
Other	Week 6	CR845	35	31 (88.6)	-2.78 (0.41)	(-3.61, -1.96)	-0.75 (0.47)	(-1.70, 0.19)	0.115
		Placebo	47	45 (95.7)	-2.03 (0.36)	(-2.75, -1.31)			
Black/African American	Week 7	CR845	135	115 (85.2)	-2.70 (0.21)	(-3.12, -2.27)	-0.85 (0.30)	(-1.44, -0.25)	0.005 *
		Placebo	114	106 (93.0)	-1.85 (0.23)	(-2.30, -1.40)			
White	Week 7	CR845	255	232 (91.0)	-2.71 (0.16)	(-3.02, -2.40)	-0.91 (0.20)	(-1.31, -0.51)	<0.001 *
		Placebo	262	245 (93.5)	-1.80 (0.15)	(-2.10, -1.50)			
Other	Week 7	CR845	35	31 (88.6)	-2.74 (0.44)	(-3.61, -1.86)	-0.72 (0.51)	(-1.74, 0.31)	0.168
		Placebo	47	44 (93.6)	-2.02 (0.38)	(-2.78, -1.26)			
Black/African American	Week 8	CR845	135	116 (85.9)	-2.67 (0.22)	(-3.11, -2.23)	-0.68 (0.31)	(-1.29, -0.06)	0.031 *
		Placebo	114	105 (92.1)	-1.99 (0.24)	(-2.46, -1.53)			
White	Week 8	CR845	255	228 (89.4)	-2.76 (0.16)	(-3.08, -2.45)	-0.90 (0.20)	(-1.30, -0.50)	<0.001 *
		Placebo	262	242 (92.4)	-1.86 (0.15)	(-2.17, -1.56)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIC_ISCC: Change from baseline in weekly WI-NRS - MMRM results by race
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Other	Week 8	CR845	35	31 (88.6)	-2.85 (0.42)	(-3.69, -2.01)	-0.52 (0.49)	(-1.49, 0.45)	0.289
		Placebo	47	45 (95.7)	-2.33 (0.37)	(-3.06, -1.60)			
Black/African American	Week 9	CR845	135	115 (85.2)	-2.93 (0.22)	(-3.36, -2.50)	-0.86 (0.31)	(-1.46, -0.26)	0.005 *
		Placebo	114	108 (94.7)	-2.07 (0.23)	(-2.53, -1.62)			
White	Week 9	CR845	255	228 (89.4)	-2.82 (0.16)	(-3.14, -2.50)	-0.85 (0.21)	(-1.26, -0.43)	<0.001 *
		Placebo	262	242 (92.4)	-1.97 (0.16)	(-2.28, -1.66)			
Other	Week 9	CR845	35	28 (80.0)	-2.70 (0.43)	(-3.56, -1.83)	-0.11 (0.50)	(-1.11, 0.89)	0.826
		Placebo	47	44 (93.6)	-2.59 (0.37)	(-3.33, -1.84)			
Black/African American	Week 10	CR845	135	115 (85.2)	-3.16 (0.22)	(-3.60, -2.72)	-1.04 (0.31)	(-1.65, -0.43)	<0.001 *
		Placebo	114	108 (94.7)	-2.12 (0.23)	(-2.58, -1.66)			
White	Week 10	CR845	255	226 (88.6)	-2.84 (0.17)	(-3.17, -2.52)	-0.81 (0.22)	(-1.24, -0.39)	<0.001 *
		Placebo	262	240 (91.6)	-2.03 (0.16)	(-2.35, -1.72)			
Other	Week 10	CR845	35	30 (85.7)	-2.92 (0.45)	(-3.80, -2.03)	-0.39 (0.52)	(-1.42, 0.65)	0.458
		Placebo	47	43 (91.5)	-2.53 (0.38)	(-3.29, -1.77)			
Black/African American	Week 11	CR845	135	106 (78.5)	-3.18 (0.22)	(-3.61, -2.74)	-1.10 (0.31)	(-1.72, -0.49)	<0.001 *
		Placebo	114	105 (92.1)	-2.07 (0.23)	(-2.54, -1.61)			
White	Week 11	CR845	255	223 (87.5)	-2.95 (0.17)	(-3.28, -2.63)	-0.92 (0.22)	(-1.34, -0.50)	<0.001 *
		Placebo	262	238 (90.8)	-2.03 (0.16)	(-2.35, -1.72)			
Other	Week 11	CR845	35	29 (82.9)	-2.95 (0.45)	(-3.83, -2.06)	-0.25 (0.52)	(-1.29, 0.78)	0.629
		Placebo	47	42 (89.4)	-2.70 (0.38)	(-3.46, -1.93)			
Black/African American	Week 12	CR845	135	104 (77.0)	-3.34 (0.23)	(-3.79, -2.89)	-1.17 (0.32)	(-1.80, -0.54)	<0.001 *
		Placebo	114	102 (89.5)	-2.18 (0.24)	(-2.65, -1.70)			
White	Week 12	CR845	255	214 (83.9)	-2.99 (0.17)	(-3.33, -2.66)	-0.86 (0.22)	(-1.29, -0.42)	<0.001 *
		Placebo	262	229 (87.4)	-2.14 (0.17)	(-2.46, -1.81)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIC_ISCC: Change from baseline in weekly WI-NRS - MMRM results by race
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Other	Week 12	CR845	35	29 (82.9)	-2.85 (0.44)	(-3.72, -1.98)	0.08 (0.51)	(-0.93, 1.10)	0.869
		Placebo	47	39 (83.0)	-2.94 (0.38)	(-3.69, -2.19)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIC_ISCD: Change from baseline in weekly WI-NRS - MMRM results by baseline WI-NRS
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
D: Baseline worst itching NRS score (WI-NRS)									0.038 i
>= 4 to < 7	Week 1	CR845	185	180 (97.3)	-0.74 (0.13)	(-0.99, -0.49)	-0.51 (0.14)	(-0.78, -0.24)	<0.001 *
		Placebo	193	186 (96.4)	-0.23 (0.12)	(-0.47, 0.02)			
>= 7	Week 1	CR845	241	234 (97.1)	-0.85 (0.09)	(-1.03, -0.67)	-0.16 (0.11)	(-0.39, 0.06)	0.158
		Placebo	232	227 (97.8)	-0.69 (0.09)	(-0.87, -0.50)			
>= 4 to < 7	Week 2	CR845	185	178 (96.2)	-1.33 (0.14)	(-1.62, -1.05)	-0.70 (0.17)	(-1.03, -0.38)	<0.001 *
		Placebo	193	185 (95.9)	-0.63 (0.14)	(-0.90, -0.35)			
>= 7	Week 2	CR845	241	226 (93.8)	-1.53 (0.12)	(-1.78, -1.29)	-0.34 (0.16)	(-0.67, -0.02)	0.037 *
		Placebo	232	225 (97.0)	-1.19 (0.13)	(-1.44, -0.94)			
>= 4 to < 7	Week 3	CR845	185	176 (95.1)	-1.73 (0.15)	(-2.03, -1.42)	-0.92 (0.18)	(-1.28, -0.56)	<0.001 *
		Placebo	193	183 (94.8)	-0.81 (0.15)	(-1.11, -0.52)			
>= 7	Week 3	CR845	241	223 (92.5)	-1.95 (0.14)	(-2.23, -1.68)	-0.48 (0.19)	(-0.85, -0.11)	0.011 *
		Placebo	232	220 (94.8)	-1.47 (0.14)	(-1.75, -1.20)			
>= 4 to < 7	Week 4	CR845	185	172 (93.0)	-1.98 (0.16)	(-2.29, -1.67)	-1.06 (0.19)	(-1.44, -0.69)	<0.001 *
		Placebo	193	183 (94.8)	-0.91 (0.15)	(-1.22, -0.61)			
>= 7	Week 4	CR845	241	218 (90.5)	-2.37 (0.15)	(-2.67, -2.06)	-0.57 (0.21)	(-0.98, -0.16)	0.007 *
		Placebo	232	220 (94.8)	-1.79 (0.16)	(-2.10, -1.49)			
>= 4 to < 7	Week 5	CR845	185	172 (93.0)	-2.06 (0.16)	(-2.38, -1.74)	-0.91 (0.20)	(-1.30, -0.52)	<0.001 *
		Placebo	193	182 (94.3)	-1.15 (0.16)	(-1.46, -0.84)			
>= 7	Week 5	CR845	241	216 (89.6)	-2.61 (0.16)	(-2.93, -2.29)	-0.58 (0.22)	(-1.01, -0.15)	0.009 *
		Placebo	232	220 (94.8)	-2.03 (0.16)	(-2.35, -1.71)			
>= 4 to < 7	Week 6	CR845	185	167 (90.3)	-2.20 (0.17)	(-2.52, -1.87)	-0.94 (0.20)	(-1.34, -0.54)	<0.001 *
		Placebo	193	181 (93.8)	-1.25 (0.16)	(-1.57, -0.94)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIC_ISCD: Change from baseline in weekly WI-NRS - MMRM results by baseline WI-NRS
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
>= 7	Week 6	CR845	241	215 (89.2)	-2.92 (0.17)	(-3.25, -2.59)	-0.77 (0.23)	(-1.22, -0.32)	<0.001 *
		Placebo	232	219 (94.4)	-2.15 (0.17)	(-2.48, -1.81)			
>= 4 to < 7	Week 7	CR845	185	168 (90.8)	-2.25 (0.17)	(-2.58, -1.91)	-0.99 (0.21)	(-1.40, -0.58)	<0.001 *
		Placebo	193	181 (93.8)	-1.25 (0.16)	(-1.57, -0.93)			
>= 7	Week 7	CR845	241	211 (87.6)	-3.03 (0.17)	(-3.36, -2.69)	-0.77 (0.23)	(-1.22, -0.31)	<0.001 *
		Placebo	232	216 (93.1)	-2.26 (0.17)	(-2.59, -1.92)			
>= 4 to < 7	Week 8	CR845	185	166 (89.7)	-2.28 (0.17)	(-2.62, -1.94)	-0.97 (0.21)	(-1.38, -0.56)	<0.001 *
		Placebo	193	179 (92.7)	-1.31 (0.17)	(-1.64, -0.99)			
>= 7	Week 8	CR845	241	210 (87.1)	-3.07 (0.17)	(-3.41, -2.74)	-0.66 (0.23)	(-1.11, -0.20)	0.005 *
		Placebo	232	215 (92.7)	-2.42 (0.17)	(-2.76, -2.08)			
>= 4 to < 7	Week 9	CR845	185	164 (88.6)	-2.39 (0.17)	(-2.72, -2.05)	-0.97 (0.21)	(-1.38, -0.55)	<0.001 *
		Placebo	193	179 (92.7)	-1.42 (0.17)	(-1.74, -1.09)			
>= 7	Week 9	CR845	241	208 (86.3)	-3.17 (0.17)	(-3.51, -2.82)	-0.63 (0.24)	(-1.10, -0.16)	0.009 *
		Placebo	232	217 (93.5)	-2.54 (0.17)	(-2.88, -2.20)			
>= 4 to < 7	Week 10	CR845	185	163 (88.1)	-2.40 (0.18)	(-2.75, -2.06)	-0.92 (0.22)	(-1.35, -0.50)	<0.001 *
		Placebo	193	180 (93.3)	-1.48 (0.17)	(-1.82, -1.15)			
>= 7	Week 10	CR845	241	209 (86.7)	-3.34 (0.18)	(-3.69, -2.99)	-0.78 (0.24)	(-1.26, -0.30)	0.001 *
		Placebo	232	213 (91.8)	-2.56 (0.18)	(-2.91, -2.21)			
>= 4 to < 7	Week 11	CR845	185	159 (85.9)	-2.47 (0.18)	(-2.82, -2.12)	-0.88 (0.22)	(-1.32, -0.45)	<0.001 *
		Placebo	193	178 (92.2)	-1.59 (0.17)	(-1.92, -1.25)			
>= 7	Week 11	CR845	241	200 (83.0)	-3.40 (0.18)	(-3.75, -3.05)	-0.91 (0.24)	(-1.39, -0.44)	<0.001 *
		Placebo	232	209 (90.1)	-2.49 (0.18)	(-2.83, -2.14)			
>= 4 to < 7	Week 12	CR845	185	151 (81.6)	-2.54 (0.18)	(-2.90, -2.19)	-0.87 (0.23)	(-1.31, -0.42)	<0.001 *
		Placebo	193	171 (88.6)	-1.68 (0.18)	(-2.02, -1.33)			
>= 7	Week 12	CR845	241	197 (81.7)	-3.47 (0.18)	(-3.83, -3.12)	-0.84 (0.25)	(-1.32, -0.35)	<0.001 *
		Placebo	232	201 (86.6)	-2.64 (0.18)	(-2.99, -2.28)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIC_ISCE: Change from baseline in weekly WI-NRS - MMRM results by specific medical condition
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
E: Presence of specific medical conditions									0.476
No	Week 1	CR845	359	351 (97.8)	-0.87 (0.07)	(-1.00, -0.73)	-0.29 (0.10)	(-0.48, -0.10)	0.003 *
		Placebo	360	348 (96.7)	-0.58 (0.07)	(-0.71, -0.44)			
Yes	Week 1	CR845	67	63 (94.0)	-0.86 (0.15)	(-1.15, -0.57)	-0.48 (0.21)	(-0.89, -0.07)	0.021 *
		Placebo	65	65 (100.0)	-0.38 (0.15)	(-0.66, -0.09)			
No	Week 2	CR845	359	343 (95.5)	-1.48 (0.09)	(-1.65, -1.30)	-0.46 (0.13)	(-0.70, -0.21)	<0.001 *
		Placebo	360	346 (96.1)	-1.02 (0.09)	(-1.20, -0.84)			
Yes	Week 2	CR845	67	61 (91.0)	-1.71 (0.23)	(-2.17, -1.26)	-0.80 (0.32)	(-1.44, -0.16)	0.014 *
		Placebo	65	64 (98.5)	-0.92 (0.23)	(-1.36, -0.47)			
No	Week 3	CR845	359	336 (93.6)	-1.87 (0.10)	(-2.07, -1.67)	-0.60 (0.14)	(-0.88, -0.32)	<0.001 *
		Placebo	360	340 (94.4)	-1.27 (0.10)	(-1.47, -1.07)			
Yes	Week 3	CR845	67	63 (94.0)	-2.19 (0.25)	(-2.69, -1.69)	-1.09 (0.36)	(-1.79, -0.38)	0.003 *
		Placebo	65	63 (96.9)	-1.10 (0.25)	(-1.60, -0.60)			
No	Week 4	CR845	359	328 (91.4)	-2.22 (0.11)	(-2.44, -2.00)	-0.73 (0.15)	(-1.03, -0.43)	<0.001 *
		Placebo	360	341 (94.7)	-1.49 (0.11)	(-1.71, -1.28)			
Yes	Week 4	CR845	67	62 (92.5)	-2.49 (0.27)	(-3.03, -1.95)	-1.15 (0.39)	(-1.92, -0.39)	0.003 *
		Placebo	65	62 (95.4)	-1.34 (0.27)	(-1.88, -0.80)			
No	Week 5	CR845	359	326 (90.8)	-2.38 (0.11)	(-2.61, -2.16)	-0.68 (0.16)	(-1.00, -0.37)	<0.001 *
		Placebo	360	340 (94.4)	-1.70 (0.11)	(-1.93, -1.48)			
Yes	Week 5	CR845	67	62 (92.5)	-2.71 (0.30)	(-3.30, -2.12)	-1.01 (0.42)	(-1.84, -0.17)	0.018 *
		Placebo	65	62 (95.4)	-1.71 (0.30)	(-2.30, -1.12)			
No	Week 6	CR845	359	323 (90.0)	-2.63 (0.12)	(-2.86, -2.39)	-0.81 (0.17)	(-1.14, -0.48)	<0.001 *
		Placebo	360	339 (94.2)	-1.81 (0.12)	(-2.04, -1.58)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor previous use of anti-itch medication is also included in the model.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIC_ISCE: Change from baseline in weekly WI-NRS - MMRM results by specific medical condition
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Yes	Week 6	CR845	67	59 (88.1)	-2.90 (0.31)	(-3.50, -2.29)	-1.07 (0.43)	(-1.93, -0.22)	0.015 *
		Placebo	65	61 (93.8)	-1.82 (0.31)	(-2.43, -1.21)			
No	Week 7	CR845	359	319 (88.9)	-2.71 (0.12)	(-2.95, -2.47)	-0.85 (0.17)	(-1.18, -0.52)	<0.001 *
		Placebo	360	334 (92.8)	-1.86 (0.12)	(-2.10, -1.62)			
Yes	Week 7	CR845	67	60 (89.6)	-2.96 (0.31)	(-3.57, -2.36)	-1.03 (0.43)	(-1.88, -0.18)	0.018 *
		Placebo	65	63 (96.9)	-1.93 (0.30)	(-2.53, -1.33)			
No	Week 8	CR845	359	316 (88.0)	-2.76 (0.12)	(-3.01, -2.52)	-0.79 (0.17)	(-1.13, -0.45)	<0.001 *
		Placebo	360	332 (92.2)	-1.97 (0.12)	(-2.21, -1.73)			
Yes	Week 8	CR845	67	60 (89.6)	-2.92 (0.30)	(-3.53, -2.32)	-0.88 (0.43)	(-1.73, -0.03)	0.042 *
		Placebo	65	62 (95.4)	-2.04 (0.30)	(-2.64, -1.44)			
No	Week 9	CR845	359	314 (87.5)	-2.86 (0.13)	(-3.11, -2.62)	-0.77 (0.18)	(-1.12, -0.43)	<0.001 *
		Placebo	360	333 (92.5)	-2.09 (0.12)	(-2.33, -1.85)			
Yes	Week 9	CR845	67	58 (86.6)	-3.04 (0.31)	(-3.65, -2.43)	-0.87 (0.43)	(-1.73, -0.02)	0.046 *
		Placebo	65	63 (96.9)	-2.17 (0.30)	(-2.77, -1.56)			
No	Week 10	CR845	359	313 (87.2)	-2.94 (0.13)	(-3.20, -2.69)	-0.81 (0.18)	(-1.17, -0.46)	<0.001 *
		Placebo	360	330 (91.7)	-2.13 (0.13)	(-2.38, -1.88)			
Yes	Week 10	CR845	67	59 (88.1)	-3.30 (0.30)	(-3.91, -2.70)	-1.09 (0.43)	(-1.94, -0.24)	0.012 *
		Placebo	65	63 (96.9)	-2.21 (0.30)	(-2.81, -1.62)			
No	Week 11	CR845	359	304 (84.7)	-3.00 (0.13)	(-3.25, -2.74)	-0.88 (0.18)	(-1.24, -0.53)	<0.001 *
		Placebo	360	327 (90.8)	-2.12 (0.13)	(-2.37, -1.87)			
Yes	Week 11	CR845	67	55 (82.1)	-3.39 (0.30)	(-3.99, -2.79)	-1.08 (0.42)	(-1.92, -0.24)	0.012 *
		Placebo	65	60 (92.3)	-2.31 (0.30)	(-2.90, -1.72)			
No	Week 12	CR845	359	293 (81.6)	-3.05 (0.13)	(-3.32, -2.79)	-0.79 (0.19)	(-1.15, -0.42)	<0.001 *
		Placebo	360	316 (87.8)	-2.27 (0.13)	(-2.52, -2.01)			
Yes	Week 12	CR845	67	55 (82.1)	-3.52 (0.31)	(-4.13, -2.91)	-1.24 (0.43)	(-2.10, -0.38)	0.005 *
		Placebo	65	56 (86.2)	-2.28 (0.30)	(-2.88, -1.67)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor previous use of anti-itch medication is also included in the model.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIC_ISCF: Change from baseline in weekly WI-NRS - MMRM results by use of concomitant itch medication
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
F: Use of concomitant itch medication									0.426
No	Week 1	CR845	267	259 (97.0)	-0.69 (0.10)	(-0.88, -0.49)	-0.25 (0.11)	(-0.46, -0.03)	0.025 *
		Placebo	262	255 (97.3)	-0.44 (0.10)	(-0.63, -0.24)			
Yes	Week 1	CR845	159	155 (97.5)	-0.98 (0.11)	(-1.21, -0.76)	-0.43 (0.14)	(-0.71, -0.15)	0.003 *
		Placebo	163	158 (96.9)	-0.55 (0.11)	(-0.78, -0.33)			
No	Week 2	CR845	267	254 (95.1)	-1.31 (0.12)	(-1.54, -1.07)	-0.40 (0.14)	(-0.68, -0.11)	0.007 *
		Placebo	262	252 (96.2)	-0.91 (0.12)	(-1.15, -0.68)			
Yes	Week 2	CR845	159	150 (94.3)	-1.67 (0.15)	(-1.97, -1.38)	-0.69 (0.20)	(-1.08, -0.30)	<0.001 *
		Placebo	163	158 (96.9)	-0.98 (0.15)	(-1.28, -0.69)			
No	Week 3	CR845	267	254 (95.1)	-1.74 (0.13)	(-2.00, -1.48)	-0.65 (0.17)	(-0.98, -0.33)	<0.001 *
		Placebo	262	246 (93.9)	-1.08 (0.13)	(-1.35, -0.82)			
Yes	Week 3	CR845	159	145 (91.2)	-2.04 (0.16)	(-2.37, -1.72)	-0.71 (0.22)	(-1.14, -0.29)	0.001 *
		Placebo	163	157 (96.3)	-1.33 (0.16)	(-1.65, -1.01)			
No	Week 4	CR845	267	250 (93.6)	-2.05 (0.14)	(-2.32, -1.77)	-0.70 (0.18)	(-1.05, -0.35)	<0.001 *
		Placebo	262	249 (95.0)	-1.35 (0.14)	(-1.63, -1.08)			
Yes	Week 4	CR845	159	140 (88.1)	-2.44 (0.18)	(-2.80, -2.08)	-0.97 (0.24)	(-1.45, -0.49)	<0.001 *
		Placebo	163	154 (94.5)	-1.47 (0.18)	(-1.82, -1.12)			
No	Week 5	CR845	267	249 (93.3)	-2.21 (0.15)	(-2.50, -1.93)	-0.67 (0.19)	(-1.03, -0.30)	<0.001 *
		Placebo	262	248 (94.7)	-1.55 (0.15)	(-1.84, -1.26)			
Yes	Week 5	CR845	159	139 (87.4)	-2.64 (0.19)	(-3.01, -2.26)	-0.86 (0.26)	(-1.36, -0.35)	<0.001 *
		Placebo	163	154 (94.5)	-1.78 (0.19)	(-2.14, -1.41)			
No	Week 6	CR845	267	247 (92.5)	-2.45 (0.15)	(-2.75, -2.15)	-0.78 (0.20)	(-1.17, -0.39)	<0.001 *
		Placebo	262	246 (93.9)	-1.67 (0.15)	(-1.97, -1.37)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor presence of medical condition is also included in the model.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIC_ISCF: Change from baseline in weekly WI-NRS - MMRM results by use of concomitant itch medication
ITT

Change from baseline in weekly WI-NRS					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Yes	Week 6	CR845	159	135 (84.9)	-2.88 (0.19)	(-3.26, -2.50)	-0.99 (0.26)	(-1.50, -0.48)	<0.001 *
		Placebo	163	154 (94.5)	-1.89 (0.19)	(-2.25, -1.52)			
No	Week 7	CR845	267	244 (91.4)	-2.54 (0.15)	(-2.84, -2.24)	-0.80 (0.20)	(-1.19, -0.41)	<0.001 *
		Placebo	262	247 (94.3)	-1.74 (0.15)	(-2.04, -1.44)			
Yes	Week 7	CR845	159	135 (84.9)	-2.93 (0.20)	(-3.32, -2.54)	-1.01 (0.27)	(-1.53, -0.49)	<0.001 *
		Placebo	163	150 (92.0)	-1.92 (0.19)	(-2.30, -1.54)			
No	Week 8	CR845	267	245 (91.8)	-2.66 (0.15)	(-2.96, -2.35)	-0.81 (0.20)	(-1.20, -0.42)	<0.001 *
		Placebo	262	245 (93.5)	-1.84 (0.15)	(-2.14, -1.54)			
Yes	Week 8	CR845	159	131 (82.4)	-2.81 (0.20)	(-3.22, -2.41)	-0.77 (0.27)	(-1.31, -0.23)	0.005 *
		Placebo	163	149 (91.4)	-2.04 (0.20)	(-2.43, -1.66)			
No	Week 9	CR845	267	239 (89.5)	-2.71 (0.16)	(-3.02, -2.40)	-0.77 (0.20)	(-1.16, -0.37)	<0.001 *
		Placebo	262	248 (94.7)	-1.94 (0.16)	(-2.25, -1.64)			
Yes	Week 9	CR845	159	133 (83.6)	-3.00 (0.20)	(-3.40, -2.60)	-0.81 (0.27)	(-1.35, -0.27)	0.003 *
		Placebo	163	148 (90.8)	-2.19 (0.20)	(-2.58, -1.80)			
No	Week 10	CR845	267	237 (88.8)	-2.79 (0.16)	(-3.11, -2.48)	-0.78 (0.21)	(-1.19, -0.37)	<0.001 *
		Placebo	262	246 (93.9)	-2.01 (0.16)	(-2.33, -1.70)			
Yes	Week 10	CR845	159	135 (84.9)	-3.15 (0.21)	(-3.55, -2.74)	-0.97 (0.28)	(-1.52, -0.43)	<0.001 *
		Placebo	163	147 (90.2)	-2.17 (0.20)	(-2.56, -1.78)			
No	Week 11	CR845	267	233 (87.3)	-2.89 (0.16)	(-3.20, -2.57)	-0.86 (0.21)	(-1.27, -0.45)	<0.001 *
		Placebo	262	243 (92.7)	-2.03 (0.16)	(-2.34, -1.71)			
Yes	Week 11	CR845	159	126 (79.2)	-3.15 (0.21)	(-3.56, -2.74)	-0.98 (0.28)	(-1.53, -0.43)	<0.001 *
		Placebo	163	144 (88.3)	-2.17 (0.20)	(-2.57, -1.78)			
No	Week 12	CR845	267	224 (83.9)	-2.94 (0.17)	(-3.27, -2.61)	-0.81 (0.22)	(-1.24, -0.38)	<0.001 *
		Placebo	262	232 (88.5)	-2.13 (0.17)	(-2.46, -1.81)			
Yes	Week 12	CR845	159	124 (78.0)	-3.24 (0.21)	(-3.65, -2.84)	-0.91 (0.27)	(-1.45, -0.37)	0.001 *
		Placebo	163	140 (85.9)	-2.33 (0.20)	(-2.72, -1.94)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor presence of medical condition is also included in the model.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WICD3_ISPA: Decrease of WI-NRS of at least 3 points by age
ITT

		CR845			Placebo						
Decrease of WI-NRS of at least 3 points		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	A: Age										0.233
	< 65 years	282	234 (83.0)	126 (44.7) [38.8, 50.7]	290	253 (87.2)	87 (30.0) [24.8, 35.6]	1.489 [1.197, 1.853]	1.885 [1.336, 2.658]	14.7 [6.5, 22.9]	<0.001 *
	>= 65 years	144	114 (79.2)	51 (35.4) [27.6, 43.8]	135	119 (88.1)	41 (30.4) [22.8, 38.9]	1.166 [0.832, 1.634]	1.257 [0.762, 2.075]	5.0 [-6.7, 16.8]	0.371

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WICD3_ISPB: Decrease of WI-NRS of at least 3 points by sex
ITT

Decrease of WI-NRS of at least 3 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	B: Sex										0.765	
	Male	249	200 (80.3)	93 (37.3) [31.3, 43.7]	258	227 (88.0)	72 (27.9) [22.5, 33.8]	1.338 [1.039, 1.725]	1.540 [1.059, 2.239]	9.4 [0.9, 18.0]	0.023	*
	Female	177	148 (83.6)	84 (47.5) [39.9, 55.1]	167	145 (86.8)	56 (33.5) [26.4, 41.2]	1.415 [1.087, 1.843]	1.790 [1.157, 2.769]	13.9 [3.1, 24.8]	0.009	*

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WICD3_ISPC: Decrease of WI-NRS of at least 3 points by race
ITT

		CR845			Placebo						
Decrease of WI-NRS of at least 3 points		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	C: Race										0.213
	Black/African American	135	104 (77.0)	60 (44.4) [35.9, 53.2]	114	102 (89.5)	34 (29.8) [21.6, 39.1]	1.490 [1.062, 2.091]	1.882 [1.113, 3.184]	14.6 [1.9, 27.3]	0.018 *
	White	255	214 (83.9)	106 (41.6) [35.5, 47.9]	262	229 (87.4)	76 (29.0) [23.6, 34.9]	1.433 [1.129, 1.820]	1.741 [1.209, 2.508]	12.6 [4.0, 21.1]	0.003 *
	Other	35	29 (82.9)	11 (31.4) [16.9, 49.3]	47	39 (83.0)	18 (38.3) [24.5, 53.6]	0.821 [0.446, 1.509]	0.738 [0.293, 1.862]	-6.9 [-30.1, 16.4]	0.522

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WICD3_ISPD: Decrease of WI-NRS of at least 3 points by baseline WI-NRS
ITT

		CR845			Placebo						
Decrease of WI-NRS of at least 3 points		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.067
	>= 4 to < 7	185	151 (81.6)	78 (42.2) [35.0, 49.6]	193	171 (88.6)	48 (24.9) [18.9, 31.6]	1.695 [1.259, 2.283]	2.202 [1.421, 3.412]	17.3 [7.4, 27.2]	<0.001 *
	>= 7	241	197 (81.7)	99 (41.1) [34.8, 47.6]	232	201 (86.6)	80 (34.5) [28.4, 41.0]	1.191 [0.944, 1.504]	1.325 [0.912, 1.924]	6.6 [-2.5, 15.7]	0.140

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WICD3_ISPE: Decrease of WI-NRS of at least 3 points by specific medical condition
ITT

		CR845			Placebo							
Decrease of WI-NRS of at least 3 points		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	E: Presence of specific medical conditions										0.184	
	No	359	293 (81.6)	146 (40.7) [35.5, 45.9]	360	316 (87.8)	112 (31.1) [26.4, 36.2]	1.307 [1.072, 1.594]	1.518 [1.117, 2.063]	9.6 [2.3, 16.8]	0.008	*
	Yes	67	55 (82.1)	31 (46.3) [34.0, 58.9]	65	56 (86.2)	16 (24.6) [14.8, 36.9]	1.880 [1.143, 3.092]	2.637 [1.257, 5.533]	21.7 [4.3, 39.0]	0.010	*

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WICD3_ISPF: Decrease of WI-NRS of at least 3 points by use of concomitant itch medication
ITT

		CR845			Placebo						
Decrease of WI-NRS of at least 3 points		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	F: Use of concomitant itch medication										0.786
	No	267	224 (83.9)	113 (42.3) [36.3, 48.5]	262	232 (88.5)	82 (31.3) [25.7, 37.3]	1.352 [1.077, 1.698]	1.611 [1.128, 2.301]	11.0 [2.5, 19.6]	0.009 *
	Yes	159	124 (78.0)	64 (40.3) [32.6, 48.3]	163	140 (85.9)	46 (28.2) [21.5, 35.8]	1.426 [1.047, 1.944]	1.714 [1.076, 2.730]	12.0 [1.1, 22.9]	0.023 *

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WICD4_ISPA: Decrease of WI-NRS of at least 4 points by age
ITT

		CR845			Placebo							
Decrease of WI-NRS of at least 4 points		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	A: Age										0.501	
	< 65 years	282	234 (83.0)	93 (33.0) [27.5, 38.8]	290	253 (87.2)	58 (20.0) [15.6, 25.1]	1.649 [1.241, 2.191]	1.968 [1.346, 2.878]	13.0 [5.5, 20.5]	<0.001	*
	>= 65 years	144	114 (79.2)	43 (29.9) [22.5, 38.0]	135	119 (88.1)	29 (21.5) [14.9, 29.4]	1.390 [0.924, 2.091]	1.556 [0.903, 2.681]	8.4 [-2.5, 19.3]	0.111	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WICD4_ISPB: Decrease of WI-NRS of at least 4 points by sex
ITT

		CR845			Placebo							
Decrease of WI-NRS of at least 4 points		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	B: Sex										0.830	
	Male	249	200 (80.3)	67 (26.9) [21.5, 32.9]	258	227 (88.0)	46 (17.8) [13.4, 23.1]	1.509 [1.082, 2.104]	1.697 [1.110, 2.593]	9.1 [1.5, 16.7]	0.014	*
	Female	177	148 (83.6)	69 (39.0) [31.8, 46.6]	167	145 (86.8)	41 (24.6) [18.2, 31.8]	1.588 [1.149, 2.194]	1.963 [1.234, 3.123]	14.4 [4.1, 24.7]	0.004	*

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WICD4_ISPC: Decrease of WI-NRS of at least 4 points by race
ITT

		CR845			Placebo							
Decrease of WI-NRS of at least 4 points		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	C: Race										0.482	
	Black/African American	135	104 (77.0)	44 (32.6) [24.8, 41.2]	114	102 (89.5)	24 (21.1) [14.0, 29.7]	1.548 [1.007, 2.381]	1.813 [1.019, 3.227]	11.5 [-0.2, 23.2]	0.042	*
	White	255	214 (83.9)	85 (33.3) [27.6, 39.5]	262	229 (87.4)	53 (20.2) [15.5, 25.6]	1.648 [1.225, 2.217]	1.972 [1.324, 2.936]	13.1 [5.2, 21.1]	<0.001	*
	Other	35	29 (82.9)	7 (20.0) [8.4, 36.9]	47	39 (83.0)	10 (21.3) [10.7, 35.7]	0.940 [0.397, 2.224]	0.925 [0.313, 2.733]	-1.3 [-21.4, 18.9]	0.889	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WICD4_ISPD: Decrease of WI-NRS of at least 4 points by baseline WI-NRS
ITT

		CR845			Placebo							
Decrease of WI-NRS of at least 4 points		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.326	
	>= 4 to < 7	185	151 (81.6)	49 (26.5) [20.3, 33.5]	193	171 (88.6)	28 (14.5) [9.9, 20.3]	1.826 [1.202, 2.774]	2.123 [1.266, 3.560]	12.0 [3.4, 20.6]	0.004	*
	>= 7	241	197 (81.7)	87 (36.1) [30.0, 42.5]	232	201 (86.6)	59 (25.4) [20.0, 31.5]	1.420 [1.076, 1.873]	1.657 [1.115, 2.460]	10.7 [2.0, 19.3]	0.012	*

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WICD4_ISPE: Decrease of WI-NRS of at least 4 points by specific medical condition
ITT

		CR845			Placebo							
Decrease of WI-NRS of at least 4 points		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	E: Presence of specific medical conditions										0.537	
	No	359	293 (81.6)	113 (31.5) [26.7, 36.6]	360	316 (87.8)	75 (20.8) [16.8, 25.4]	1.511 [1.174, 1.945]	1.746 [1.245, 2.448]	10.6 [4.0, 17.3]	0.001	*
	Yes	67	55 (82.1)	23 (34.3) [23.2, 46.9]	65	56 (86.2)	12 (18.5) [9.9, 30.0]	1.859 [1.011, 3.418]	2.309 [1.033, 5.160]	15.9 [-0.4, 32.2]	0.040	*

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WICD4_ISPF: Decrease of WI-NRS of at least 4 points by use of concomitant itch medication
ITT

		CR845			Placebo							
Decrease of WI-NRS of at least 4 points		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	F: Use of concomitant itch medication										0.484	
	No	267	224 (83.9)	85 (31.8) [26.3, 37.8]	262	232 (88.5)	57 (21.8) [16.9, 27.2]	1.463 [1.096, 1.954]	1.680 [1.137, 2.482]	10.1 [2.2, 18.0]	0.009	*
	Yes	159	124 (78.0)	51 (32.1) [24.9, 39.9]	163	140 (85.9)	30 (18.4) [12.8, 25.2]	1.743 [1.175, 2.586]	2.094 [1.248, 3.513]	13.7 [3.7, 23.7]	0.005	*

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIR_ISPA: Complete WI-NRS responder by age
ITT

		CR845			Placebo							
Complete WI-NRS responder		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	A: Age										0.123	
	< 65 years	282	282 (100.0)	41 (14.5) [10.6, 19.2]	290	290 (100.0)	19 (6.6) [4.0, 10.0]	2.219 [1.321, 3.728]	2.427 [1.371, 4.295]	8.0 [2.6, 13.3]	0.002	*
	>= 65 years	144	144 (100.0)	14 (9.7) [5.4, 15.8]	135	135 (100.0)	12 (8.9) [4.7, 15.0]	1.094 [0.525, 2.280]	1.104 [0.491, 2.480]	0.8 [-6.7, 8.4]	0.811	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIR_ISPB: Complete WI-NRS responder by sex
ITT

		CR845			Placebo						
Complete WI-NRS responder		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	B: Sex										0.382
	Male	249	249 (100.0)	22 (8.8) [5.6, 13.1]	258	258 (100.0)	16 (6.2) [3.6, 9.9]	1.425 [0.766, 2.648]	1.466 [0.751, 2.862]	2.6 [-2.4, 7.6]	0.261
	Female	177	177 (100.0)	33 (18.6) [13.2, 25.2]	167	167 (100.0)	15 (9.0) [5.1, 14.4]	2.076 [1.171, 3.680]	2.322 [1.210, 4.455]	9.7 [1.9, 17.4]	0.010 *

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIR_ISPC: Complete WI-NRS responder by race
ITT

		CR845			Placebo						
Complete WI-NRS responder		N	nval	n (%) [95 % CI]	N	nval	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	C: Race										0.699
	Black/African American	135	135 (100.0)	15 (11.1) [6.4, 17.7]	114	114 (100.0)	8 (7.0) [3.1, 13.4]	1.583 [0.697, 3.599]	1.656 [0.675, 4.061]	4.1 [-3.8, 12.0]	0.267
	White	255	255 (100.0)	35 (13.7) [9.8, 18.6]	262	262 (100.0)	21 (8.0) [5.0, 12.0]	1.712 [1.025, 2.860]	1.826 [1.031, 3.232]	5.7 [-0.0, 11.4]	0.037 *
	Other	35	35 (100.0)	5 (14.3) [4.8, 30.3]	47	47 (100.0)	2 (4.3) [0.5, 14.5]	3.357 [0.691, 16.305]	3.750 [0.683, 20.602]	10.0 [-5.4, 25.5]	0.131 #

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIR_ISPD: Complete WI-NRS responder by baseline WI-NRS
ITT

		CR845			Placebo						
Complete WI-NRS responder		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.355
	>= 4 to < 7	185	185 (100.0)	29 (15.7) [10.8, 21.7]	193	193 (100.0)	20 (10.4) [6.4, 15.6]	1.513 [0.888, 2.577]	1.608 [0.874, 2.958]	5.3 [-2.0, 12.6]	0.125
	>= 7	241	241 (100.0)	26 (10.8) [7.2, 15.4]	232	232 (100.0)	11 (4.7) [2.4, 8.3]	2.275 [1.151, 4.498]	2.430 [1.171, 5.039]	6.0 [0.8, 11.2]	0.014 *

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIR_ISPE: Complete WI-NRS responder by specific medical condition
ITT

Complete WI-NRS responder		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	E: Presence of specific medical conditions										0.149	
	No	359	359 (100.0)	45 (12.5) [9.3, 16.4]	360	360 (100.0)	29 (8.1) [5.5, 11.4]	1.556 [0.999, 2.424]	1.636 [1.000, 2.674]	4.5 [-0.2, 9.2]	0.048	*
	Yes	67	67 (100.0)	10 (14.9) [7.4, 25.7]	65	65 (100.0)	2 (3.1) [0.4, 10.7]	4.851 [1.105, 21.295]	5.526 [1.161, 26.296]	11.8 [0.8, 22.9]	0.018	*

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek_i, created on: 17FEB2022

Table IT2WIR_ISPF: Complete WI-NRS responder by use of concomitant itch medication
ITT

		CR845			Placebo						
Complete WI-NRS responder		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	F: Use of concomitant itch medication										0.198
	No	267	267 (100.0)	36 (13.5) [9.6, 18.2]	262	262 (100.0)	24 (9.2) [6.0, 13.3]	1.472 [0.904, 2.397]	1.545 [0.894, 2.671]	4.3 [-1.4, 10.1]	0.117
	Yes	159	159 (100.0)	19 (11.9) [7.4, 18.0]	163	163 (100.0)	7 (4.3) [1.7, 8.6]	2.783 [1.203, 6.436]	3.024 [1.234, 7.410]	7.7 [1.1, 14.2]	0.012 *

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. WI-NRS = worst itching intensity numerical rating scale.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aweek_i, created on: 17FEB2022

Table IT2DTC_ISHA: Change from baseline in 5-D total score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
< 65 years	5-D total score	Baseline	CR845	282	274 (97.2)	16.8 (3.4)	7	17.0	25	
			Placebo	290	290 (100.0)	17.1 (3.5)	7	17.0	25	
		Week 4	CR845	282	253 (89.7)	13.1 (3.5)	5	13.0	24	
			Placebo	290	261 (90.0)	14.8 (4.1)	6	14.0	25	
		Week 8	CR845	282	242 (85.8)	12.3 (3.7)	5	12.0	25	
			Placebo	290	264 (91.0)	13.6 (4.2)	5	13.0	25	
		Week 10	CR845	282	243 (86.2)	12.0 (3.7)	5	11.0	23	
			Placebo	290	259 (89.3)	13.5 (4.2)	5	13.0	25	
		Week 12	CR845	282	244 (86.5)	11.8 (3.9)	5	11.0	23	
			Placebo	290	260 (89.7)	13.3 (4.4)	5	13.0	25	
	Change from baseline in 5-D total score	Week 4	CR845	282	247 (87.6)	-3.7 (3.3)	-14	-4.0	4	-0.39 [-0.57, -0.22]
			Placebo	290	261 (90.0)	-2.2 (4.1)	-12	-2.0	9	
		Week 8	CR845	282	236 (83.7)	-4.6 (3.8)	-16	-4.5	6	-0.29 [-0.46, -0.11]
			Placebo	290	264 (91.0)	-3.4 (4.2)	-18	-3.0	9	
		Week 10	CR845	282	237 (84.0)	-4.8 (4.0)	-17	-5.0	8	-0.29 [-0.47, -0.11]
			Placebo	290	259 (89.3)	-3.6 (4.3)	-18	-4.0	10	
		Week 12	CR845	282	239 (84.8)	-5.0 (4.2)	-19	-5.0	8	-0.32 [-0.49, -0.14]
			Placebo	290	260 (89.7)	-3.7 (4.3)	-17	-3.0	8	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DTC_ISHA: Change from baseline in 5-D total score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 65 years	5-D total score	Baseline	CR845	144	143 (99.3)	16.8 (3.7)	7	17.0	25	
			Placebo	135	135 (100.0)	16.7 (3.5)	9	16.0	25	
		Week 4	CR845	144	129 (89.6)	13.1 (4.1)	5	13.0	22	
			Placebo	135	129 (95.6)	14.1 (3.7)	5	14.0	24	
		Week 8	CR845	144	126 (87.5)	12.6 (4.1)	5	12.0	25	
			Placebo	135	128 (94.8)	13.6 (3.8)	5	14.0	25	
		Week 10	CR845	144	120 (83.3)	12.3 (4.1)	5	12.0	23	
			Placebo	135	125 (92.6)	13.4 (3.7)	5	13.0	25	
		Week 12	CR845	144	120 (83.3)	12.3 (4.3)	5	11.0	25	
			Placebo	135	125 (92.6)	13.0 (3.9)	5	13.0	23	
	Change from baseline in 5-D total score	Week 4	CR845	144	129 (89.6)	-3.7 (3.8)	-15	-3.0	4	-0.31 [-0.56, -0.06]
			Placebo	135	129 (95.6)	-2.5 (3.7)	-13	-2.0	11	
		Week 8	CR845	144	126 (87.5)	-4.1 (3.9)	-16	-4.0	5	-0.27 [-0.52, -0.03]
			Placebo	135	128 (94.8)	-3.0 (4.0)	-16	-3.0	8	
		Week 10	CR845	144	120 (83.3)	-4.5 (4.2)	-16	-5.0	6	-0.33 [-0.59, -0.08]
			Placebo	135	125 (92.6)	-3.2 (3.9)	-12	-3.0	12	
		Week 12	CR845	144	120 (83.3)	-4.5 (4.6)	-16	-4.5	6	-0.20 [-0.45, 0.06]
			Placebo	135	125 (92.6)	-3.7 (3.7)	-13	-4.0	10	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DTC_ISHB: Change from baseline in 5-D total score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Male	5-D total score	Baseline	CR845	249	245 (98.4)	16.6 (3.4)	7	17.0	25	
			Placebo	258	258 (100.0)	16.7 (3.5)	7	17.0	25	
		Week 4	CR845	249	222 (89.2)	13.4 (3.5)	5	13.5	24	
			Placebo	258	231 (89.5)	14.4 (4.0)	5	14.0	25	
		Week 8	CR845	249	213 (85.5)	12.8 (3.7)	5	13.0	22	
			Placebo	258	238 (92.2)	13.6 (4.1)	5	13.0	25	
		Week 10	CR845	249	209 (83.9)	12.6 (3.9)	5	12.0	23	
			Placebo	258	233 (90.3)	13.2 (3.9)	5	13.0	25	
		Week 12	CR845	249	209 (83.9)	12.3 (4.1)	5	12.0	23	
			Placebo	258	232 (89.9)	13.1 (4.0)	5	13.0	25	
	Change from baseline in 5-D total score	Week 4	CR845	249	220 (88.4)	-3.1 (3.1)	-15	-3.0	4	-0.25 [-0.44, -0.07]
			Placebo	258	231 (89.5)	-2.2 (3.9)	-12	-2.0	9	
		Week 8	CR845	249	211 (84.7)	-3.8 (3.6)	-16	-4.0	6	-0.18 [-0.36, 0.01]
			Placebo	258	238 (92.2)	-3.1 (3.9)	-18	-3.0	9	
		Week 10	CR845	249	207 (83.1)	-4.0 (3.7)	-16	-4.0	8	-0.13 [-0.32, 0.05]
			Placebo	258	233 (90.3)	-3.5 (3.8)	-18	-3.0	10	
		Week 12	CR845	249	207 (83.1)	-4.3 (4.1)	-16	-4.0	8	-0.20 [-0.39, -0.01]
			Placebo	258	232 (89.9)	-3.5 (3.8)	-16	-3.0	8	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DTC_ISHB: Change from baseline in 5-D total score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Female	5-D total score	Baseline	CR845	177	172 (97.2)	17.1 (3.6)	7	17.0	25	
			Placebo	167	167 (100.0)	17.4 (3.3)	10	17.0	25	
		Week 4	CR845	177	160 (90.4)	12.7 (3.9)	5	12.0	23	
			Placebo	167	159 (95.2)	14.8 (3.9)	8	14.0	25	
		Week 8	CR845	177	155 (87.6)	11.8 (3.9)	5	11.0	25	
			Placebo	167	154 (92.2)	13.7 (4.1)	5	13.5	25	
		Week 10	CR845	177	154 (87.0)	11.3 (3.7)	5	11.0	22	
			Placebo	167	151 (90.4)	13.8 (4.3)	5	13.0	25	
		Week 12	CR845	177	155 (87.6)	11.4 (4.0)	5	11.0	25	
			Placebo	167	153 (91.6)	13.3 (4.5)	5	13.0	24	
	Change from baseline in 5-D total score	Week 4	CR845	177	156 (88.1)	-4.5 (3.8)	-14	-4.0	4	-0.51 [-0.74, -0.29]
			Placebo	167	159 (95.2)	-2.5 (4.0)	-13	-2.0	11	
		Week 8	CR845	177	151 (85.3)	-5.3 (4.1)	-16	-5.0	4	-0.41 [-0.64, -0.18]
			Placebo	167	154 (92.2)	-3.6 (4.4)	-17	-3.0	8	
		Week 10	CR845	177	150 (84.7)	-5.8 (4.3)	-17	-6.0	4	-0.51 [-0.74, -0.28]
			Placebo	167	151 (90.4)	-3.5 (4.7)	-18	-3.0	12	
		Week 12	CR845	177	152 (85.9)	-5.7 (4.6)	-19	-5.5	6	-0.37 [-0.59, -0.14]
			Placebo	167	153 (91.6)	-4.0 (4.5)	-17	-4.0	10	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DTC_ISHC: Change from baseline in 5-D total score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Black/African American	5-D total score	Baseline	CR845	135	131 (97.0)	16.8 (3.4)	8	16.0	25	
			Placebo	114	114 (100.0)	17.3 (3.7)	9	17.0	25	
		Week 4	CR845	135	116 (85.9)	13.3 (3.8)	6	13.0	22	
			Placebo	114	101 (88.6)	15.0 (4.1)	8	14.0	25	
		Week 8	CR845	135	113 (83.7)	12.4 (4.0)	5	12.0	25	
			Placebo	114	105 (92.1)	13.8 (4.0)	5	13.0	25	
		Week 10	CR845	135	108 (80.0)	11.7 (3.7)	5	11.0	23	
			Placebo	114	102 (89.5)	13.8 (4.4)	5	13.0	25	
		Week 12	CR845	135	110 (81.5)	11.6 (4.0)	5	11.0	22	
			Placebo	114	103 (90.4)	13.5 (4.4)	5	13.0	24	
	Change from baseline in 5-D total score	Week 4	CR845	135	113 (83.7)	-3.6 (3.5)	-15	-3.0	4	-0.34 [-0.61, -0.07]
			Placebo	114	101 (88.6)	-2.2 (4.6)	-12	-2.0	11	
		Week 8	CR845	135	110 (81.5)	-4.6 (3.9)	-16	-5.0	6	-0.24 [-0.50, 0.03]
			Placebo	114	105 (92.1)	-3.6 (4.7)	-18	-3.0	9	
		Week 10	CR845	135	105 (77.8)	-5.1 (3.9)	-16	-5.0	4	-0.32 [-0.60, -0.05]
			Placebo	114	102 (89.5)	-3.7 (5.0)	-18	-4.0	12	
		Week 12	CR845	135	107 (79.3)	-5.3 (4.2)	-16	-5.0	6	-0.37 [-0.64, -0.09]
			Placebo	114	103 (90.4)	-3.7 (4.6)	-17	-4.0	10	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DTC_ISHC: Change from baseline in 5-D total score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
White	5-D total score	Baseline	CR845	255	250 (98.0)	16.8 (3.6)	7	17.0	25	
			Placebo	262	262 (100.0)	16.8 (3.4)	7	17.0	25	
		Week 4	CR845	255	234 (91.8)	13.1 (3.7)	5	13.0	24	
			Placebo	262	243 (92.7)	14.4 (3.8)	5	14.0	24	
		Week 8	CR845	255	223 (87.5)	12.4 (3.8)	5	12.0	25	
			Placebo	262	242 (92.4)	13.5 (4.1)	5	13.0	25	
		Week 10	CR845	255	225 (88.2)	12.3 (3.9)	5	12.0	23	
			Placebo	262	238 (90.8)	13.4 (3.9)	5	13.0	25	
		Week 12	CR845	255	224 (87.8)	12.0 (4.0)	5	12.0	23	
			Placebo	262	239 (91.2)	13.2 (4.1)	5	13.0	23	
	Change from baseline in 5-D total score	Week 4	CR845	255	231 (90.6)	-3.7 (3.6)	-13	-3.0	4	-0.38 [-0.56, -0.20]
			Placebo	262	243 (92.7)	-2.4 (3.7)	-13	-2.0	9	
		Week 8	CR845	255	220 (86.3)	-4.3 (3.8)	-16	-4.0	5	-0.30 [-0.48, -0.11]
			Placebo	262	242 (92.4)	-3.2 (3.9)	-16	-3.0	8	
		Week 10	CR845	255	222 (87.1)	-4.5 (4.1)	-16	-4.0	8	-0.29 [-0.48, -0.11]
			Placebo	262	238 (90.8)	-3.3 (3.8)	-14	-3.0	10	
		Week 12	CR845	255	222 (87.1)	-4.8 (4.3)	-19	-5.0	8	-0.33 [-0.51, -0.15]
			Placebo	262	239 (91.2)	-3.5 (3.8)	-15	-3.0	8	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DTC_ISHC: Change from baseline in 5-D total score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Other	5-D total score	Baseline	CR845	35	35 (100.0)	16.6 (3.4)	9	16.0	25	
			Placebo	47	47 (100.0)	17.0 (3.7)	9	17.0	24	
		Week 4	CR845	35	31 (88.6)	12.7 (3.6)	5	12.0	22	
			Placebo	47	44 (93.6)	14.2 (4.3)	7	14.5	25	
		Week 8	CR845	35	31 (88.6)	12.1 (3.6)	6	11.0	22	
			Placebo	47	43 (91.5)	13.4 (3.9)	7	13.0	25	
		Week 10	CR845	35	29 (82.9)	11.4 (3.9)	5	10.0	18	
			Placebo	47	42 (89.4)	12.9 (4.4)	7	12.0	25	
		Week 12	CR845	35	29 (82.9)	13.0 (4.7)	6	13.0	25	
			Placebo	47	41 (87.2)	12.2 (4.5)	5	11.0	25	
	Change from baseline in 5-D total score	Week 4	CR845	35	31 (88.6)	-3.9 (2.8)	-10	-4.0	1	-0.34 [-0.80, 0.13]
			Placebo	47	44 (93.6)	-2.8 (3.8)	-10	-2.0	3	
		Week 8	CR845	35	31 (88.6)	-4.7 (4.0)	-13	-4.0	5	-0.26 [-0.72, 0.21]
			Placebo	47	43 (91.5)	-3.7 (3.9)	-12	-4.0	5	
		Week 10	CR845	35	29 (82.9)	-5.4 (4.3)	-17	-5.0	0	-0.34 [-0.82, 0.13]
			Placebo	47	42 (89.4)	-4.0 (4.0)	-12	-4.0	3	
		Week 12	CR845	35	29 (82.9)	-3.7 (4.8)	-14	-4.0	6	0.26 [-0.22, 0.74]
			Placebo	47	41 (87.2)	-4.9 (4.5)	-13	-5.0	5	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DTC_ISHD: Change from baseline in 5-D total score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 4 to < 7	5-D total score	Baseline	CR845	185	182 (98.4)	15.0 (2.9)	7	15.0	22	
			Placebo	193	193 (100.0)	15.0 (3.0)	7	15.0	23	
		Week 4	CR845	185	168 (90.8)	11.8 (3.0)	5	12.0	23	
			Placebo	193	179 (92.7)	13.4 (3.6)	5	13.0	23	
		Week 8	CR845	185	164 (88.6)	11.4 (3.0)	5	11.0	22	
			Placebo	193	177 (91.7)	12.7 (3.6)	5	13.0	23	
		Week 10	CR845	185	161 (87.0)	11.0 (3.1)	5	11.0	23	
			Placebo	193	173 (89.6)	12.6 (3.9)	5	12.0	25	
		Week 12	CR845	185	159 (85.9)	10.9 (3.3)	5	10.0	23	
			Placebo	193	175 (90.7)	12.1 (3.9)	5	11.0	22	
	Change from baseline in 5-D total score	Week 4	CR845	185	166 (89.7)	-3.1 (3.2)	-15	-3.0	4	-0.45 [-0.67, -0.24]
			Placebo	193	179 (92.7)	-1.6 (3.6)	-11	-1.0	9	
		Week 8	CR845	185	162 (87.6)	-3.6 (3.1)	-13	-4.0	6	-0.40 [-0.62, -0.19]
			Placebo	193	177 (91.7)	-2.3 (3.5)	-12	-2.0	8	
		Week 10	CR845	185	159 (85.9)	-4.0 (3.2)	-13	-4.0	6	-0.45 [-0.67, -0.23]
			Placebo	193	173 (89.6)	-2.4 (3.6)	-14	-2.0	10	
		Week 12	CR845	185	157 (84.9)	-4.2 (3.7)	-13	-4.0	6	-0.34 [-0.56, -0.12]
			Placebo	193	175 (90.7)	-2.9 (3.6)	-15	-3.0	8	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DTC_ISHD: Change from baseline in 5-D total score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 7	5-D total score	Baseline	CR845	241	235 (97.5)	18.2 (3.3)	7	18.0	25	
			Placebo	232	232 (100.0)	18.5 (3.1)	10	19.0	25	
		Week 4	CR845	241	214 (88.8)	14.2 (3.9)	5	14.0	24	
			Placebo	232	211 (90.9)	15.5 (4.0)	8	15.0	25	
		Week 8	CR845	241	204 (84.6)	13.2 (4.3)	5	13.0	25	
			Placebo	232	215 (92.7)	14.4 (4.3)	5	14.0	25	
		Week 10	CR845	241	202 (83.8)	12.9 (4.2)	5	13.0	23	
			Placebo	232	211 (90.9)	14.1 (4.1)	5	14.0	25	
		Week 12	CR845	241	205 (85.1)	12.8 (4.4)	5	13.0	25	
			Placebo	232	210 (90.5)	14.1 (4.3)	5	14.0	25	
	Change from baseline in 5-D total score	Week 4	CR845	241	210 (87.1)	-4.1 (3.6)	-14	-4.0	4	-0.30 [-0.49, -0.11]
			Placebo	232	211 (90.9)	-3.0 (4.1)	-13	-3.0	11	
		Week 8	CR845	241	200 (83.0)	-5.0 (4.3)	-16	-5.0	5	-0.21 [-0.41, -0.02]
			Placebo	232	215 (92.7)	-4.1 (4.4)	-18	-4.0	9	
		Week 10	CR845	241	198 (82.2)	-5.3 (4.5)	-17	-5.0	8	-0.22 [-0.42, -0.03]
			Placebo	232	211 (90.9)	-4.3 (4.4)	-18	-4.0	12	
		Week 12	CR845	241	202 (83.8)	-5.4 (4.7)	-19	-5.0	8	-0.23 [-0.43, -0.04]
			Placebo	232	210 (90.5)	-4.4 (4.5)	-17	-5.0	10	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DTC_ISHE: Change from baseline in 5-D total score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	5-D total score	Baseline	CR845	359	350 (97.5)	16.7 (3.5)	7	17.0	25	
			Placebo	360	360 (100.0)	16.8 (3.5)	7	17.0	25	
		Week 4	CR845	359	320 (89.1)	13.0 (3.7)	5	13.0	24	
			Placebo	360	330 (91.7)	14.5 (4.0)	5	14.0	25	
		Week 8	CR845	359	309 (86.1)	12.4 (3.8)	5	12.0	25	
			Placebo	360	328 (91.1)	13.5 (4.1)	5	13.0	25	
		Week 10	CR845	359	306 (85.2)	12.0 (3.7)	5	11.0	23	
			Placebo	360	322 (89.4)	13.3 (4.1)	5	13.0	25	
		Week 12	CR845	359	306 (85.2)	12.0 (4.0)	5	11.0	25	
			Placebo	360	322 (89.4)	13.1 (4.3)	5	13.0	25	
	Change from baseline in 5-D total score	Week 4	CR845	359	314 (87.5)	-3.7 (3.5)	-15	-3.5	4	-0.38 [-0.54, -0.22]
			Placebo	360	330 (91.7)	-2.3 (4.0)	-13	-2.0	11	
		Week 8	CR845	359	303 (84.4)	-4.3 (3.8)	-16	-4.0	6	-0.27 [-0.43, -0.12]
			Placebo	360	328 (91.1)	-3.3 (4.2)	-18	-3.0	9	
		Week 10	CR845	359	300 (83.6)	-4.7 (3.8)	-16	-5.0	8	-0.31 [-0.47, -0.15]
			Placebo	360	322 (89.4)	-3.4 (4.3)	-18	-3.0	12	
		Week 12	CR845	359	301 (83.8)	-4.7 (4.2)	-19	-4.0	8	-0.26 [-0.42, -0.11]
			Placebo	360	322 (89.4)	-3.6 (4.2)	-17	-3.5	10	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DTC_ISHE: Change from baseline in 5-D total score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	5-D total score	Baseline	CR845	67	67 (100.0)	17.2 (3.3)	11	17.0	24	
			Placebo	65	65 (100.0)	17.9 (3.2)	9	18.0	24	
		Week 4	CR845	67	62 (92.5)	13.5 (3.8)	5	13.0	22	
			Placebo	65	60 (92.3)	15.1 (4.0)	7	15.0	24	
		Week 8	CR845	67	59 (88.1)	12.5 (3.9)	5	12.0	21	
			Placebo	65	64 (98.5)	14.3 (3.9)	7	14.5	23	
		Week 10	CR845	67	57 (85.1)	12.4 (4.3)	5	12.0	23	
			Placebo	65	62 (95.4)	14.2 (3.8)	7	14.0	22	
		Week 12	CR845	67	58 (86.6)	11.7 (4.1)	5	11.5	23	
			Placebo	65	63 (96.9)	13.7 (4.0)	5	14.0	23	
	Change from baseline in 5-D total score	Week 4	CR845	67	62 (92.5)	-3.6 (3.6)	-14	-3.0	4	-0.27 [-0.63, 0.08]
			Placebo	65	60 (92.3)	-2.7 (3.5)	-11	-2.0	4	
		Week 8	CR845	67	59 (88.1)	-4.8 (4.3)	-16	-4.0	3	-0.31 [-0.67, 0.04]
			Placebo	65	64 (98.5)	-3.6 (3.5)	-12	-4.0	6	
		Week 10	CR845	67	57 (85.1)	-4.9 (5.0)	-17	-5.0	4	-0.28 [-0.64, 0.08]
			Placebo	65	62 (95.4)	-3.7 (3.6)	-14	-4.0	3	
		Week 12	CR845	67	58 (86.6)	-5.5 (4.8)	-16	-5.0	3	-0.34 [-0.70, 0.02]
			Placebo	65	63 (96.9)	-4.1 (3.6)	-13	-4.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DTC_ISHF: Change from baseline in 5-D total score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	5-D total score	Baseline	CR845	267	261 (97.8)	16.5 (3.6)	7	16.0	25	
			Placebo	262	262 (100.0)	16.6 (3.4)	7	17.0	25	
		Week 4	CR845	267	246 (92.1)	13.0 (3.7)	5	13.0	24	
			Placebo	262	240 (91.6)	14.4 (3.7)	5	14.0	24	
		Week 8	CR845	267	238 (89.1)	12.2 (3.7)	5	12.0	22	
			Placebo	262	242 (92.4)	13.4 (3.8)	5	13.0	25	
		Week 10	CR845	267	232 (86.9)	12.0 (3.8)	5	11.0	23	
			Placebo	262	238 (90.8)	13.1 (3.8)	5	13.0	25	
		Week 12	CR845	267	234 (87.6)	11.9 (4.0)	5	11.0	25	
			Placebo	262	241 (92.0)	13.0 (4.1)	5	13.0	24	
	Change from baseline in 5-D total score	Week 4	CR845	267	242 (90.6)	-3.6 (3.4)	-14	-3.0	4	-0.37 [-0.55, -0.19]
			Placebo	262	240 (91.6)	-2.2 (3.9)	-12	-2.0	9	
		Week 8	CR845	267	234 (87.6)	-4.4 (3.7)	-14	-4.0	6	-0.28 [-0.46, -0.10]
			Placebo	262	242 (92.4)	-3.2 (4.2)	-18	-3.0	9	
		Week 10	CR845	267	228 (85.4)	-4.5 (3.8)	-15	-5.0	8	-0.23 [-0.42, -0.05]
			Placebo	262	238 (90.8)	-3.5 (4.3)	-18	-3.0	10	
		Week 12	CR845	267	231 (86.5)	-4.6 (4.2)	-16	-4.0	8	-0.23 [-0.41, -0.05]
			Placebo	262	241 (92.0)	-3.7 (4.2)	-17	-4.0	8	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DTC_ISHF: Change from baseline in 5-D total score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	5-D total score	Baseline	CR845	159	156 (98.1)	17.2 (3.4)	9	17.0	24	
			Placebo	163	163 (100.0)	17.4 (3.6)	9	18.0	25	
		Week 4	CR845	159	136 (85.5)	13.3 (3.8)	5	13.0	22	
			Placebo	163	150 (92.0)	14.8 (4.5)	6	14.0	25	
		Week 8	CR845	159	130 (81.8)	12.7 (4.2)	5	13.0	25	
			Placebo	163	150 (92.0)	14.0 (4.5)	6	13.0	25	
		Week 10	CR845	159	131 (82.4)	12.1 (3.9)	5	12.0	21	
			Placebo	163	146 (89.6)	14.0 (4.4)	6	13.0	25	
		Week 12	CR845	159	130 (81.8)	12.1 (4.1)	5	12.0	23	
			Placebo	163	144 (88.3)	13.5 (4.5)	5	13.0	25	
	Change from baseline in 5-D total score	Week 4	CR845	159	134 (84.3)	-3.9 (3.6)	-15	-4.0	3	-0.35 [-0.59, -0.12]
			Placebo	163	150 (92.0)	-2.6 (4.0)	-13	-2.0	11	
		Week 8	CR845	159	128 (80.5)	-4.5 (4.2)	-16	-4.0	5	-0.28 [-0.52, -0.04]
			Placebo	163	150 (92.0)	-3.4 (4.0)	-16	-3.0	8	
		Week 10	CR845	159	129 (81.1)	-5.2 (4.4)	-17	-5.0	6	-0.43 [-0.67, -0.19]
			Placebo	163	146 (89.6)	-3.4 (3.9)	-14	-4.0	12	
		Week 12	CR845	159	128 (80.5)	-5.3 (4.6)	-19	-5.0	7	-0.35 [-0.59, -0.11]
			Placebo	163	144 (88.3)	-3.8 (4.0)	-13	-3.0	10	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DDC_ISHA: Change from baseline in 5-D degree score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
< 65 years	5-D degree score	Baseline	CR845	282	276 (97.9)	3.5 (0.7)	1	3.0	5	
			Placebo	290	290 (100.0)	3.6 (0.8)	1	3.0	5	
		Week 4	CR845	282	253 (89.7)	2.8 (0.8)	1	3.0	5	
			Placebo	290	261 (90.0)	3.1 (0.8)	1	3.0	5	
		Week 8	CR845	282	243 (86.2)	2.7 (0.8)	1	3.0	5	
			Placebo	290	264 (91.0)	2.9 (0.8)	1	3.0	5	
		Week 10	CR845	282	243 (86.2)	2.6 (0.8)	1	2.0	5	
			Placebo	290	259 (89.3)	2.9 (0.9)	1	3.0	5	
		Week 12	CR845	282	244 (86.5)	2.5 (0.8)	1	2.0	5	
			Placebo	290	260 (89.7)	2.8 (0.9)	1	3.0	5	
	Change from baseline in 5-D degree score	Week 4	CR845	282	249 (88.3)	-0.6 (0.9)	-3	-1.0	3	-0.24 [-0.42, -0.07]
			Placebo	290	261 (90.0)	-0.4 (0.9)	-3	0.0	2	
		Week 8	CR845	282	239 (84.8)	-0.8 (1.0)	-4	-1.0	3	-0.12 [-0.30, 0.05]
			Placebo	290	264 (91.0)	-0.7 (0.9)	-4	-1.0	2	
		Week 10	CR845	282	239 (84.8)	-0.9 (1.0)	-4	-1.0	3	-0.22 [-0.39, -0.04]
			Placebo	290	259 (89.3)	-0.7 (1.0)	-4	-1.0	2	
		Week 12	CR845	282	241 (85.5)	-0.9 (1.0)	-4	-1.0	3	-0.16 [-0.34, 0.01]
			Placebo	290	260 (89.7)	-0.8 (0.9)	-3	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DDC_ISHA: Change from baseline in 5-D degree score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 65 years	5-D degree score	Baseline	CR845	144	144 (100.0)	3.5 (0.7)	2	3.0	5	
			Placebo	135	135 (100.0)	3.4 (0.7)	2	3.0	5	
		Week 4	CR845	144	130 (90.3)	2.7 (0.8)	1	3.0	5	
			Placebo	135	129 (95.6)	3.0 (0.7)	1	3.0	5	
		Week 8	CR845	144	126 (87.5)	2.7 (0.9)	1	3.0	5	
			Placebo	135	128 (94.8)	3.0 (0.8)	1	3.0	5	
		Week 10	CR845	144	120 (83.3)	2.6 (0.8)	1	3.0	5	
			Placebo	135	125 (92.6)	2.9 (0.7)	1	3.0	5	
		Week 12	CR845	144	121 (84.0)	2.6 (0.9)	1	3.0	5	
			Placebo	135	125 (92.6)	2.8 (0.8)	1	3.0	5	
	Change from baseline in 5-D degree score	Week 4	CR845	144	130 (90.3)	-0.8 (0.9)	-4	-1.0	2	-0.37 [-0.62, -0.12]
			Placebo	135	129 (95.6)	-0.4 (0.8)	-3	0.0	1	
		Week 8	CR845	144	126 (87.5)	-0.7 (1.0)	-4	-1.0	2	-0.24 [-0.49, 0.01]
			Placebo	135	128 (94.8)	-0.5 (0.9)	-3	0.0	1	
		Week 10	CR845	144	120 (83.3)	-0.9 (1.0)	-4	-1.0	1	-0.32 [-0.57, -0.07]
			Placebo	135	125 (92.6)	-0.6 (0.8)	-3	-1.0	1	
		Week 12	CR845	144	121 (84.0)	-0.9 (1.1)	-4	-1.0	2	-0.19 [-0.44, 0.06]
			Placebo	135	125 (92.6)	-0.7 (0.8)	-3	-1.0	1	

ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DDC_ISHB: Change from baseline in 5-D degree score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Male	5-D degree score	Baseline	CR845	249	245 (98.4)	3.4 (0.7)	1	3.0	5	
			Placebo	258	258 (100.0)	3.5 (0.7)	1	3.0	5	
		Week 4	CR845	249	222 (89.2)	2.8 (0.8)	1	3.0	5	
			Placebo	258	231 (89.5)	3.0 (0.8)	1	3.0	5	
		Week 8	CR845	249	214 (85.9)	2.8 (0.8)	1	3.0	5	
			Placebo	258	238 (92.2)	2.9 (0.8)	1	3.0	5	
		Week 10	CR845	249	209 (83.9)	2.7 (0.8)	1	3.0	5	
			Placebo	258	233 (90.3)	2.9 (0.8)	1	3.0	5	
		Week 12	CR845	249	209 (83.9)	2.6 (0.8)	1	3.0	5	
			Placebo	258	232 (89.9)	2.8 (0.8)	1	3.0	5	
	Change from baseline in 5-D degree score	Week 4	CR845	249	220 (88.4)	-0.6 (0.8)	-3	-1.0	2	-0.13 [-0.32, 0.05]
			Placebo	258	231 (89.5)	-0.5 (0.9)	-3	0.0	2	
		Week 8	CR845	249	212 (85.1)	-0.6 (0.9)	-3	-1.0	2	-0.04 [-0.22, 0.15]
			Placebo	258	238 (92.2)	-0.6 (0.9)	-4	0.0	2	
		Week 10	CR845	249	207 (83.1)	-0.7 (0.9)	-3	-1.0	2	-0.09 [-0.28, 0.10]
			Placebo	258	233 (90.3)	-0.6 (0.9)	-4	-1.0	2	
		Week 12	CR845	249	207 (83.1)	-0.8 (0.9)	-3	-1.0	2	-0.06 [-0.25, 0.13]
			Placebo	258	232 (89.9)	-0.7 (0.9)	-3	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DDC_ISHB: Change from baseline in 5-D degree score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Female	5-D degree score	Baseline	CR845	177	175 (98.9)	3.6 (0.8)	1	4.0	5	
			Placebo	167	167 (100.0)	3.6 (0.8)	2	4.0	5	
		Week 4	CR845	177	161 (91.0)	2.7 (0.8)	1	3.0	5	
			Placebo	167	159 (95.2)	3.2 (0.8)	2	3.0	5	
		Week 8	CR845	177	155 (87.6)	2.6 (0.9)	1	2.0	5	
			Placebo	167	154 (92.2)	2.9 (0.9)	1	3.0	5	
		Week 10	CR845	177	154 (87.0)	2.5 (0.8)	1	2.0	5	
			Placebo	167	151 (90.4)	3.0 (0.8)	1	3.0	5	
		Week 12	CR845	177	156 (88.1)	2.4 (0.8)	1	2.0	5	
			Placebo	167	153 (91.6)	2.8 (0.9)	1	3.0	5	
	Change from baseline in 5-D degree score	Week 4	CR845	177	159 (89.8)	-0.8 (1.0)	-4	-1.0	3	-0.49 [-0.71, -0.26]
			Placebo	167	159 (95.2)	-0.4 (0.8)	-2	0.0	2	
		Week 8	CR845	177	153 (86.4)	-1.0 (1.1)	-4	-1.0	3	-0.30 [-0.52, -0.07]
			Placebo	167	154 (92.2)	-0.7 (0.9)	-4	-1.0	1	
		Week 10	CR845	177	152 (85.9)	-1.1 (1.1)	-4	-1.0	3	-0.45 [-0.67, -0.22]
			Placebo	167	151 (90.4)	-0.6 (0.9)	-3	-1.0	2	
		Week 12	CR845	177	155 (87.6)	-1.1 (1.1)	-4	-1.0	3	-0.30 [-0.52, -0.07]
			Placebo	167	153 (91.6)	-0.8 (0.9)	-3	-1.0	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DDC_ISHC: Change from baseline in 5-D degree score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Black/African American	5-D degree score	Baseline	CR845	135	133 (98.5)	3.5 (0.7)	1	3.0	5	
			Placebo	114	114 (100.0)	3.5 (0.8)	1	3.0	5	
		Week 4	CR845	135	116 (85.9)	2.8 (0.9)	1	3.0	5	
			Placebo	114	101 (88.6)	3.2 (0.8)	2	3.0	5	
		Week 8	CR845	135	113 (83.7)	2.7 (0.9)	1	3.0	5	
			Placebo	114	105 (92.1)	2.9 (0.9)	1	3.0	5	
		Week 10	CR845	135	108 (80.0)	2.6 (0.8)	1	2.0	5	
			Placebo	114	102 (89.5)	2.9 (0.9)	1	3.0	5	
		Week 12	CR845	135	111 (82.2)	2.5 (0.8)	1	2.0	5	
			Placebo	114	103 (90.4)	2.8 (0.9)	1	3.0	5	
	Change from baseline in 5-D degree score	Week 4	CR845	135	114 (84.4)	-0.6 (1.0)	-4	-1.0	2	-0.33 [-0.60, -0.06]
			Placebo	114	101 (88.6)	-0.3 (1.0)	-3	0.0	2	
		Week 8	CR845	135	111 (82.2)	-0.8 (1.1)	-4	-1.0	2	-0.15 [-0.42, 0.12]
			Placebo	114	105 (92.1)	-0.7 (1.0)	-4	-1.0	2	
		Week 10	CR845	135	106 (78.5)	-0.9 (1.0)	-4	-1.0	3	-0.31 [-0.59, -0.04]
			Placebo	114	102 (89.5)	-0.6 (1.1)	-4	-1.0	2	
		Week 12	CR845	135	109 (80.7)	-1.0 (1.0)	-4	-1.0	2	-0.32 [-0.59, -0.05]
			Placebo	114	103 (90.4)	-0.7 (1.0)	-3	-1.0	2	

ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DDC_ISHC: Change from baseline in 5-D degree score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
White	5-D degree score	Baseline	CR845	255	251 (98.4)	3.5 (0.7)	1	3.0	5	
			Placebo	262	262 (100.0)	3.5 (0.7)	2	3.0	5	
		Week 4	CR845	255	235 (92.2)	2.8 (0.8)	1	3.0	5	
			Placebo	262	243 (92.7)	3.1 (0.8)	1	3.0	5	
		Week 8	CR845	255	224 (87.8)	2.7 (0.8)	1	3.0	5	
			Placebo	262	242 (92.4)	2.9 (0.8)	1	3.0	5	
		Week 10	CR845	255	225 (88.2)	2.6 (0.8)	1	3.0	5	
			Placebo	262	238 (90.8)	2.9 (0.8)	1	3.0	5	
		Week 12	CR845	255	224 (87.8)	2.6 (0.8)	1	3.0	5	
			Placebo	262	239 (91.2)	2.8 (0.8)	1	3.0	5	
	Change from baseline in 5-D degree score	Week 4	CR845	255	233 (91.4)	-0.7 (0.9)	-3	-1.0	3	-0.24 [-0.42, -0.06]
			Placebo	262	243 (92.7)	-0.5 (0.8)	-3	0.0	2	
		Week 8	CR845	255	222 (87.1)	-0.7 (1.0)	-4	-1.0	3	-0.13 [-0.31, 0.05]
			Placebo	262	242 (92.4)	-0.6 (0.9)	-4	0.0	1	
		Week 10	CR845	255	223 (87.5)	-0.8 (1.0)	-4	-1.0	3	-0.21 [-0.39, -0.03]
			Placebo	262	238 (90.8)	-0.6 (0.8)	-3	-1.0	2	
		Week 12	CR845	255	223 (87.5)	-0.9 (1.0)	-4	-1.0	3	-0.16 [-0.35, 0.02]
			Placebo	262	239 (91.2)	-0.7 (0.9)	-3	-1.0	2	

ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DDC_ISHC: Change from baseline in 5-D degree score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Other	5-D degree score	Baseline	CR845	35	35 (100.0)	3.5 (0.6)	3	3.0	5	
			Placebo	47	47 (100.0)	3.4 (0.8)	2	3.0	5	
		Week 4	CR845	35	31 (88.6)	2.7 (0.7)	1	3.0	5	
			Placebo	47	44 (93.6)	3.0 (0.9)	2	3.0	5	
		Week 8	CR845	35	31 (88.6)	2.5 (0.7)	1	3.0	4	
			Placebo	47	43 (91.5)	2.8 (0.8)	1	3.0	5	
		Week 10	CR845	35	29 (82.9)	2.6 (0.9)	1	2.0	5	
			Placebo	47	42 (89.4)	2.8 (0.9)	2	3.0	5	
		Week 12	CR845	35	29 (82.9)	2.8 (1.0)	1	3.0	5	
			Placebo	47	41 (87.2)	2.5 (0.9)	1	2.0	5	
	Change from baseline in 5-D degree score	Week 4	CR845	35	31 (88.6)	-0.8 (0.7)	-2	-1.0	0	-0.47 [-0.93, -0.00]
			Placebo	47	44 (93.6)	-0.5 (0.9)	-2	0.0	1	
		Week 8	CR845	35	31 (88.6)	-1.0 (0.9)	-3	-1.0	1	-0.35 [-0.82, 0.11]
			Placebo	47	43 (91.5)	-0.7 (1.0)	-3	-1.0	1	
		Week 10	CR845	35	29 (82.9)	-1.0 (1.0)	-3	-1.0	1	-0.30 [-0.78, 0.18]
			Placebo	47	42 (89.4)	-0.7 (1.0)	-3	-1.0	1	
		Week 12	CR845	35	29 (82.9)	-0.8 (1.1)	-3	-1.0	2	0.19 [-0.29, 0.66]
			Placebo	47	41 (87.2)	-1.0 (1.0)	-3	-1.0	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DDC_ISHD: Change from baseline in 5-D degree score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 4 to < 7	5-D degree score	Baseline	CR845	185	183 (98.9)	3.2 (0.6)	2	3.0	5	
			Placebo	193	193 (100.0)	3.1 (0.6)	1	3.0	5	
		Week 4	CR845	185	168 (90.8)	2.6 (0.7)	1	3.0	5	
			Placebo	193	179 (92.7)	2.8 (0.7)	1	3.0	5	
		Week 8	CR845	185	164 (88.6)	2.6 (0.8)	1	2.0	5	
			Placebo	193	177 (91.7)	2.7 (0.7)	1	3.0	4	
		Week 10	CR845	185	161 (87.0)	2.5 (0.7)	1	2.0	5	
			Placebo	193	173 (89.6)	2.7 (0.7)	1	3.0	5	
		Week 12	CR845	185	159 (85.9)	2.4 (0.7)	1	2.0	5	
			Placebo	193	175 (90.7)	2.6 (0.8)	1	3.0	4	
	Change from baseline in 5-D degree score	Week 4	CR845	185	167 (90.3)	-0.5 (0.8)	-3	-1.0	3	-0.23 [-0.44, -0.01]
			Placebo	193	179 (92.7)	-0.3 (0.8)	-2	0.0	2	
		Week 8	CR845	185	163 (88.1)	-0.6 (0.9)	-3	-1.0	3	-0.20 [-0.42, 0.01]
			Placebo	193	177 (91.7)	-0.4 (0.8)	-3	0.0	2	
		Week 10	CR845	185	160 (86.5)	-0.7 (0.9)	-3	-1.0	3	-0.34 [-0.55, -0.12]
			Placebo	193	173 (89.6)	-0.4 (0.8)	-2	0.0	2	
		Week 12	CR845	185	158 (85.4)	-0.8 (0.9)	-3	-1.0	3	-0.26 [-0.48, -0.05]
			Placebo	193	175 (90.7)	-0.5 (0.8)	-2	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DDC_ISHD: Change from baseline in 5-D degree score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 7	5-D degree score	Baseline	CR845	241	237 (98.3)	3.7 (0.7)	1	4.0	5	
			Placebo	232	232 (100.0)	3.9 (0.7)	2	4.0	5	
		Week 4	CR845	241	215 (89.2)	2.9 (0.8)	1	3.0	5	
			Placebo	232	211 (90.9)	3.3 (0.8)	2	3.0	5	
		Week 8	CR845	241	205 (85.1)	2.8 (0.9)	1	3.0	5	
			Placebo	232	215 (92.7)	3.0 (0.9)	1	3.0	5	
		Week 10	CR845	241	202 (83.8)	2.7 (0.9)	1	3.0	5	
			Placebo	232	211 (90.9)	3.0 (0.9)	1	3.0	5	
		Week 12	CR845	241	206 (85.5)	2.7 (0.9)	1	3.0	5	
			Placebo	232	210 (90.5)	2.9 (0.9)	1	3.0	5	
	Change from baseline in 5-D degree score	Week 4	CR845	241	212 (88.0)	-0.8 (0.9)	-4	-1.0	2	-0.33 [-0.52, -0.14]
			Placebo	232	211 (90.9)	-0.5 (0.9)	-3	0.0	2	
		Week 8	CR845	241	202 (83.8)	-0.9 (1.1)	-4	-1.0	2	-0.13 [-0.32, 0.06]
			Placebo	232	215 (92.7)	-0.8 (1.0)	-4	-1.0	1	
		Week 10	CR845	241	199 (82.6)	-1.0 (1.0)	-4	-1.0	3	-0.19 [-0.38, 0.00]
			Placebo	232	211 (90.9)	-0.8 (1.0)	-4	-1.0	2	
		Week 12	CR845	241	204 (84.6)	-1.0 (1.1)	-4	-1.0	2	-0.10 [-0.29, 0.09]
			Placebo	232	210 (90.5)	-0.9 (0.9)	-3	-1.0	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DDC_ISHE: Change from baseline in 5-D degree score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	5-D degree score	Baseline	CR845	359	353 (98.3)	3.5 (0.7)	1	3.0	5	
			Placebo	360	360 (100.0)	3.5 (0.8)	1	3.0	5	
		Week 4	CR845	359	321 (89.4)	2.8 (0.8)	1	3.0	5	
			Placebo	360	330 (91.7)	3.1 (0.8)	1	3.0	5	
		Week 8	CR845	359	310 (86.4)	2.7 (0.8)	1	3.0	5	
			Placebo	360	328 (91.1)	2.9 (0.8)	1	3.0	5	
		Week 10	CR845	359	306 (85.2)	2.6 (0.8)	1	3.0	5	
			Placebo	360	322 (89.4)	2.9 (0.9)	1	3.0	5	
		Week 12	CR845	359	306 (85.2)	2.6 (0.8)	1	2.0	5	
			Placebo	360	322 (89.4)	2.7 (0.9)	1	3.0	5	
	Change from baseline in 5-D degree score	Week 4	CR845	359	317 (88.3)	-0.7 (0.9)	-3	-1.0	3	-0.27 [-0.42, -0.11]
			Placebo	360	330 (91.7)	-0.4 (0.9)	-3	0.0	2	
		Week 8	CR845	359	306 (85.2)	-0.8 (1.0)	-4	-1.0	3	-0.13 [-0.28, 0.03]
			Placebo	360	328 (91.1)	-0.6 (0.9)	-4	0.0	2	
		Week 10	CR845	359	302 (84.1)	-0.8 (1.0)	-4	-1.0	3	-0.21 [-0.37, -0.06]
			Placebo	360	322 (89.4)	-0.6 (0.9)	-4	-1.0	2	
		Week 12	CR845	359	303 (84.4)	-0.9 (1.0)	-4	-1.0	3	-0.14 [-0.30, 0.02]
			Placebo	360	322 (89.4)	-0.7 (0.9)	-3	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DDC_ISHE: Change from baseline in 5-D degree score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	5-D degree score	Baseline	CR845	67	67 (100.0)	3.5 (0.7)	2	4.0	5	
			Placebo	65	65 (100.0)	3.7 (0.7)	2	4.0	5	
		Week 4	CR845	67	62 (92.5)	2.7 (0.9)	1	3.0	5	
			Placebo	65	60 (92.3)	3.2 (0.7)	2	3.0	5	
		Week 8	CR845	67	59 (88.1)	2.7 (0.9)	1	3.0	5	
			Placebo	65	64 (98.5)	3.1 (0.9)	1	3.0	5	
		Week 10	CR845	67	57 (85.1)	2.5 (0.8)	1	3.0	4	
			Placebo	65	62 (95.4)	3.0 (0.7)	2	3.0	5	
		Week 12	CR845	67	59 (88.1)	2.5 (0.9)	1	2.0	5	
			Placebo	65	63 (96.9)	2.9 (0.8)	1	3.0	5	
	Change from baseline in 5-D degree score	Week 4	CR845	67	62 (92.5)	-0.8 (1.0)	-4	-1.0	2	-0.36 [-0.72, -0.01]
			Placebo	65	60 (92.3)	-0.5 (0.9)	-3	0.0	2	
		Week 8	CR845	67	59 (88.1)	-0.9 (1.1)	-4	-1.0	2	-0.30 [-0.66, 0.05]
			Placebo	65	64 (98.5)	-0.6 (0.7)	-3	-1.0	1	
		Week 10	CR845	67	57 (85.1)	-1.1 (1.0)	-4	-1.0	1	-0.45 [-0.81, -0.08]
			Placebo	65	62 (95.4)	-0.6 (0.8)	-2	-1.0	1	
		Week 12	CR845	67	59 (88.1)	-1.1 (1.1)	-4	-1.0	2	-0.32 [-0.68, 0.04]
			Placebo	65	63 (96.9)	-0.8 (0.9)	-3	-1.0	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DDC_ISHF: Change from baseline in 5-D degree score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	5-D degree score	Baseline	CR845	267	262 (98.1)	3.4 (0.7)	1	3.0	5	
			Placebo	262	262 (100.0)	3.5 (0.8)	1	3.0	5	
		Week 4	CR845	267	247 (92.5)	2.8 (0.8)	1	3.0	5	
			Placebo	262	240 (91.6)	3.1 (0.7)	1	3.0	5	
		Week 8	CR845	267	239 (89.5)	2.7 (0.8)	1	3.0	5	
			Placebo	262	242 (92.4)	2.9 (0.8)	1	3.0	5	
		Week 10	CR845	267	232 (86.9)	2.6 (0.8)	1	2.0	5	
			Placebo	262	238 (90.8)	2.9 (0.8)	1	3.0	5	
		Week 12	CR845	267	234 (87.6)	2.6 (0.8)	1	2.0	5	
			Placebo	262	241 (92.0)	2.7 (0.8)	1	3.0	5	
	Change from baseline in 5-D degree score	Week 4	CR845	267	244 (91.4)	-0.6 (0.9)	-3	-1.0	3	-0.24 [-0.42, -0.06]
			Placebo	262	240 (91.6)	-0.4 (0.9)	-3	0.0	2	
		Week 8	CR845	267	236 (88.4)	-0.7 (1.0)	-4	-1.0	3	-0.10 [-0.28, 0.08]
			Placebo	262	242 (92.4)	-0.6 (0.9)	-4	0.0	2	
		Week 10	CR845	267	229 (85.8)	-0.8 (1.0)	-3	-1.0	3	-0.16 [-0.34, 0.02]
			Placebo	262	238 (90.8)	-0.6 (1.0)	-4	-1.0	2	
		Week 12	CR845	267	232 (86.9)	-0.8 (1.0)	-4	-1.0	3	-0.08 [-0.26, 0.10]
			Placebo	262	241 (92.0)	-0.8 (0.9)	-3	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DDC_ISHF: Change from baseline in 5-D degree score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	5-D degree score	Baseline	CR845	159	158 (99.4)	3.6 (0.7)	1	4.0	5	
			Placebo	163	163 (100.0)	3.6 (0.7)	2	4.0	5	
		Week 4	CR845	159	136 (85.5)	2.8 (0.8)	1	3.0	5	
			Placebo	163	150 (92.0)	3.1 (0.9)	1	3.0	5	
		Week 8	CR845	159	130 (81.8)	2.7 (0.9)	1	3.0	5	
			Placebo	163	150 (92.0)	3.0 (0.9)	1	3.0	5	
		Week 10	CR845	159	131 (82.4)	2.6 (0.9)	1	3.0	5	
			Placebo	163	146 (89.6)	3.0 (0.8)	1	3.0	5	
		Week 12	CR845	159	131 (82.4)	2.5 (0.9)	1	3.0	5	
			Placebo	163	144 (88.3)	2.8 (0.9)	1	3.0	5	
	Change from baseline in 5-D degree score	Week 4	CR845	159	135 (84.9)	-0.8 (0.9)	-4	-1.0	2	-0.38 [-0.62, -0.15]
			Placebo	163	150 (92.0)	-0.5 (0.8)	-2	0.0	2	
		Week 8	CR845	159	129 (81.1)	-0.9 (1.1)	-4	-1.0	2	-0.25 [-0.49, -0.02]
			Placebo	163	150 (92.0)	-0.6 (0.9)	-4	-1.0	1	
		Week 10	CR845	159	130 (81.8)	-1.0 (1.1)	-4	-1.0	3	-0.40 [-0.64, -0.16]
			Placebo	163	146 (89.6)	-0.6 (0.8)	-3	-1.0	2	
		Week 12	CR845	159	130 (81.8)	-1.0 (1.1)	-4	-1.0	2	-0.33 [-0.57, -0.09]
			Placebo	163	144 (88.3)	-0.7 (0.9)	-3	-1.0	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DLC_ISHA: Change from baseline in 5-D duration score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
< 65 years	5-D duration score	Baseline	CR845	282	274 (97.2)	2.7 (1.4)	1	2.0	5	
			Placebo	290	290 (100.0)	2.8 (1.4)	1	2.5	5	
		Week 4	CR845	282	254 (90.1)	2.0 (1.2)	1	2.0	5	
			Placebo	290	261 (90.0)	2.4 (1.4)	1	2.0	5	
		Week 8	CR845	282	243 (86.2)	1.8 (1.1)	1	1.0	5	
			Placebo	290	264 (91.0)	2.1 (1.3)	1	2.0	5	
		Week 10	CR845	282	243 (86.2)	1.8 (1.1)	1	1.0	5	
			Placebo	290	259 (89.3)	2.1 (1.3)	1	2.0	5	
		Week 12	CR845	282	244 (86.5)	1.8 (1.1)	1	1.0	5	
			Placebo	290	260 (89.7)	2.1 (1.3)	1	2.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	282	248 (87.9)	-0.7 (1.3)	-4	-1.0	4	-0.21 [-0.38, -0.03]
			Placebo	290	261 (90.0)	-0.4 (1.6)	-4	0.0	4	
		Week 8	CR845	282	237 (84.0)	-0.9 (1.4)	-4	-1.0	3	-0.10 [-0.27, 0.08]
			Placebo	290	264 (91.0)	-0.8 (1.5)	-4	-1.0	4	
		Week 10	CR845	282	237 (84.0)	-0.9 (1.5)	-4	-1.0	4	-0.09 [-0.27, 0.09]
			Placebo	290	259 (89.3)	-0.8 (1.5)	-4	-1.0	4	
		Week 12	CR845	282	239 (84.8)	-0.9 (1.5)	-4	-1.0	3	-0.14 [-0.31, 0.04]
			Placebo	290	260 (89.7)	-0.7 (1.6)	-4	-1.0	4	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DLC_ISHA: Change from baseline in 5-D duration score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 65 years	5-D duration score	Baseline	CR845	144	144 (100.0)	2.8 (1.4)	1	3.0	5	
			Placebo	135	135 (100.0)	2.7 (1.4)	1	2.0	5	
		Week 4	CR845	144	129 (89.6)	2.0 (1.2)	1	2.0	5	
			Placebo	135	129 (95.6)	2.3 (1.4)	1	2.0	5	
		Week 8	CR845	144	126 (87.5)	1.8 (1.1)	1	1.0	5	
			Placebo	135	128 (94.8)	2.1 (1.2)	1	2.0	5	
		Week 10	CR845	144	120 (83.3)	1.9 (1.1)	1	1.5	5	
			Placebo	135	125 (92.6)	2.1 (1.2)	1	2.0	5	
		Week 12	CR845	144	121 (84.0)	1.8 (1.1)	1	1.0	5	
			Placebo	135	125 (92.6)	2.0 (1.2)	1	2.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	144	129 (89.6)	-0.8 (1.4)	-4	-1.0	2	-0.22 [-0.47, 0.02]
			Placebo	135	129 (95.6)	-0.4 (1.6)	-4	0.0	4	
		Week 8	CR845	144	126 (87.5)	-1.0 (1.4)	-4	-1.0	3	-0.28 [-0.53, -0.03]
			Placebo	135	128 (94.8)	-0.6 (1.6)	-4	0.0	4	
		Week 10	CR845	144	120 (83.3)	-1.0 (1.4)	-4	-1.0	4	-0.24 [-0.49, 0.01]
			Placebo	135	125 (92.6)	-0.6 (1.5)	-4	0.0	4	
		Week 12	CR845	144	121 (84.0)	-1.1 (1.5)	-4	-1.0	4	-0.25 [-0.50, 0.00]
			Placebo	135	125 (92.6)	-0.7 (1.4)	-4	-1.0	4	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DLC_ISHB: Change from baseline in 5-D duration score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Male	5-D duration score	Baseline	CR845	249	245 (98.4)	2.6 (1.3)	1	2.0	5	
			Placebo	258	258 (100.0)	2.8 (1.4)	1	2.0	5	
		Week 4	CR845	249	223 (89.6)	2.1 (1.2)	1	2.0	5	
			Placebo	258	231 (89.5)	2.4 (1.4)	1	2.0	5	
		Week 8	CR845	249	214 (85.9)	1.9 (1.1)	1	2.0	5	
			Placebo	258	238 (92.2)	2.1 (1.2)	1	2.0	5	
		Week 10	CR845	249	209 (83.9)	2.0 (1.1)	1	2.0	5	
			Placebo	258	233 (90.3)	2.0 (1.2)	1	2.0	5	
		Week 12	CR845	249	209 (83.9)	1.9 (1.2)	1	2.0	5	
			Placebo	258	232 (89.9)	2.1 (1.2)	1	2.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	249	221 (88.8)	-0.5 (1.2)	-4	-1.0	4	-0.13 [-0.31, 0.05]
			Placebo	258	231 (89.5)	-0.3 (1.5)	-4	0.0	4	
		Week 8	CR845	249	212 (85.1)	-0.8 (1.4)	-4	-1.0	3	-0.05 [-0.24, 0.13]
			Placebo	258	238 (92.2)	-0.7 (1.4)	-4	-1.0	4	
		Week 10	CR845	249	207 (83.1)	-0.7 (1.4)	-4	-1.0	4	0.06 [-0.13, 0.24]
			Placebo	258	233 (90.3)	-0.8 (1.3)	-4	-1.0	4	
		Week 12	CR845	249	207 (83.1)	-0.8 (1.5)	-4	-1.0	4	-0.07 [-0.26, 0.12]
			Placebo	258	232 (89.9)	-0.7 (1.4)	-4	-1.0	4	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DLC_ISHB: Change from baseline in 5-D duration score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Female	5-D duration score	Baseline	CR845	177	173 (97.7)	2.9 (1.4)	1	3.0	5	
			Placebo	167	167 (100.0)	2.8 (1.4)	1	3.0	5	
		Week 4	CR845	177	160 (90.4)	1.9 (1.1)	1	2.0	5	
			Placebo	167	159 (95.2)	2.3 (1.3)	1	2.0	5	
		Week 8	CR845	177	155 (87.6)	1.7 (1.1)	1	1.0	5	
			Placebo	167	154 (92.2)	2.1 (1.3)	1	2.0	5	
		Week 10	CR845	177	154 (87.0)	1.6 (0.9)	1	1.0	5	
			Placebo	167	151 (90.4)	2.1 (1.3)	1	2.0	5	
		Week 12	CR845	177	156 (88.1)	1.7 (1.0)	1	1.0	5	
			Placebo	167	153 (91.6)	2.0 (1.3)	1	2.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	177	156 (88.1)	-1.0 (1.4)	-4	-1.0	2	-0.32 [-0.55, -0.10]
			Placebo	167	159 (95.2)	-0.5 (1.6)	-4	0.0	4	
		Week 8	CR845	177	151 (85.3)	-1.2 (1.5)	-4	-1.0	3	-0.29 [-0.52, -0.07]
			Placebo	167	154 (92.2)	-0.7 (1.7)	-4	0.0	4	
		Week 10	CR845	177	150 (84.7)	-1.3 (1.4)	-4	-1.0	2	-0.38 [-0.61, -0.15]
			Placebo	167	151 (90.4)	-0.7 (1.8)	-4	0.0	4	
		Week 12	CR845	177	153 (86.4)	-1.2 (1.5)	-4	-1.0	3	-0.30 [-0.53, -0.08]
			Placebo	167	153 (91.6)	-0.7 (1.7)	-4	-1.0	4	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DLC_ISHC: Change from baseline in 5-D duration score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Black/African American	5-D duration score	Baseline	CR845	135	132 (97.8)	2.8 (1.4)	1	2.0	5	
			Placebo	114	114 (100.0)	2.9 (1.5)	1	3.0	5	
		Week 4	CR845	135	116 (85.9)	2.1 (1.2)	1	2.0	5	
			Placebo	114	101 (88.6)	2.4 (1.5)	1	2.0	5	
		Week 8	CR845	135	113 (83.7)	1.8 (1.1)	1	1.0	5	
			Placebo	114	105 (92.1)	2.2 (1.4)	1	2.0	5	
		Week 10	CR845	135	108 (80.0)	1.7 (0.9)	1	1.0	5	
			Placebo	114	102 (89.5)	2.3 (1.4)	1	2.0	5	
		Week 12	CR845	135	111 (82.2)	1.7 (1.0)	1	1.0	5	
			Placebo	114	103 (90.4)	2.1 (1.3)	1	2.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	135	113 (83.7)	-0.8 (1.2)	-4	-1.0	2	-0.21 [-0.48, 0.06]
			Placebo	114	101 (88.6)	-0.5 (1.6)	-4	0.0	4	
		Week 8	CR845	135	110 (81.5)	-1.1 (1.4)	-4	-1.0	3	-0.23 [-0.50, 0.03]
			Placebo	114	105 (92.1)	-0.7 (1.7)	-4	0.0	4	
		Week 10	CR845	135	105 (77.8)	-1.2 (1.4)	-4	-1.0	2	-0.38 [-0.66, -0.11]
			Placebo	114	102 (89.5)	-0.6 (1.6)	-4	0.0	4	
		Week 12	CR845	135	108 (80.0)	-1.2 (1.4)	-4	-1.0	2	-0.34 [-0.61, -0.07]
			Placebo	114	103 (90.4)	-0.7 (1.5)	-4	-1.0	4	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DLC_ISHC: Change from baseline in 5-D duration score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
White	5-D duration score	Baseline	CR845	255	250 (98.0)	2.8 (1.4)	1	2.5	5	
			Placebo	262	262 (100.0)	2.7 (1.4)	1	2.0	5	
		Week 4	CR845	255	235 (92.2)	2.0 (1.2)	1	2.0	5	
			Placebo	262	243 (92.7)	2.4 (1.4)	1	2.0	5	
		Week 8	CR845	255	224 (87.8)	1.8 (1.1)	1	1.5	5	
			Placebo	262	242 (92.4)	2.1 (1.2)	1	2.0	5	
		Week 10	CR845	255	225 (88.2)	1.9 (1.1)	1	2.0	5	
			Placebo	262	238 (90.8)	2.0 (1.2)	1	2.0	5	
		Week 12	CR845	255	224 (87.8)	1.8 (1.1)	1	1.0	5	
			Placebo	262	239 (91.2)	2.1 (1.3)	1	2.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	255	232 (91.0)	-0.7 (1.3)	-4	-1.0	3	-0.27 [-0.45, -0.09]
			Placebo	262	243 (92.7)	-0.3 (1.6)	-4	0.0	4	
		Week 8	CR845	255	221 (86.7)	-0.9 (1.4)	-4	-1.0	3	-0.15 [-0.34, 0.03]
			Placebo	262	242 (92.4)	-0.7 (1.4)	-4	0.0	4	
		Week 10	CR845	255	222 (87.1)	-0.8 (1.5)	-4	-1.0	4	-0.08 [-0.26, 0.10]
			Placebo	262	238 (90.8)	-0.7 (1.5)	-4	-1.0	4	
		Week 12	CR845	255	222 (87.1)	-0.9 (1.5)	-4	-1.0	3	-0.22 [-0.40, -0.03]
			Placebo	262	239 (91.2)	-0.6 (1.5)	-4	0.0	4	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DLC_ISHC: Change from baseline in 5-D duration score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Other	5-D duration score	Baseline	CR845	35	35 (100.0)	2.3 (1.4)	1	2.0	5	
			Placebo	47	47 (100.0)	3.0 (1.4)	1	3.0	5	
		Week 4	CR845	35	31 (88.6)	1.9 (1.1)	1	2.0	5	
			Placebo	47	44 (93.6)	2.3 (1.3)	1	2.0	5	
		Week 8	CR845	35	31 (88.6)	1.5 (1.1)	1	1.0	5	
			Placebo	47	43 (91.5)	2.0 (1.1)	1	2.0	5	
		Week 10	CR845	35	29 (82.9)	1.6 (0.9)	1	1.0	4	
			Placebo	47	42 (89.4)	1.9 (1.2)	1	2.0	5	
		Week 12	CR845	35	29 (82.9)	2.1 (1.4)	1	2.0	5	
			Placebo	47	41 (87.2)	1.9 (1.2)	1	1.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	35	31 (88.6)	-0.5 (1.3)	-4	0.0	2	0.11 [-0.35, 0.57]
			Placebo	47	44 (93.6)	-0.7 (1.3)	-4	0.0	2	
		Week 8	CR845	35	31 (88.6)	-0.9 (1.7)	-4	0.0	3	0.00 [-0.46, 0.46]
			Placebo	47	43 (91.5)	-0.9 (1.5)	-4	-1.0	3	
		Week 10	CR845	35	29 (82.9)	-0.8 (1.4)	-4	0.0	2	0.18 [-0.30, 0.65]
			Placebo	47	42 (89.4)	-1.1 (1.4)	-4	-1.0	2	
		Week 12	CR845	35	29 (82.9)	-0.3 (2.0)	-4	0.0	4	0.48 [-0.00, 0.96]
			Placebo	47	41 (87.2)	-1.1 (1.4)	-4	-1.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DLC_ISHD: Change from baseline in 5-D duration score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 4 to < 7	5-D duration score	Baseline	CR845	185	182 (98.4)	2.2 (1.2)	1	2.0	5	
			Placebo	193	193 (100.0)	2.2 (1.2)	1	2.0	5	
		Week 4	CR845	185	169 (91.4)	1.7 (1.1)	1	1.0	5	
			Placebo	193	179 (92.7)	2.1 (1.2)	1	2.0	5	
		Week 8	CR845	185	164 (88.6)	1.6 (0.9)	1	1.0	5	
			Placebo	193	177 (91.7)	1.9 (1.1)	1	2.0	5	
		Week 10	CR845	185	161 (87.0)	1.6 (0.9)	1	1.0	5	
			Placebo	193	173 (89.6)	1.8 (1.1)	1	1.0	5	
		Week 12	CR845	185	159 (85.9)	1.6 (1.0)	1	1.0	5	
			Placebo	193	175 (90.7)	1.8 (1.1)	1	1.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	185	167 (90.3)	-0.5 (1.3)	-4	0.0	4	-0.26 [-0.47, -0.05]
			Placebo	193	179 (92.7)	-0.1 (1.4)	-4	0.0	4	
		Week 8	CR845	185	162 (87.6)	-0.7 (1.3)	-4	0.0	2	-0.27 [-0.48, -0.06]
			Placebo	193	177 (91.7)	-0.3 (1.3)	-4	0.0	4	
		Week 10	CR845	185	159 (85.9)	-0.6 (1.3)	-4	0.0	4	-0.18 [-0.39, 0.04]
			Placebo	193	173 (89.6)	-0.4 (1.4)	-4	0.0	4	
		Week 12	CR845	185	157 (84.9)	-0.6 (1.4)	-4	0.0	4	-0.17 [-0.39, 0.04]
			Placebo	193	175 (90.7)	-0.4 (1.3)	-4	0.0	4	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DLC_ISHD: Change from baseline in 5-D duration score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 7	5-D duration score	Baseline	CR845	241	236 (97.9)	3.1 (1.4)	1	3.0	5	
			Placebo	232	232 (100.0)	3.3 (1.4)	1	3.0	5	
		Week 4	CR845	241	214 (88.8)	2.3 (1.2)	1	2.0	5	
			Placebo	232	211 (90.9)	2.6 (1.5)	1	2.0	5	
		Week 8	CR845	241	205 (85.1)	2.0 (1.2)	1	2.0	5	
			Placebo	232	215 (92.7)	2.3 (1.4)	1	2.0	5	
		Week 10	CR845	241	202 (83.8)	2.0 (1.1)	1	2.0	5	
			Placebo	232	211 (90.9)	2.3 (1.3)	1	2.0	5	
		Week 12	CR845	241	206 (85.5)	2.0 (1.1)	1	2.0	5	
			Placebo	232	210 (90.5)	2.3 (1.3)	1	2.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	241	210 (87.1)	-0.9 (1.3)	-4	-1.0	3	-0.17 [-0.37, 0.02]
			Placebo	232	211 (90.9)	-0.7 (1.6)	-4	0.0	4	
		Week 8	CR845	241	201 (83.4)	-1.1 (1.5)	-4	-1.0	3	-0.09 [-0.28, 0.10]
			Placebo	232	215 (92.7)	-1.0 (1.6)	-4	-1.0	4	
		Week 10	CR845	241	198 (82.2)	-1.2 (1.6)	-4	-1.0	4	-0.11 [-0.31, 0.08]
			Placebo	232	211 (90.9)	-1.0 (1.6)	-4	-1.0	4	
		Week 12	CR845	241	203 (84.2)	-1.2 (1.5)	-4	-1.0	3	-0.17 [-0.36, 0.02]
			Placebo	232	210 (90.5)	-1.0 (1.6)	-4	-1.0	4	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DLC_ISHE: Change from baseline in 5-D duration score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	5-D duration score	Baseline	CR845	359	351 (97.8)	2.7 (1.4)	1	2.0	5	
			Placebo	360	360 (100.0)	2.8 (1.4)	1	2.0	5	
		Week 4	CR845	359	321 (89.4)	2.0 (1.2)	1	2.0	5	
			Placebo	360	330 (91.7)	2.4 (1.4)	1	2.0	5	
		Week 8	CR845	359	310 (86.4)	1.8 (1.1)	1	1.0	5	
			Placebo	360	328 (91.1)	2.1 (1.2)	1	2.0	5	
		Week 10	CR845	359	306 (85.2)	1.8 (1.0)	1	1.0	5	
			Placebo	360	322 (89.4)	2.0 (1.3)	1	2.0	5	
		Week 12	CR845	359	306 (85.2)	1.8 (1.1)	1	1.0	5	
			Placebo	360	322 (89.4)	2.0 (1.3)	1	2.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	359	315 (87.7)	-0.7 (1.3)	-4	-1.0	4	-0.24 [-0.40, -0.09]
			Placebo	360	330 (91.7)	-0.4 (1.6)	-4	0.0	4	
		Week 8	CR845	359	304 (84.7)	-0.9 (1.4)	-4	-1.0	3	-0.16 [-0.31, 0.00]
			Placebo	360	328 (91.1)	-0.7 (1.5)	-4	0.0	4	
		Week 10	CR845	359	300 (83.6)	-0.9 (1.4)	-4	-1.0	2	-0.14 [-0.30, 0.01]
			Placebo	360	322 (89.4)	-0.7 (1.6)	-4	-1.0	4	
		Week 12	CR845	359	301 (83.8)	-1.0 (1.5)	-4	-1.0	4	-0.17 [-0.33, -0.02]
			Placebo	360	322 (89.4)	-0.7 (1.6)	-4	-1.0	4	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DLC_ISHE: Change from baseline in 5-D duration score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	5-D duration score	Baseline	CR845	67	67 (100.0)	2.9 (1.4)	1	3.0	5	
			Placebo	65	65 (100.0)	3.0 (1.3)	1	3.0	5	
		Week 4	CR845	67	62 (92.5)	2.2 (1.2)	1	2.0	5	
			Placebo	65	60 (92.3)	2.4 (1.4)	1	2.0	5	
		Week 8	CR845	67	59 (88.1)	1.9 (1.1)	1	2.0	5	
			Placebo	65	64 (98.5)	2.3 (1.3)	1	2.0	5	
		Week 10	CR845	67	57 (85.1)	2.0 (1.3)	1	1.0	5	
			Placebo	65	62 (95.4)	2.3 (1.3)	1	2.0	5	
		Week 12	CR845	67	59 (88.1)	1.8 (0.9)	1	2.0	5	
			Placebo	65	63 (96.9)	2.2 (1.2)	1	2.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	67	62 (92.5)	-0.6 (1.3)	-4	0.0	2	-0.02 [-0.38, 0.33]
			Placebo	65	60 (92.3)	-0.6 (1.4)	-4	-1.0	3	
		Week 8	CR845	67	59 (88.1)	-1.0 (1.4)	-4	-1.0	3	-0.18 [-0.53, 0.18]
			Placebo	65	64 (98.5)	-0.7 (1.4)	-3	-1.0	4	
		Week 10	CR845	67	57 (85.1)	-0.9 (1.8)	-4	-1.0	4	-0.11 [-0.47, 0.25]
			Placebo	65	62 (95.4)	-0.7 (1.4)	-4	-1.0	2	
		Week 12	CR845	67	59 (88.1)	-1.1 (1.5)	-4	-1.0	1	-0.18 [-0.53, 0.18]
			Placebo	65	63 (96.9)	-0.8 (1.2)	-4	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DLC_ISHF: Change from baseline in 5-D duration score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	5-D duration score	Baseline	CR845	267	261 (97.8)	2.8 (1.4)	1	3.0	5	
			Placebo	262	262 (100.0)	2.7 (1.3)	1	2.0	5	
		Week 4	CR845	267	247 (92.5)	2.0 (1.2)	1	2.0	5	
			Placebo	262	240 (91.6)	2.3 (1.3)	1	2.0	5	
		Week 8	CR845	267	239 (89.5)	1.8 (1.1)	1	1.0	5	
			Placebo	262	242 (92.4)	2.1 (1.2)	1	2.0	5	
		Week 10	CR845	267	232 (86.9)	1.8 (1.1)	1	1.0	5	
			Placebo	262	238 (90.8)	2.0 (1.1)	1	2.0	5	
		Week 12	CR845	267	234 (87.6)	1.8 (1.1)	1	1.0	5	
			Placebo	262	241 (92.0)	2.0 (1.2)	1	2.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	267	243 (91.0)	-0.7 (1.3)	-4	-1.0	4	-0.26 [-0.44, -0.08]
			Placebo	262	240 (91.6)	-0.3 (1.6)	-4	0.0	4	
		Week 8	CR845	267	235 (88.0)	-1.0 (1.4)	-4	-1.0	3	-0.25 [-0.43, -0.07]
			Placebo	262	242 (92.4)	-0.6 (1.5)	-4	0.0	4	
		Week 10	CR845	267	228 (85.4)	-0.9 (1.4)	-4	-1.0	4	-0.17 [-0.35, 0.01]
			Placebo	262	238 (90.8)	-0.7 (1.6)	-4	0.0	4	
		Week 12	CR845	267	231 (86.5)	-1.0 (1.5)	-4	-1.0	4	-0.22 [-0.40, -0.04]
			Placebo	262	241 (92.0)	-0.6 (1.6)	-4	0.0	4	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DLC_ISHF: Change from baseline in 5-D duration score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	5-D duration score	Baseline	CR845	159	157 (98.7)	2.7 (1.4)	1	2.0	5	
			Placebo	163	163 (100.0)	3.0 (1.5)	1	3.0	5	
		Week 4	CR845	159	136 (85.5)	2.0 (1.2)	1	2.0	5	
			Placebo	163	150 (92.0)	2.5 (1.5)	1	2.0	5	
		Week 8	CR845	159	130 (81.8)	1.9 (1.1)	1	2.0	5	
			Placebo	163	150 (92.0)	2.2 (1.4)	1	2.0	5	
		Week 10	CR845	159	131 (82.4)	1.8 (1.0)	1	2.0	5	
			Placebo	163	146 (89.6)	2.2 (1.4)	1	2.0	5	
		Week 12	CR845	159	131 (82.4)	1.8 (1.0)	1	1.0	5	
			Placebo	163	144 (88.3)	2.1 (1.4)	1	2.0	5	
	Change from baseline in 5-D duration score	Week 4	CR845	159	134 (84.3)	-0.7 (1.3)	-4	-1.0	3	-0.13 [-0.37, 0.10]
			Placebo	163	150 (92.0)	-0.5 (1.5)	-4	0.0	4	
		Week 8	CR845	159	128 (80.5)	-0.9 (1.5)	-4	-1.0	3	-0.01 [-0.25, 0.22]
			Placebo	163	150 (92.0)	-0.8 (1.5)	-4	-1.0	4	
		Week 10	CR845	159	129 (81.1)	-1.0 (1.5)	-4	-1.0	3	-0.09 [-0.33, 0.15]
			Placebo	163	146 (89.6)	-0.8 (1.4)	-4	-1.0	4	
		Week 12	CR845	159	129 (81.1)	-1.0 (1.5)	-4	-1.0	3	-0.09 [-0.33, 0.15]
			Placebo	163	144 (88.3)	-0.8 (1.4)	-4	-1.0	4	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DWC_ISHA: Change from baseline in 5-D direction score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
< 65 years	5-D direction score	Baseline	CR845	282	276 (97.9)	3.9 (0.6)	2	4.0	5	
			Placebo	290	290 (100.0)	3.9 (0.7)	2	4.0	5	
		Week 4	CR845	282	254 (90.1)	2.7 (0.8)	1	3.0	5	
			Placebo	290	261 (90.0)	3.2 (0.9)	1	3.0	5	
		Week 8	CR845	282	242 (85.8)	2.5 (0.8)	1	2.0	5	
			Placebo	290	264 (91.0)	3.0 (0.9)	1	3.0	5	
		Week 10	CR845	282	243 (86.2)	2.5 (0.8)	1	2.0	5	
			Placebo	290	259 (89.3)	2.9 (0.9)	1	3.0	5	
		Week 12	CR845	282	244 (86.5)	2.5 (0.9)	1	2.0	5	
			Placebo	290	260 (89.7)	2.9 (1.0)	1	3.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	282	250 (88.7)	-1.3 (1.0)	-4	-1.0	2	-0.53 [-0.71, -0.36]
			Placebo	290	261 (90.0)	-0.7 (1.1)	-3	-1.0	3	
		Week 8	CR845	282	238 (84.4)	-1.4 (0.9)	-3	-1.0	2	-0.54 [-0.72, -0.37]
			Placebo	290	264 (91.0)	-0.9 (1.1)	-4	-1.0	2	
		Week 10	CR845	282	239 (84.8)	-1.4 (1.0)	-4	-1.0	1	-0.43 [-0.61, -0.25]
			Placebo	290	259 (89.3)	-0.9 (1.1)	-4	-1.0	3	
		Week 12	CR845	282	241 (85.5)	-1.4 (1.0)	-4	-2.0	2	-0.43 [-0.61, -0.25]
			Placebo	290	260 (89.7)	-0.9 (1.1)	-4	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DWC_ISHA: Change from baseline in 5-D direction score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 65 years	5-D direction score	Baseline	CR845	144	144 (100.0)	3.8 (0.7)	1	4.0	5	
			Placebo	135	135 (100.0)	3.9 (0.7)	2	4.0	5	
		Week 4	CR845	144	130 (90.3)	2.7 (0.8)	1	3.0	5	
			Placebo	135	129 (95.6)	3.0 (0.8)	1	3.0	5	
		Week 8	CR845	144	126 (87.5)	2.8 (0.9)	1	3.0	5	
			Placebo	135	128 (94.8)	2.8 (0.8)	1	3.0	5	
		Week 10	CR845	144	120 (83.3)	2.6 (0.8)	1	2.0	5	
			Placebo	135	125 (92.6)	3.0 (0.9)	1	3.0	5	
		Week 12	CR845	144	120 (83.3)	2.6 (1.0)	1	2.0	5	
			Placebo	135	125 (92.6)	2.8 (1.0)	1	3.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	144	130 (90.3)	-1.1 (1.0)	-3	-1.0	2	-0.26 [-0.50, -0.01]
			Placebo	135	129 (95.6)	-0.8 (1.0)	-4	-1.0	2	
		Week 8	CR845	144	126 (87.5)	-1.0 (1.1)	-4	-1.0	2	0.01 [-0.23, 0.26]
			Placebo	135	128 (94.8)	-1.0 (1.0)	-4	-1.0	2	
		Week 10	CR845	144	120 (83.3)	-1.2 (0.9)	-4	-1.0	1	-0.33 [-0.58, -0.08]
			Placebo	135	125 (92.6)	-0.9 (1.1)	-3	-1.0	3	
		Week 12	CR845	144	120 (83.3)	-1.1 (1.1)	-4	-1.0	1	-0.08 [-0.33, 0.17]
			Placebo	135	125 (92.6)	-1.0 (1.1)	-3	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DWC_ISHB: Change from baseline in 5-D direction score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Male	5-D direction score	Baseline	CR845	249	245 (98.4)	3.9 (0.6)	1	4.0	5	
			Placebo	258	258 (100.0)	3.9 (0.7)	2	4.0	5	
		Week 4	CR845	249	223 (89.6)	2.7 (0.8)	1	3.0	5	
			Placebo	258	231 (89.5)	3.1 (0.9)	1	3.0	5	
		Week 8	CR845	249	213 (85.5)	2.8 (0.8)	1	3.0	5	
			Placebo	258	238 (92.2)	3.0 (0.9)	1	3.0	5	
		Week 10	CR845	249	209 (83.9)	2.7 (0.8)	1	2.0	5	
			Placebo	258	233 (90.3)	2.9 (0.9)	1	3.0	5	
		Week 12	CR845	249	209 (83.9)	2.7 (0.9)	1	2.0	5	
			Placebo	258	232 (89.9)	2.9 (1.0)	1	3.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	249	221 (88.8)	-1.1 (0.9)	-3	-1.0	2	-0.37 [-0.55, -0.18]
			Placebo	258	231 (89.5)	-0.8 (1.0)	-4	-1.0	2	
		Week 8	CR845	249	211 (84.7)	-1.1 (0.9)	-3	-1.0	2	-0.22 [-0.40, -0.03]
			Placebo	258	238 (92.2)	-0.9 (1.0)	-4	-1.0	2	
		Week 10	CR845	249	207 (83.1)	-1.2 (0.9)	-3	-1.0	1	-0.26 [-0.44, -0.07]
			Placebo	258	233 (90.3)	-0.9 (1.0)	-4	-1.0	2	
		Week 12	CR845	249	207 (83.1)	-1.2 (1.0)	-4	-1.0	2	-0.24 [-0.43, -0.05]
			Placebo	258	232 (89.9)	-0.9 (1.1)	-3	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DWC_ISHB: Change from baseline in 5-D direction score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Female	5-D direction score	Baseline	CR845	177	175 (98.9)	3.9 (0.7)	2	4.0	5	
			Placebo	167	167 (100.0)	3.9 (0.7)	2	4.0	5	
		Week 4	CR845	177	161 (91.0)	2.6 (0.8)	1	3.0	5	
			Placebo	167	159 (95.2)	3.1 (0.9)	2	3.0	5	
		Week 8	CR845	177	155 (87.6)	2.4 (0.7)	1	2.0	5	
			Placebo	167	154 (92.2)	2.9 (0.9)	1	3.0	5	
		Week 10	CR845	177	154 (87.0)	2.4 (0.8)	1	2.0	5	
			Placebo	167	151 (90.4)	3.0 (1.0)	1	3.0	5	
		Week 12	CR845	177	155 (87.6)	2.4 (0.9)	1	2.0	5	
			Placebo	167	153 (91.6)	2.9 (1.0)	1	3.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	177	159 (89.8)	-1.3 (1.0)	-4	-1.0	1	-0.54 [-0.76, -0.32]
			Placebo	167	159 (95.2)	-0.7 (1.1)	-3	-1.0	3	
		Week 8	CR845	177	153 (86.4)	-1.5 (1.0)	-4	-2.0	2	-0.50 [-0.73, -0.28]
			Placebo	167	154 (92.2)	-1.0 (1.1)	-4	-1.0	2	
		Week 10	CR845	177	152 (85.9)	-1.5 (1.0)	-4	-2.0	1	-0.57 [-0.80, -0.34]
			Placebo	167	151 (90.4)	-0.9 (1.2)	-3	-1.0	3	
		Week 12	CR845	177	154 (87.0)	-1.4 (1.1)	-4	-1.5	2	-0.39 [-0.61, -0.16]
			Placebo	167	153 (91.6)	-1.0 (1.1)	-4	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DWC_ISHC: Change from baseline in 5-D direction score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Black/African American	5-D direction score	Baseline	CR845	135	133 (98.5)	3.9 (0.6)	2	4.0	5	
			Placebo	114	114 (100.0)	3.8 (0.7)	2	4.0	5	
		Week 4	CR845	135	116 (85.9)	2.7 (0.8)	1	3.0	5	
			Placebo	114	101 (88.6)	3.1 (0.8)	2	3.0	5	
		Week 8	CR845	135	113 (83.7)	2.5 (0.8)	1	2.0	5	
			Placebo	114	105 (92.1)	2.8 (0.9)	1	3.0	5	
		Week 10	CR845	135	108 (80.0)	2.4 (0.7)	1	2.0	5	
			Placebo	114	102 (89.5)	2.9 (0.9)	1	3.0	5	
		Week 12	CR845	135	110 (81.5)	2.4 (0.7)	1	2.0	4	
			Placebo	114	103 (90.4)	2.9 (1.0)	1	3.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	135	114 (84.4)	-1.3 (1.0)	-4	-1.0	1	-0.59 [-0.86, -0.32]
			Placebo	114	101 (88.6)	-0.6 (1.1)	-3	-1.0	3	
		Week 8	CR845	135	111 (82.2)	-1.4 (1.0)	-4	-2.0	2	-0.38 [-0.65, -0.11]
			Placebo	114	105 (92.1)	-1.0 (1.1)	-4	-1.0	2	
		Week 10	CR845	135	106 (78.5)	-1.5 (1.0)	-4	-2.0	1	-0.49 [-0.77, -0.22]
			Placebo	114	102 (89.5)	-1.0 (1.2)	-4	-1.0	3	
		Week 12	CR845	135	108 (80.0)	-1.5 (1.1)	-4	-2.0	2	-0.49 [-0.77, -0.22]
			Placebo	114	103 (90.4)	-1.0 (1.2)	-3	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DWC_ISHC: Change from baseline in 5-D direction score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
White	5-D direction score	Baseline	CR845	255	251 (98.4)	3.9 (0.6)	2	4.0	5	
			Placebo	262	262 (100.0)	3.9 (0.7)	2	4.0	5	
		Week 4	CR845	255	236 (92.5)	2.7 (0.8)	1	3.0	5	
			Placebo	262	243 (92.7)	3.1 (0.9)	1	3.0	5	
		Week 8	CR845	255	223 (87.5)	2.7 (0.8)	1	3.0	5	
			Placebo	262	242 (92.4)	3.0 (0.9)	1	3.0	5	
		Week 10	CR845	255	225 (88.2)	2.6 (0.9)	1	2.0	5	
			Placebo	262	238 (90.8)	3.0 (0.9)	1	3.0	5	
		Week 12	CR845	255	224 (87.8)	2.6 (1.0)	1	2.0	5	
			Placebo	262	239 (91.2)	3.0 (1.0)	1	3.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	255	234 (91.8)	-1.2 (1.0)	-4	-1.0	2	-0.37 [-0.55, -0.19]
			Placebo	262	243 (92.7)	-0.8 (1.0)	-4	-1.0	2	
		Week 8	CR845	255	221 (86.7)	-1.2 (0.9)	-3	-1.0	1	-0.33 [-0.51, -0.15]
			Placebo	262	242 (92.4)	-0.9 (1.1)	-4	-1.0	2	
		Week 10	CR845	255	223 (87.5)	-1.2 (1.0)	-3	-1.0	1	-0.36 [-0.55, -0.18]
			Placebo	262	238 (90.8)	-0.9 (1.1)	-3	-1.0	2	
		Week 12	CR845	255	223 (87.5)	-1.2 (1.0)	-3	-1.0	2	-0.27 [-0.46, -0.09]
			Placebo	262	239 (91.2)	-0.9 (1.1)	-4	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DWC_ISHC: Change from baseline in 5-D direction score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Other	5-D direction score	Baseline	CR845	35	35 (100.0)	3.8 (0.8)	1	4.0	5	
			Placebo	47	47 (100.0)	3.9 (0.6)	2	4.0	5	
		Week 4	CR845	35	31 (88.6)	2.6 (0.7)	1	3.0	4	
			Placebo	47	44 (93.6)	3.1 (0.9)	2	3.0	5	
		Week 8	CR845	35	31 (88.6)	2.6 (0.7)	1	3.0	4	
			Placebo	47	43 (91.5)	2.9 (0.9)	2	3.0	5	
		Week 10	CR845	35	29 (82.9)	2.5 (0.7)	1	2.0	4	
			Placebo	47	42 (89.4)	2.8 (0.9)	2	3.0	5	
		Week 12	CR845	35	29 (82.9)	2.7 (0.9)	2	2.0	5	
			Placebo	47	41 (87.2)	2.7 (1.0)	1	2.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	35	31 (88.6)	-1.2 (1.0)	-3	-1.0	2	-0.42 [-0.88, 0.05]
			Placebo	47	44 (93.6)	-0.8 (1.0)	-3	-1.0	1	
		Week 8	CR845	35	31 (88.6)	-1.2 (1.1)	-3	-1.0	2	-0.20 [-0.66, 0.26]
			Placebo	47	43 (91.5)	-1.0 (0.9)	-2	-1.0	2	
		Week 10	CR845	35	29 (82.9)	-1.3 (0.9)	-3	-1.0	1	-0.28 [-0.75, 0.20]
			Placebo	47	42 (89.4)	-1.1 (0.8)	-2	-1.0	0	
		Week 12	CR845	35	29 (82.9)	-1.1 (1.0)	-3	-1.0	1	0.07 [-0.40, 0.55]
			Placebo	47	41 (87.2)	-1.1 (1.1)	-3	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DWC_ISHD: Change from baseline in 5-D direction score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 4 to < 7	5-D direction score	Baseline	CR845	185	183 (98.9)	3.7 (0.7)	1	4.0	5	
			Placebo	193	193 (100.0)	3.7 (0.7)	2	4.0	5	
		Week 4	CR845	185	169 (91.4)	2.5 (0.7)	1	2.0	5	
			Placebo	193	179 (92.7)	3.0 (0.9)	1	3.0	5	
		Week 8	CR845	185	164 (88.6)	2.5 (0.7)	1	2.0	5	
			Placebo	193	177 (91.7)	2.9 (0.9)	1	3.0	5	
		Week 10	CR845	185	161 (87.0)	2.4 (0.7)	1	2.0	5	
			Placebo	193	173 (89.6)	2.8 (0.9)	1	3.0	5	
		Week 12	CR845	185	159 (85.9)	2.5 (0.9)	1	2.0	5	
			Placebo	193	175 (90.7)	2.8 (1.0)	1	3.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	185	168 (90.8)	-1.2 (1.0)	-4	-1.0	2	-0.46 [-0.67, -0.25]
			Placebo	193	179 (92.7)	-0.7 (1.0)	-3	-1.0	3	
		Week 8	CR845	185	163 (88.1)	-1.2 (0.9)	-3	-1.0	2	-0.39 [-0.61, -0.18]
			Placebo	193	177 (91.7)	-0.8 (1.0)	-3	-1.0	2	
		Week 10	CR845	185	160 (86.5)	-1.3 (0.9)	-3	-1.0	1	-0.44 [-0.66, -0.22]
			Placebo	193	173 (89.6)	-0.8 (1.1)	-3	-1.0	2	
		Week 12	CR845	185	158 (85.4)	-1.2 (1.0)	-4	-1.0	2	-0.28 [-0.50, -0.06]
			Placebo	193	175 (90.7)	-0.9 (1.1)	-3	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DWC_ISHD: Change from baseline in 5-D direction score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 7	5-D direction score	Baseline	CR845	241	237 (98.3)	4.0 (0.6)	2	4.0	5	
			Placebo	232	232 (100.0)	4.0 (0.6)	2	4.0	5	
		Week 4	CR845	241	215 (89.2)	2.8 (0.8)	1	3.0	5	
			Placebo	232	211 (90.9)	3.2 (0.9)	1	3.0	5	
		Week 8	CR845	241	204 (84.6)	2.7 (0.9)	1	3.0	5	
			Placebo	232	215 (92.7)	3.0 (0.9)	1	3.0	5	
		Week 10	CR845	241	202 (83.8)	2.6 (0.9)	1	3.0	5	
			Placebo	232	211 (90.9)	3.0 (0.9)	1	3.0	5	
		Week 12	CR845	241	205 (85.1)	2.6 (0.9)	1	2.0	5	
			Placebo	232	210 (90.5)	3.0 (1.0)	1	3.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	241	212 (88.0)	-1.2 (1.0)	-3	-1.0	2	-0.42 [-0.62, -0.23]
			Placebo	232	211 (90.9)	-0.8 (1.0)	-4	-1.0	2	
		Week 8	CR845	241	201 (83.4)	-1.3 (1.0)	-4	-1.0	2	-0.31 [-0.50, -0.11]
			Placebo	232	215 (92.7)	-1.0 (1.1)	-4	-1.0	2	
		Week 10	CR845	241	199 (82.6)	-1.4 (1.0)	-4	-1.0	1	-0.36 [-0.56, -0.17]
			Placebo	232	211 (90.9)	-1.0 (1.1)	-4	-1.0	3	
		Week 12	CR845	241	203 (84.2)	-1.3 (1.1)	-4	-1.0	2	-0.33 [-0.52, -0.13]
			Placebo	232	210 (90.5)	-1.0 (1.1)	-4	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DWC_ISHE: Change from baseline in 5-D direction score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	5-D direction score	Baseline	CR845	359	353 (98.3)	3.8 (0.6)	1	4.0	5	
			Placebo	360	360 (100.0)	3.9 (0.7)	2	4.0	5	
		Week 4	CR845	359	322 (89.7)	2.7 (0.8)	1	3.0	5	
			Placebo	360	330 (91.7)	3.1 (0.9)	1	3.0	5	
		Week 8	CR845	359	309 (86.1)	2.7 (0.8)	1	3.0	5	
			Placebo	360	328 (91.1)	2.9 (0.9)	1	3.0	5	
		Week 10	CR845	359	306 (85.2)	2.5 (0.8)	1	2.0	5	
			Placebo	360	322 (89.4)	2.9 (0.9)	1	3.0	5	
		Week 12	CR845	359	306 (85.2)	2.6 (0.9)	1	2.0	5	
			Placebo	360	322 (89.4)	2.9 (1.0)	1	3.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	359	318 (88.6)	-1.2 (1.0)	-4	-1.0	2	-0.42 [-0.58, -0.26]
			Placebo	360	330 (91.7)	-0.8 (1.1)	-4	-1.0	3	
		Week 8	CR845	359	305 (85.0)	-1.2 (0.9)	-3	-1.0	2	-0.31 [-0.47, -0.15]
			Placebo	360	328 (91.1)	-0.9 (1.1)	-4	-1.0	2	
		Week 10	CR845	359	302 (84.1)	-1.3 (0.9)	-3	-1.0	1	-0.39 [-0.55, -0.23]
			Placebo	360	322 (89.4)	-0.9 (1.1)	-4	-1.0	3	
		Week 12	CR845	359	303 (84.4)	-1.2 (1.0)	-3	-1.0	2	-0.27 [-0.43, -0.12]
			Placebo	360	322 (89.4)	-0.9 (1.1)	-4	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DWC_ISHE: Change from baseline in 5-D direction score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	5-D direction score	Baseline	CR845	67	67 (100.0)	4.0 (0.7)	2	4.0	5	
			Placebo	65	65 (100.0)	4.0 (0.7)	2	4.0	5	
		Week 4	CR845	67	62 (92.5)	2.8 (0.8)	1	3.0	5	
			Placebo	65	60 (92.3)	3.3 (0.9)	2	3.0	5	
		Week 8	CR845	67	59 (88.1)	2.4 (0.8)	1	2.0	5	
			Placebo	65	64 (98.5)	2.9 (0.8)	2	3.0	5	
		Week 10	CR845	67	57 (85.1)	2.5 (0.9)	1	2.0	5	
			Placebo	65	62 (95.4)	3.0 (0.8)	2	3.0	5	
		Week 12	CR845	67	58 (86.6)	2.4 (0.9)	1	2.0	5	
			Placebo	65	63 (96.9)	3.0 (1.0)	1	3.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	67	62 (92.5)	-1.2 (1.1)	-3	-1.0	1	-0.56 [-0.92, -0.19]
			Placebo	65	60 (92.3)	-0.7 (0.9)	-2	-1.0	1	
		Week 8	CR845	67	59 (88.1)	-1.6 (1.0)	-4	-2.0	1	-0.51 [-0.87, -0.15]
			Placebo	65	64 (98.5)	-1.1 (1.0)	-3	-1.0	1	
		Week 10	CR845	67	57 (85.1)	-1.5 (1.2)	-4	-1.0	1	-0.42 [-0.79, -0.06]
			Placebo	65	62 (95.4)	-1.0 (1.1)	-3	-1.0	2	
		Week 12	CR845	67	58 (86.6)	-1.6 (1.2)	-4	-2.0	1	-0.48 [-0.84, -0.11]
			Placebo	65	63 (96.9)	-1.0 (1.1)	-3	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DWC_ISHF: Change from baseline in 5-D direction score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	5-D direction score	Baseline	CR845	267	262 (98.1)	3.9 (0.7)	1	4.0	5	
			Placebo	262	262 (100.0)	3.9 (0.7)	2	4.0	5	
		Week 4	CR845	267	248 (92.9)	2.7 (0.8)	1	3.0	5	
			Placebo	262	240 (91.6)	3.1 (0.8)	1	3.0	5	
		Week 8	CR845	267	238 (89.1)	2.6 (0.8)	1	2.5	5	
			Placebo	262	242 (92.4)	2.9 (0.9)	1	3.0	5	
		Week 10	CR845	267	232 (86.9)	2.6 (0.8)	1	2.0	5	
			Placebo	262	238 (90.8)	2.9 (0.9)	1	3.0	5	
		Week 12	CR845	267	234 (87.6)	2.6 (0.9)	1	2.0	5	
			Placebo	262	241 (92.0)	2.9 (1.0)	1	3.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	267	245 (91.8)	-1.2 (1.0)	-4	-1.0	2	-0.41 [-0.59, -0.23]
			Placebo	262	240 (91.6)	-0.8 (1.0)	-4	-1.0	2	
		Week 8	CR845	267	235 (88.0)	-1.2 (0.9)	-3	-1.0	2	-0.30 [-0.48, -0.12]
			Placebo	262	242 (92.4)	-0.9 (1.0)	-4	-1.0	2	
		Week 10	CR845	267	229 (85.8)	-1.2 (0.9)	-3	-1.0	1	-0.24 [-0.42, -0.06]
			Placebo	262	238 (90.8)	-1.0 (1.1)	-4	-1.0	2	
		Week 12	CR845	267	232 (86.9)	-1.2 (1.0)	-4	-1.0	2	-0.26 [-0.44, -0.08]
			Placebo	262	241 (92.0)	-1.0 (1.1)	-3	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DWC_ISHF: Change from baseline in 5-D direction score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	5-D direction score	Baseline	CR845	159	158 (99.4)	3.9 (0.6)	2	4.0	5	
			Placebo	163	163 (100.0)	3.9 (0.6)	2	4.0	5	
		Week 4	CR845	159	136 (85.5)	2.6 (0.8)	1	3.0	5	
			Placebo	163	150 (92.0)	3.1 (0.9)	1	3.0	5	
		Week 8	CR845	159	130 (81.8)	2.6 (0.9)	1	3.0	5	
			Placebo	163	150 (92.0)	3.0 (1.0)	1	3.0	5	
		Week 10	CR845	159	131 (82.4)	2.4 (0.7)	1	2.0	4	
			Placebo	163	146 (89.6)	3.1 (1.0)	1	3.0	5	
		Week 12	CR845	159	130 (81.8)	2.5 (0.9)	1	2.0	5	
			Placebo	163	144 (88.3)	2.9 (1.0)	1	3.0	5	
	Change from baseline in 5-D direction score	Week 4	CR845	159	135 (84.9)	-1.3 (1.0)	-3	-1.0	1	-0.50 [-0.74, -0.27]
			Placebo	163	150 (92.0)	-0.8 (1.1)	-3	-1.0	3	
		Week 8	CR845	159	129 (81.1)	-1.3 (1.0)	-4	-1.0	2	-0.41 [-0.64, -0.17]
			Placebo	163	150 (92.0)	-0.9 (1.1)	-4	-1.0	2	
		Week 10	CR845	159	130 (81.8)	-1.5 (1.0)	-4	-2.0	1	-0.67 [-0.91, -0.42]
			Placebo	163	146 (89.6)	-0.8 (1.1)	-3	-1.0	3	
		Week 12	CR845	159	129 (81.1)	-1.4 (1.0)	-4	-1.0	1	-0.40 [-0.64, -0.16]
			Placebo	163	144 (88.3)	-1.0 (1.1)	-4	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DNC_ISHA: Change from baseline in 5-D disability score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
< 65 years	5-D disability score	Baseline	CR845	282	276 (97.9)	3.5 (1.1)	1	4.0	5	
			Placebo	290	290 (100.0)	3.7 (1.1)	1	4.0	5	
		Week 4	CR845	282	254 (90.1)	2.9 (1.1)	1	3.0	5	
			Placebo	290	261 (90.0)	3.1 (1.2)	1	3.0	5	
		Week 8	CR845	282	243 (86.2)	2.7 (1.2)	1	3.0	5	
			Placebo	290	264 (91.0)	2.9 (1.2)	1	3.0	5	
		Week 10	CR845	282	243 (86.2)	2.5 (1.1)	1	2.0	5	
			Placebo	290	259 (89.3)	2.7 (1.2)	1	3.0	5	
		Week 12	CR845	282	244 (86.5)	2.4 (1.2)	1	2.0	5	
			Placebo	290	260 (89.7)	2.7 (1.3)	1	3.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	282	250 (88.7)	-0.6 (1.2)	-4	-1.0	2	-0.11 [-0.28, 0.07]
			Placebo	290	261 (90.0)	-0.5 (1.4)	-4	0.0	3	
		Week 8	CR845	282	239 (84.8)	-0.9 (1.3)	-4	-1.0	4	-0.06 [-0.23, 0.12]
			Placebo	290	264 (91.0)	-0.8 (1.3)	-4	-1.0	4	
		Week 10	CR845	282	239 (84.8)	-1.1 (1.3)	-4	-1.0	2	-0.09 [-0.27, 0.08]
			Placebo	290	259 (89.3)	-0.9 (1.4)	-4	-1.0	3	
		Week 12	CR845	282	241 (85.5)	-1.1 (1.4)	-4	-1.0	3	-0.10 [-0.27, 0.08]
			Placebo	290	260 (89.7)	-1.0 (1.4)	-4	-1.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DNC_ISHA: Change from baseline in 5-D disability score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 65 years	5-D disability score	Baseline	CR845	144	143 (99.3)	3.5 (1.2)	1	4.0	5	
			Placebo	135	135 (100.0)	3.5 (1.2)	1	4.0	5	
		Week 4	CR845	144	130 (90.3)	2.9 (1.2)	1	3.0	5	
			Placebo	135	129 (95.6)	2.9 (1.1)	1	3.0	5	
		Week 8	CR845	144	126 (87.5)	2.6 (1.3)	1	2.0	5	
			Placebo	135	128 (94.8)	2.9 (1.2)	1	3.0	5	
		Week 10	CR845	144	120 (83.3)	2.5 (1.3)	1	2.0	5	
			Placebo	135	125 (92.6)	2.8 (1.2)	1	3.0	5	
		Week 12	CR845	144	121 (84.0)	2.6 (1.3)	1	2.0	5	
			Placebo	135	125 (92.6)	2.5 (1.1)	1	2.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	144	130 (90.3)	-0.6 (1.2)	-4	0.0	3	-0.03 [-0.28, 0.21]
			Placebo	135	129 (95.6)	-0.6 (1.3)	-4	-1.0	4	
		Week 8	CR845	144	126 (87.5)	-0.9 (1.2)	-3	-1.0	3	-0.18 [-0.42, 0.07]
			Placebo	135	128 (94.8)	-0.6 (1.3)	-4	-1.0	3	
		Week 10	CR845	144	120 (83.3)	-1.0 (1.4)	-4	-1.0	3	-0.19 [-0.44, 0.06]
			Placebo	135	125 (92.6)	-0.7 (1.3)	-4	-1.0	3	
		Week 12	CR845	144	121 (84.0)	-1.0 (1.4)	-4	-1.0	4	0.01 [-0.24, 0.26]
			Placebo	135	125 (92.6)	-1.0 (1.2)	-4	-1.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DNC_ISHB: Change from baseline in 5-D disability score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Male	5-D disability score	Baseline	CR845	249	245 (98.4)	3.5 (1.1)	1	4.0	5	
			Placebo	258	258 (100.0)	3.5 (1.2)	1	4.0	5	
		Week 4	CR845	249	223 (89.6)	3.0 (1.1)	1	3.0	5	
			Placebo	258	231 (89.5)	3.0 (1.2)	1	3.0	5	
		Week 8	CR845	249	214 (85.9)	2.7 (1.2)	1	3.0	5	
			Placebo	258	238 (92.2)	2.8 (1.2)	1	3.0	5	
		Week 10	CR845	249	209 (83.9)	2.6 (1.2)	1	2.0	5	
			Placebo	258	233 (90.3)	2.6 (1.2)	1	3.0	5	
		Week 12	CR845	249	209 (83.9)	2.6 (1.2)	1	2.0	5	
			Placebo	258	232 (89.9)	2.6 (1.2)	1	2.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	249	221 (88.8)	-0.6 (1.1)	-4	0.0	2	-0.08 [-0.27, 0.10]
			Placebo	258	231 (89.5)	-0.5 (1.3)	-4	0.0	4	
		Week 8	CR845	249	212 (85.1)	-0.8 (1.3)	-4	-1.0	4	-0.06 [-0.24, 0.13]
			Placebo	258	238 (92.2)	-0.7 (1.3)	-4	-1.0	3	
		Week 10	CR845	249	207 (83.1)	-0.9 (1.3)	-4	-1.0	3	-0.03 [-0.22, 0.16]
			Placebo	258	233 (90.3)	-0.9 (1.3)	-4	-1.0	3	
		Week 12	CR845	249	207 (83.1)	-1.0 (1.4)	-4	-1.0	4	-0.04 [-0.23, 0.15]
			Placebo	258	232 (89.9)	-0.9 (1.3)	-4	-1.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DNC_ISHB: Change from baseline in 5-D disability score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Female	5-D disability score	Baseline	CR845	177	174 (98.3)	3.5 (1.1)	1	4.0	5	
			Placebo	167	167 (100.0)	3.8 (1.0)	1	4.0	5	
		Week 4	CR845	177	161 (91.0)	2.8 (1.2)	1	3.0	5	
			Placebo	167	159 (95.2)	3.2 (1.2)	1	3.0	5	
		Week 8	CR845	177	155 (87.6)	2.5 (1.2)	1	2.0	5	
			Placebo	167	154 (92.2)	3.0 (1.2)	1	3.0	5	
		Week 10	CR845	177	154 (87.0)	2.3 (1.1)	1	2.0	5	
			Placebo	167	151 (90.4)	2.9 (1.3)	1	3.0	5	
		Week 12	CR845	177	156 (88.1)	2.3 (1.2)	1	2.0	5	
			Placebo	167	153 (91.6)	2.7 (1.3)	1	3.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	177	159 (89.8)	-0.7 (1.3)	-4	-1.0	3	-0.08 [-0.30, 0.14]
			Placebo	167	159 (95.2)	-0.6 (1.3)	-4	-1.0	3	
		Week 8	CR845	177	153 (86.4)	-1.0 (1.2)	-4	-1.0	3	-0.15 [-0.37, 0.08]
			Placebo	167	154 (92.2)	-0.8 (1.3)	-4	-1.0	4	
		Week 10	CR845	177	152 (85.9)	-1.2 (1.3)	-4	-1.0	3	-0.25 [-0.47, -0.02]
			Placebo	167	151 (90.4)	-0.9 (1.4)	-4	-1.0	3	
		Week 12	CR845	177	155 (87.6)	-1.2 (1.4)	-4	-1.0	3	-0.08 [-0.31, 0.14]
			Placebo	167	153 (91.6)	-1.1 (1.3)	-4	-1.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DNC_ISHC: Change from baseline in 5-D disability score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Black/African American	5-D disability score	Baseline	CR845	135	132 (97.8)	3.4 (1.1)	1	3.5	5	
			Placebo	114	114 (100.0)	3.8 (1.0)	1	4.0	5	
		Week 4	CR845	135	116 (85.9)	2.9 (1.2)	1	3.0	5	
			Placebo	114	101 (88.6)	3.1 (1.2)	1	3.0	5	
		Week 8	CR845	135	113 (83.7)	2.6 (1.2)	1	2.0	5	
			Placebo	114	105 (92.1)	2.9 (1.2)	1	3.0	5	
		Week 10	CR845	135	108 (80.0)	2.4 (1.2)	1	2.0	5	
			Placebo	114	102 (89.5)	2.7 (1.3)	1	3.0	5	
		Week 12	CR845	135	111 (82.2)	2.4 (1.2)	1	2.0	5	
			Placebo	114	103 (90.4)	2.6 (1.3)	1	3.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	135	114 (84.4)	-0.6 (1.1)	-4	-1.0	2	0.06 [-0.21, 0.33]
			Placebo	114	101 (88.6)	-0.7 (1.4)	-3	-1.0	3	
		Week 8	CR845	135	111 (82.2)	-0.9 (1.2)	-4	-1.0	4	0.04 [-0.22, 0.31]
			Placebo	114	105 (92.1)	-0.9 (1.5)	-4	-1.0	3	
		Week 10	CR845	135	106 (78.5)	-1.0 (1.3)	-4	-1.0	2	0.06 [-0.21, 0.34]
			Placebo	114	102 (89.5)	-1.1 (1.5)	-4	-1.0	3	
		Week 12	CR845	135	109 (80.7)	-1.1 (1.4)	-4	-1.0	2	0.05 [-0.22, 0.32]
			Placebo	114	103 (90.4)	-1.2 (1.4)	-4	-1.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DNC_ISHC: Change from baseline in 5-D disability score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
White	5-D disability score	Baseline	CR845	255	251 (98.4)	3.5 (1.1)	1	4.0	5	
			Placebo	262	262 (100.0)	3.5 (1.2)	1	4.0	5	
		Week 4	CR845	255	236 (92.5)	2.9 (1.1)	1	3.0	5	
			Placebo	262	243 (92.7)	3.0 (1.2)	1	3.0	5	
		Week 8	CR845	255	224 (87.8)	2.6 (1.2)	1	2.0	5	
			Placebo	262	242 (92.4)	2.8 (1.2)	1	3.0	5	
		Week 10	CR845	255	225 (88.2)	2.6 (1.2)	1	2.0	5	
			Placebo	262	238 (90.8)	2.8 (1.2)	1	3.0	5	
		Week 12	CR845	255	224 (87.8)	2.5 (1.2)	1	2.0	5	
			Placebo	262	239 (91.2)	2.6 (1.2)	1	3.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	255	234 (91.8)	-0.7 (1.2)	-4	-1.0	3	-0.12 [-0.30, 0.06]
			Placebo	262	243 (92.7)	-0.5 (1.3)	-4	0.0	3	
		Week 8	CR845	255	222 (87.1)	-0.9 (1.3)	-4	-1.0	3	-0.12 [-0.30, 0.06]
			Placebo	262	242 (92.4)	-0.7 (1.3)	-4	-1.0	3	
		Week 10	CR845	255	223 (87.5)	-1.0 (1.4)	-4	-1.0	3	-0.15 [-0.33, 0.04]
			Placebo	262	238 (90.8)	-0.8 (1.3)	-4	-1.0	3	
		Week 12	CR845	255	223 (87.5)	-1.1 (1.4)	-4	-1.0	3	-0.13 [-0.31, 0.05]
			Placebo	262	239 (91.2)	-0.9 (1.3)	-4	-1.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DNC_ISHC: Change from baseline in 5-D disability score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Other	5-D disability score	Baseline	CR845	35	35 (100.0)	3.9 (1.0)	1	4.0	5	
			Placebo	47	47 (100.0)	3.6 (1.2)	1	4.0	5	
		Week 4	CR845	35	31 (88.6)	3.1 (1.1)	1	3.0	5	
			Placebo	47	44 (93.6)	3.1 (1.2)	1	3.0	5	
		Week 8	CR845	35	31 (88.6)	2.9 (1.2)	1	3.0	5	
			Placebo	47	43 (91.5)	3.0 (1.1)	1	3.0	5	
		Week 10	CR845	35	29 (82.9)	2.3 (1.3)	1	2.0	5	
			Placebo	47	42 (89.4)	2.8 (1.2)	1	3.0	5	
		Week 12	CR845	35	29 (82.9)	2.8 (1.4)	1	3.0	5	
			Placebo	47	41 (87.2)	2.6 (1.2)	1	2.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	35	31 (88.6)	-0.8 (1.1)	-3	-1.0	2	-0.21 [-0.67, 0.25]
			Placebo	47	44 (93.6)	-0.6 (1.2)	-3	-1.0	2	
		Week 8	CR845	35	31 (88.6)	-1.0 (1.1)	-3	-1.0	1	-0.33 [-0.79, 0.14]
			Placebo	47	43 (91.5)	-0.6 (1.2)	-3	-1.0	4	
		Week 10	CR845	35	29 (82.9)	-1.6 (1.3)	-4	-1.0	0	-0.61 [-1.10, -0.13]
			Placebo	47	42 (89.4)	-0.8 (1.2)	-3	-1.0	2	
		Week 12	CR845	35	29 (82.9)	-1.1 (1.5)	-3	-1.0	4	-0.03 [-0.50, 0.45]
			Placebo	47	41 (87.2)	-1.1 (1.4)	-4	-1.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DNC_ISHD: Change from baseline in 5-D disability score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 4 to < 7	5-D disability score	Baseline	CR845	185	183 (98.9)	3.1 (1.1)	1	3.0	5	
			Placebo	193	193 (100.0)	3.2 (1.1)	1	3.0	5	
		Week 4	CR845	185	169 (91.4)	2.5 (1.0)	1	2.0	5	
			Placebo	193	179 (92.7)	2.8 (1.2)	1	3.0	5	
		Week 8	CR845	185	164 (88.6)	2.4 (1.1)	1	2.0	5	
			Placebo	193	177 (91.7)	2.6 (1.2)	1	2.0	5	
		Week 10	CR845	185	161 (87.0)	2.2 (1.0)	1	2.0	5	
			Placebo	193	173 (89.6)	2.6 (1.2)	1	2.0	5	
		Week 12	CR845	185	159 (85.9)	2.1 (1.1)	1	2.0	5	
			Placebo	193	175 (90.7)	2.4 (1.2)	1	2.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	185	168 (90.8)	-0.6 (1.2)	-4	-1.0	2	-0.14 [-0.35, 0.07]
			Placebo	193	179 (92.7)	-0.4 (1.4)	-4	0.0	3	
		Week 8	CR845	185	163 (88.1)	-0.7 (1.3)	-4	-1.0	4	-0.14 [-0.35, 0.07]
			Placebo	193	177 (91.7)	-0.6 (1.3)	-3	0.0	4	
		Week 10	CR845	185	160 (86.5)	-0.9 (1.3)	-4	-1.0	3	-0.20 [-0.42, 0.01]
			Placebo	193	173 (89.6)	-0.6 (1.3)	-4	-1.0	3	
		Week 12	CR845	185	158 (85.4)	-1.0 (1.3)	-4	-1.0	4	-0.12 [-0.33, 0.10]
			Placebo	193	175 (90.7)	-0.8 (1.3)	-4	-1.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DNC_ISHD: Change from baseline in 5-D disability score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 7	5-D disability score	Baseline	CR845	241	236 (97.9)	3.9 (1.0)	1	4.0	5	
			Placebo	232	232 (100.0)	4.0 (1.0)	1	4.0	5	
		Week 4	CR845	241	215 (89.2)	3.2 (1.1)	1	3.0	5	
			Placebo	232	211 (90.9)	3.3 (1.1)	1	3.0	5	
		Week 8	CR845	241	205 (85.1)	2.9 (1.2)	1	3.0	5	
			Placebo	232	215 (92.7)	3.1 (1.2)	1	3.0	5	
		Week 10	CR845	241	202 (83.8)	2.7 (1.2)	1	3.0	5	
			Placebo	232	211 (90.9)	2.9 (1.2)	1	3.0	5	
		Week 12	CR845	241	206 (85.5)	2.7 (1.3)	1	3.0	5	
			Placebo	232	210 (90.5)	2.8 (1.2)	1	3.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	241	212 (88.0)	-0.7 (1.1)	-4	-1.0	3	-0.03 [-0.22, 0.16]
			Placebo	232	211 (90.9)	-0.7 (1.3)	-4	-1.0	4	
		Week 8	CR845	241	202 (83.8)	-1.0 (1.2)	-4	-1.0	3	-0.06 [-0.25, 0.13]
			Placebo	232	215 (92.7)	-0.9 (1.3)	-4	-1.0	3	
		Week 10	CR845	241	199 (82.6)	-1.2 (1.4)	-4	-1.0	3	-0.06 [-0.26, 0.13]
			Placebo	232	211 (90.9)	-1.1 (1.4)	-4	-1.0	3	
		Week 12	CR845	241	204 (84.6)	-1.2 (1.5)	-4	-1.0	3	-0.02 [-0.21, 0.18]
			Placebo	232	210 (90.5)	-1.1 (1.3)	-4	-1.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DNC_ISHE: Change from baseline in 5-D disability score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	5-D disability score	Baseline	CR845	359	352 (98.1)	3.5 (1.1)	1	4.0	5	
			Placebo	360	360 (100.0)	3.6 (1.1)	1	4.0	5	
		Week 4	CR845	359	322 (89.7)	2.8 (1.1)	1	3.0	5	
			Placebo	360	330 (91.7)	3.0 (1.2)	1	3.0	5	
		Week 8	CR845	359	310 (86.4)	2.6 (1.2)	1	2.0	5	
			Placebo	360	328 (91.1)	2.8 (1.2)	1	3.0	5	
		Week 10	CR845	359	306 (85.2)	2.5 (1.2)	1	2.0	5	
			Placebo	360	322 (89.4)	2.7 (1.2)	1	3.0	5	
		Week 12	CR845	359	306 (85.2)	2.5 (1.2)	1	2.0	5	
			Placebo	360	322 (89.4)	2.6 (1.2)	1	2.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	359	318 (88.6)	-0.7 (1.2)	-4	-1.0	3	-0.11 [-0.26, 0.05]
			Placebo	360	330 (91.7)	-0.5 (1.3)	-4	0.0	3	
		Week 8	CR845	359	306 (85.2)	-0.9 (1.2)	-4	-1.0	4	-0.08 [-0.24, 0.07]
			Placebo	360	328 (91.1)	-0.8 (1.4)	-4	-1.0	4	
		Week 10	CR845	359	302 (84.1)	-1.0 (1.3)	-4	-1.0	3	-0.14 [-0.30, 0.02]
			Placebo	360	322 (89.4)	-0.9 (1.4)	-4	-1.0	3	
		Week 12	CR845	359	303 (84.4)	-1.0 (1.4)	-4	-1.0	4	-0.06 [-0.22, 0.09]
			Placebo	360	322 (89.4)	-1.0 (1.4)	-4	-1.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DNC_ISHE: Change from baseline in 5-D disability score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	5-D disability score	Baseline	CR845	67	67 (100.0)	3.7 (1.1)	1	4.0	5	
			Placebo	65	65 (100.0)	3.9 (1.1)	1	4.0	5	
		Week 4	CR845	67	62 (92.5)	3.1 (1.2)	1	3.0	5	
			Placebo	65	60 (92.3)	3.2 (1.2)	1	3.0	5	
		Week 8	CR845	67	59 (88.1)	2.8 (1.3)	1	3.0	5	
			Placebo	65	64 (98.5)	3.1 (1.1)	1	3.0	5	
		Week 10	CR845	67	57 (85.1)	2.7 (1.3)	1	3.0	5	
			Placebo	65	62 (95.4)	2.9 (1.2)	1	3.0	5	
		Week 12	CR845	67	59 (88.1)	2.5 (1.2)	1	2.0	5	
			Placebo	65	63 (96.9)	2.7 (1.1)	1	3.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	67	62 (92.5)	-0.6 (1.1)	-3	-1.0	2	0.04 [-0.31, 0.40]
			Placebo	65	60 (92.3)	-0.6 (1.3)	-3	-0.5	4	
		Week 8	CR845	67	59 (88.1)	-0.9 (1.3)	-4	-1.0	3	-0.17 [-0.52, 0.19]
			Placebo	65	64 (98.5)	-0.7 (1.3)	-3	-1.0	3	
		Week 10	CR845	67	57 (85.1)	-1.0 (1.5)	-4	-1.0	2	-0.04 [-0.40, 0.32]
			Placebo	65	62 (95.4)	-1.0 (1.2)	-3	-1.0	1	
		Week 12	CR845	67	59 (88.1)	-1.2 (1.4)	-4	-1.0	2	-0.05 [-0.40, 0.31]
			Placebo	65	63 (96.9)	-1.2 (1.1)	-3	-1.0	1	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DNC_ISHF: Change from baseline in 5-D disability score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	5-D disability score	Baseline	CR845	267	262 (98.1)	3.4 (1.1)	1	4.0	5	
			Placebo	262	262 (100.0)	3.6 (1.1)	1	4.0	5	
		Week 4	CR845	267	248 (92.9)	2.8 (1.1)	1	3.0	5	
			Placebo	262	240 (91.6)	3.1 (1.2)	1	3.0	5	
		Week 8	CR845	267	239 (89.5)	2.6 (1.2)	1	2.0	5	
			Placebo	262	242 (92.4)	2.8 (1.2)	1	3.0	5	
		Week 10	CR845	267	232 (86.9)	2.4 (1.1)	1	2.0	5	
			Placebo	262	238 (90.8)	2.7 (1.2)	1	3.0	5	
		Week 12	CR845	267	234 (87.6)	2.4 (1.2)	1	2.0	5	
			Placebo	262	241 (92.0)	2.5 (1.2)	1	2.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	267	245 (91.8)	-0.6 (1.1)	-4	-1.0	3	-0.08 [-0.26, 0.09]
			Placebo	262	240 (91.6)	-0.5 (1.3)	-4	0.0	3	
		Week 8	CR845	267	236 (88.4)	-0.8 (1.2)	-4	-1.0	4	-0.04 [-0.22, 0.13]
			Placebo	262	242 (92.4)	-0.8 (1.3)	-4	-1.0	3	
		Week 10	CR845	267	229 (85.8)	-1.0 (1.3)	-4	-1.0	3	-0.08 [-0.26, 0.10]
			Placebo	262	238 (90.8)	-0.9 (1.4)	-4	-1.0	3	
		Week 12	CR845	267	232 (86.9)	-1.0 (1.4)	-4	-1.0	3	0.03 [-0.15, 0.21]
			Placebo	262	241 (92.0)	-1.0 (1.3)	-4	-1.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DNC_ISHF: Change from baseline in 5-D disability score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	5-D disability score	Baseline	CR845	159	157 (98.7)	3.7 (1.1)	1	4.0	5	
			Placebo	163	163 (100.0)	3.7 (1.2)	1	4.0	5	
		Week 4	CR845	159	136 (85.5)	3.0 (1.2)	1	3.0	5	
			Placebo	163	150 (92.0)	3.1 (1.3)	1	3.0	5	
		Week 8	CR845	159	130 (81.8)	2.8 (1.3)	1	3.0	5	
			Placebo	163	150 (92.0)	3.0 (1.3)	1	3.0	5	
		Week 10	CR845	159	131 (82.4)	2.6 (1.3)	1	2.0	5	
			Placebo	163	146 (89.6)	2.8 (1.3)	1	3.0	5	
		Week 12	CR845	159	131 (82.4)	2.5 (1.2)	1	2.0	5	
			Placebo	163	144 (88.3)	2.8 (1.3)	1	3.0	5	
	Change from baseline in 5-D disability score	Week 4	CR845	159	135 (84.9)	-0.7 (1.2)	-4	-1.0	2	-0.09 [-0.32, 0.15]
			Placebo	163	150 (92.0)	-0.6 (1.5)	-4	-1.0	4	
		Week 8	CR845	159	129 (81.1)	-0.9 (1.3)	-4	-1.0	3	-0.18 [-0.42, 0.05]
			Placebo	163	150 (92.0)	-0.7 (1.3)	-4	-1.0	4	
		Week 10	CR845	159	130 (81.8)	-1.1 (1.4)	-4	-1.0	3	-0.20 [-0.44, 0.03]
			Placebo	163	146 (89.6)	-0.8 (1.3)	-4	-1.0	3	
		Week 12	CR845	159	130 (81.8)	-1.2 (1.4)	-4	-1.0	4	-0.22 [-0.46, 0.02]
			Placebo	163	144 (88.3)	-0.9 (1.3)	-4	-1.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DVC_ISHA: Change from baseline in 5-D distribution score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
< 65 years	5-D distribution score	Baseline	CR845	282	276 (97.9)	3.2 (1.2)	1	3.0	5	
			Placebo	290	290 (100.0)	3.1 (1.1)	1	3.0	5	
		Week 4	CR845	282	254 (90.1)	2.7 (1.2)	1	3.0	5	
			Placebo	290	261 (90.0)	2.9 (1.2)	1	3.0	5	
		Week 8	CR845	282	243 (86.2)	2.6 (1.2)	1	2.0	5	
			Placebo	290	264 (91.0)	2.8 (1.2)	1	3.0	5	
		Week 10	CR845	282	243 (86.2)	2.6 (1.2)	1	2.0	5	
			Placebo	290	259 (89.3)	2.8 (1.2)	1	3.0	5	
		Week 12	CR845	282	244 (86.5)	2.5 (1.2)	1	2.0	5	
			Placebo	290	260 (89.7)	2.8 (1.2)	1	3.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	282	250 (88.7)	-0.5 (1.0)	-4	0.0	3	-0.25 [-0.42, -0.07]
			Placebo	290	261 (90.0)	-0.2 (1.0)	-4	0.0	2	
		Week 8	CR845	282	239 (84.8)	-0.6 (1.2)	-4	0.0	4	-0.21 [-0.38, -0.03]
			Placebo	290	264 (91.0)	-0.3 (1.2)	-4	0.0	3	
		Week 10	CR845	282	239 (84.8)	-0.6 (1.2)	-4	0.0	3	-0.24 [-0.42, -0.07]
			Placebo	290	259 (89.3)	-0.3 (1.1)	-4	0.0	3	
		Week 12	CR845	282	241 (85.5)	-0.7 (1.2)	-4	0.0	2	-0.31 [-0.49, -0.14]
			Placebo	290	260 (89.7)	-0.3 (1.1)	-4	0.0	3	

ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DVC_ISHA: Change from baseline in 5-D distribution score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 65 years	5-D distribution score	Baseline	CR845	144	144 (100.0)	3.2 (1.2)	1	3.0	5	
			Placebo	135	135 (100.0)	3.1 (1.1)	1	3.0	5	
		Week 4	CR845	144	130 (90.3)	2.7 (1.2)	1	3.0	5	
			Placebo	135	129 (95.6)	2.9 (1.2)	1	3.0	5	
		Week 8	CR845	144	126 (87.5)	2.7 (1.2)	1	3.0	5	
			Placebo	135	128 (94.8)	2.8 (1.1)	1	3.0	5	
		Week 10	CR845	144	120 (83.3)	2.7 (1.2)	1	3.0	5	
			Placebo	135	125 (92.6)	2.7 (1.2)	1	3.0	5	
		Week 12	CR845	144	121 (84.0)	2.7 (1.2)	1	3.0	5	
			Placebo	135	125 (92.6)	2.8 (1.2)	1	3.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	144	130 (90.3)	-0.4 (1.1)	-4	0.0	2	-0.22 [-0.47, 0.02]
			Placebo	135	129 (95.6)	-0.2 (1.1)	-4	0.0	3	
		Week 8	CR845	144	126 (87.5)	-0.5 (1.1)	-4	0.0	3	-0.20 [-0.45, 0.04]
			Placebo	135	128 (94.8)	-0.3 (1.1)	-3	0.0	4	
		Week 10	CR845	144	120 (83.3)	-0.5 (1.3)	-4	0.0	3	-0.09 [-0.34, 0.16]
			Placebo	135	125 (92.6)	-0.4 (1.1)	-4	0.0	2	
		Week 12	CR845	144	121 (84.0)	-0.5 (1.3)	-4	0.0	4	-0.18 [-0.43, 0.07]
			Placebo	135	125 (92.6)	-0.3 (1.1)	-3	0.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DVC_ISHB: Change from baseline in 5-D distribution score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Male	5-D distribution score	Baseline	CR845	249	245 (98.4)	3.1 (1.2)	1	3.0	5	
			Placebo	258	258 (100.0)	3.0 (1.1)	1	3.0	5	
		Week 4	CR845	249	223 (89.6)	2.8 (1.2)	1	3.0	5	
			Placebo	258	231 (89.5)	2.8 (1.2)	1	3.0	5	
		Week 8	CR845	249	214 (85.9)	2.6 (1.2)	1	2.0	5	
			Placebo	258	238 (92.2)	2.8 (1.2)	1	3.0	5	
		Week 10	CR845	249	209 (83.9)	2.6 (1.2)	1	3.0	5	
			Placebo	258	233 (90.3)	2.7 (1.2)	1	3.0	5	
		Week 12	CR845	249	209 (83.9)	2.6 (1.2)	1	2.0	5	
			Placebo	258	232 (89.9)	2.8 (1.2)	1	3.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	249	221 (88.8)	-0.4 (1.0)	-3	0.0	3	-0.15 [-0.33, 0.04]
			Placebo	258	231 (89.5)	-0.2 (1.1)	-4	0.0	2	
		Week 8	CR845	249	212 (85.1)	-0.5 (1.0)	-4	0.0	2	-0.23 [-0.42, -0.04]
			Placebo	258	238 (92.2)	-0.3 (1.2)	-3	0.0	4	
		Week 10	CR845	249	207 (83.1)	-0.5 (1.1)	-4	0.0	3	-0.19 [-0.38, -0.00]
			Placebo	258	233 (90.3)	-0.3 (1.1)	-4	0.0	3	
		Week 12	CR845	249	207 (83.1)	-0.6 (1.2)	-4	0.0	2	-0.28 [-0.47, -0.09]
			Placebo	258	232 (89.9)	-0.2 (1.1)	-3	0.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DVC_ISHB: Change from baseline in 5-D distribution score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Female	5-D distribution score	Baseline	CR845	177	175 (98.9)	3.3 (1.2)	1	3.0	5	
			Placebo	167	167 (100.0)	3.3 (1.0)	1	3.0	5	
		Week 4	CR845	177	161 (91.0)	2.6 (1.1)	1	3.0	5	
			Placebo	167	159 (95.2)	3.1 (1.2)	1	3.0	5	
		Week 8	CR845	177	155 (87.6)	2.6 (1.2)	1	3.0	5	
			Placebo	167	154 (92.2)	2.9 (1.2)	1	3.0	5	
		Week 10	CR845	177	154 (87.0)	2.5 (1.2)	1	2.0	5	
			Placebo	167	151 (90.4)	2.8 (1.2)	1	3.0	5	
		Week 12	CR845	177	156 (88.1)	2.5 (1.2)	1	2.0	5	
			Placebo	167	153 (91.6)	2.9 (1.2)	1	3.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	177	159 (89.8)	-0.6 (1.1)	-4	0.0	3	-0.36 [-0.59, -0.14]
			Placebo	167	159 (95.2)	-0.2 (1.0)	-3	0.0	3	
		Week 8	CR845	177	153 (86.4)	-0.6 (1.3)	-4	-1.0	4	-0.17 [-0.39, 0.05]
			Placebo	167	154 (92.2)	-0.4 (1.1)	-4	0.0	3	
		Week 10	CR845	177	152 (85.9)	-0.7 (1.4)	-4	0.0	3	-0.19 [-0.41, 0.04]
			Placebo	167	151 (90.4)	-0.4 (1.0)	-4	0.0	2	
		Week 12	CR845	177	155 (87.6)	-0.7 (1.3)	-4	0.0	4	-0.24 [-0.46, -0.02]
			Placebo	167	153 (91.6)	-0.4 (1.1)	-4	0.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DVC_ISHC: Change from baseline in 5-D distribution score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Black/African American	5-D distribution score	Baseline	CR845	135	133 (98.5)	3.2 (1.1)	1	3.0	5	
			Placebo	114	114 (100.0)	3.3 (1.1)	1	3.0	5	
		Week 4	CR845	135	116 (85.9)	2.8 (1.1)	1	3.0	5	
			Placebo	114	101 (88.6)	3.2 (1.3)	1	3.0	5	
		Week 8	CR845	135	113 (83.7)	2.7 (1.2)	1	3.0	5	
			Placebo	114	105 (92.1)	3.0 (1.3)	1	3.0	5	
		Week 10	CR845	135	108 (80.0)	2.7 (1.2)	1	3.0	5	
			Placebo	114	102 (89.5)	3.0 (1.3)	1	3.0	5	
		Week 12	CR845	135	111 (82.2)	2.6 (1.2)	1	2.0	5	
			Placebo	114	103 (90.4)	3.1 (1.3)	1	3.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	135	114 (84.4)	-0.4 (1.0)	-4	0.0	3	-0.24 [-0.51, 0.03]
			Placebo	114	101 (88.6)	-0.1 (1.0)	-3	0.0	2	
		Week 8	CR845	135	111 (82.2)	-0.4 (1.1)	-4	0.0	4	-0.13 [-0.39, 0.14]
			Placebo	114	105 (92.1)	-0.3 (1.2)	-4	0.0	2	
		Week 10	CR845	135	106 (78.5)	-0.4 (1.2)	-4	0.0	2	-0.08 [-0.36, 0.19]
			Placebo	114	102 (89.5)	-0.3 (1.2)	-4	0.0	3	
		Week 12	CR845	135	109 (80.7)	-0.5 (1.1)	-4	0.0	2	-0.30 [-0.57, -0.03]
			Placebo	114	103 (90.4)	-0.2 (1.2)	-4	0.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DVC_ISHC: Change from baseline in 5-D distribution score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
White	5-D distribution score	Baseline	CR845	255	251 (98.4)	3.2 (1.2)	1	3.0	5	
			Placebo	262	262 (100.0)	3.1 (1.1)	1	3.0	5	
		Week 4	CR845	255	236 (92.5)	2.7 (1.2)	1	3.0	5	
			Placebo	262	243 (92.7)	2.8 (1.2)	1	3.0	5	
		Week 8	CR845	255	224 (87.8)	2.6 (1.2)	1	2.0	5	
			Placebo	262	242 (92.4)	2.8 (1.2)	1	3.0	5	
		Week 10	CR845	255	225 (88.2)	2.6 (1.3)	1	2.0	5	
			Placebo	262	238 (90.8)	2.7 (1.1)	1	3.0	5	
		Week 12	CR845	255	224 (87.8)	2.5 (1.2)	1	2.0	5	
			Placebo	262	239 (91.2)	2.8 (1.2)	1	3.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	255	234 (91.8)	-0.5 (1.0)	-4	0.0	3	-0.23 [-0.41, -0.05]
			Placebo	262	243 (92.7)	-0.2 (1.0)	-4	0.0	3	
		Week 8	CR845	255	222 (87.1)	-0.6 (1.2)	-4	-0.5	3	-0.25 [-0.43, -0.07]
			Placebo	262	242 (92.4)	-0.3 (1.1)	-4	0.0	4	
		Week 10	CR845	255	223 (87.5)	-0.6 (1.3)	-4	0.0	3	-0.22 [-0.40, -0.04]
			Placebo	262	238 (90.8)	-0.3 (1.1)	-3	0.0	3	
		Week 12	CR845	255	223 (87.5)	-0.7 (1.3)	-4	-1.0	4	-0.32 [-0.50, -0.14]
			Placebo	262	239 (91.2)	-0.3 (1.1)	-3	0.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DVC_ISHC: Change from baseline in 5-D distribution score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Other	5-D distribution score	Baseline	CR845	35	35 (100.0)	3.0 (1.2)	1	3.0	5	
			Placebo	47	47 (100.0)	3.0 (1.1)	1	3.0	5	
		Week 4	CR845	35	31 (88.6)	2.5 (1.2)	1	2.0	5	
			Placebo	47	44 (93.6)	2.8 (1.3)	1	3.0	5	
		Week 8	CR845	35	31 (88.6)	2.5 (1.1)	1	2.0	5	
			Placebo	47	43 (91.5)	2.6 (1.1)	1	3.0	5	
		Week 10	CR845	35	29 (82.9)	2.4 (1.1)	1	2.0	5	
			Placebo	47	42 (89.4)	2.6 (1.1)	1	2.5	5	
		Week 12	CR845	35	29 (82.9)	2.7 (1.3)	1	2.0	5	
			Placebo	47	41 (87.2)	2.5 (1.0)	1	2.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	35	31 (88.6)	-0.5 (1.0)	-3	0.0	1	-0.23 [-0.69, 0.23]
			Placebo	47	44 (93.6)	-0.3 (1.3)	-4	0.0	2	
		Week 8	CR845	35	31 (88.6)	-0.6 (1.0)	-3	0.0	1	-0.10 [-0.57, 0.36]
			Placebo	47	43 (91.5)	-0.5 (1.2)	-3	0.0	2	
		Week 10	CR845	35	29 (82.9)	-0.7 (1.3)	-4	0.0	1	-0.30 [-0.77, 0.18]
			Placebo	47	42 (89.4)	-0.4 (1.0)	-4	0.0	1	
		Week 12	CR845	35	29 (82.9)	-0.4 (1.2)	-4	0.0	2	0.14 [-0.33, 0.62]
			Placebo	47	41 (87.2)	-0.6 (1.2)	-3	0.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DVC_ISHD: Change from baseline in 5-D distribution score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 4 to < 7	5-D distribution score	Baseline	CR845	185	183 (98.9)	2.8 (1.1)	1	3.0	5	
			Placebo	193	193 (100.0)	2.8 (1.0)	1	3.0	5	
		Week 4	CR845	185	169 (91.4)	2.4 (1.0)	1	2.0	5	
			Placebo	193	179 (92.7)	2.7 (1.2)	1	3.0	5	
		Week 8	CR845	185	164 (88.6)	2.4 (1.1)	1	2.0	5	
			Placebo	193	177 (91.7)	2.6 (1.1)	1	3.0	5	
		Week 10	CR845	185	161 (87.0)	2.3 (1.1)	1	2.0	5	
			Placebo	193	173 (89.6)	2.6 (1.2)	1	2.0	5	
		Week 12	CR845	185	159 (85.9)	2.3 (1.1)	1	2.0	5	
			Placebo	193	175 (90.7)	2.6 (1.1)	1	2.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	185	168 (90.8)	-0.4 (1.0)	-3	0.0	2	-0.34 [-0.55, -0.12]
			Placebo	193	179 (92.7)	-0.1 (1.0)	-3	0.0	3	
		Week 8	CR845	185	163 (88.1)	-0.4 (1.0)	-4	0.0	2	-0.22 [-0.43, -0.00]
			Placebo	193	177 (91.7)	-0.2 (1.1)	-3	0.0	3	
		Week 10	CR845	185	160 (86.5)	-0.5 (1.1)	-4	0.0	2	-0.28 [-0.49, -0.06]
			Placebo	193	173 (89.6)	-0.2 (1.0)	-3	0.0	3	
		Week 12	CR845	185	158 (85.4)	-0.5 (1.2)	-4	0.0	4	-0.27 [-0.48, -0.05]
			Placebo	193	175 (90.7)	-0.3 (1.0)	-3	0.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DVC_ISHD: Change from baseline in 5-D distribution score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 7	5-D distribution score	Baseline	CR845	241	237 (98.3)	3.5 (1.1)	1	3.0	5	
			Placebo	232	232 (100.0)	3.4 (1.1)	1	3.0	5	
		Week 4	CR845	241	215 (89.2)	3.0 (1.2)	1	3.0	5	
			Placebo	232	211 (90.9)	3.1 (1.2)	1	3.0	5	
		Week 8	CR845	241	205 (85.1)	2.8 (1.3)	1	3.0	5	
			Placebo	232	215 (92.7)	3.0 (1.2)	1	3.0	5	
		Week 10	CR845	241	202 (83.8)	2.8 (1.3)	1	3.0	5	
			Placebo	232	211 (90.9)	2.9 (1.2)	1	3.0	5	
		Week 12	CR845	241	206 (85.5)	2.7 (1.3)	1	3.0	5	
			Placebo	232	210 (90.5)	3.0 (1.2)	1	3.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	241	212 (88.0)	-0.5 (1.1)	-4	0.0	3	-0.16 [-0.35, 0.03]
			Placebo	232	211 (90.9)	-0.3 (1.1)	-4	0.0	2	
		Week 8	CR845	241	202 (83.8)	-0.6 (1.3)	-4	-0.5	4	-0.20 [-0.39, -0.00]
			Placebo	232	215 (92.7)	-0.4 (1.2)	-4	0.0	4	
		Week 10	CR845	241	199 (82.6)	-0.6 (1.4)	-4	0.0	3	-0.13 [-0.33, 0.06]
			Placebo	232	211 (90.9)	-0.5 (1.1)	-4	0.0	3	
		Week 12	CR845	241	204 (84.6)	-0.7 (1.3)	-4	0.0	2	-0.27 [-0.46, -0.08]
			Placebo	232	210 (90.5)	-0.3 (1.2)	-4	0.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DVC_ISHE: Change from baseline in 5-D distribution score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	5-D distribution score	Baseline	CR845	359	353 (98.3)	3.2 (1.2)	1	3.0	5	
			Placebo	360	360 (100.0)	3.1 (1.1)	1	3.0	5	
		Week 4	CR845	359	322 (89.7)	2.7 (1.2)	1	3.0	5	
			Placebo	360	330 (91.7)	2.9 (1.2)	1	3.0	5	
		Week 8	CR845	359	310 (86.4)	2.6 (1.2)	1	2.0	5	
			Placebo	360	328 (91.1)	2.8 (1.2)	1	3.0	5	
		Week 10	CR845	359	306 (85.2)	2.6 (1.2)	1	2.0	5	
			Placebo	360	322 (89.4)	2.7 (1.2)	1	3.0	5	
		Week 12	CR845	359	306 (85.2)	2.6 (1.2)	1	2.0	5	
			Placebo	360	322 (89.4)	2.8 (1.2)	1	3.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	359	318 (88.6)	-0.5 (1.0)	-4	0.0	3	-0.26 [-0.42, -0.11]
			Placebo	360	330 (91.7)	-0.2 (1.1)	-4	0.0	3	
		Week 8	CR845	359	306 (85.2)	-0.6 (1.1)	-4	0.0	3	-0.25 [-0.41, -0.10]
			Placebo	360	328 (91.1)	-0.3 (1.2)	-4	0.0	4	
		Week 10	CR845	359	302 (84.1)	-0.6 (1.2)	-4	0.0	3	-0.21 [-0.37, -0.05]
			Placebo	360	322 (89.4)	-0.3 (1.1)	-4	0.0	3	
		Week 12	CR845	359	303 (84.4)	-0.6 (1.2)	-4	0.0	4	-0.27 [-0.43, -0.11]
			Placebo	360	322 (89.4)	-0.3 (1.1)	-4	0.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DVC_ISHE: Change from baseline in 5-D distribution score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	5-D distribution score	Baseline	CR845	67	67 (100.0)	3.1 (1.2)	1	3.0	5	
			Placebo	65	65 (100.0)	3.4 (1.1)	1	3.0	5	
		Week 4	CR845	67	62 (92.5)	2.8 (1.2)	1	3.0	5	
			Placebo	65	60 (92.3)	3.0 (1.2)	1	3.0	5	
		Week 8	CR845	67	59 (88.1)	2.8 (1.2)	1	3.0	5	
			Placebo	65	64 (98.5)	2.9 (1.2)	1	3.0	5	
		Week 10	CR845	67	57 (85.1)	2.6 (1.2)	1	3.0	5	
			Placebo	65	62 (95.4)	3.0 (1.1)	1	3.0	5	
		Week 12	CR845	67	59 (88.1)	2.5 (1.1)	1	2.0	5	
			Placebo	65	63 (96.9)	3.0 (1.1)	1	3.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	67	62 (92.5)	-0.4 (1.2)	-4	0.0	3	-0.10 [-0.45, 0.26]
			Placebo	65	60 (92.3)	-0.3 (0.9)	-3	0.0	2	
		Week 8	CR845	67	59 (88.1)	-0.4 (1.4)	-4	0.0	4	0.04 [-0.31, 0.39]
			Placebo	65	64 (98.5)	-0.5 (1.0)	-3	0.0	2	
		Week 10	CR845	67	57 (85.1)	-0.5 (1.5)	-4	0.0	2	-0.10 [-0.46, 0.26]
			Placebo	65	62 (95.4)	-0.4 (1.0)	-4	0.0	2	
		Week 12	CR845	67	59 (88.1)	-0.6 (1.2)	-4	0.0	2	-0.27 [-0.62, 0.09]
			Placebo	65	63 (96.9)	-0.3 (1.0)	-3	0.0	2	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DVC_ISHF: Change from baseline in 5-D distribution score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	5-D distribution score	Baseline	CR845	267	262 (98.1)	3.1 (1.1)	1	3.0	5	
			Placebo	262	262 (100.0)	3.0 (1.1)	1	3.0	5	
		Week 4	CR845	267	248 (92.9)	2.6 (1.2)	1	3.0	5	
			Placebo	262	240 (91.6)	2.9 (1.2)	1	3.0	5	
		Week 8	CR845	267	239 (89.5)	2.6 (1.2)	1	2.0	5	
			Placebo	262	242 (92.4)	2.8 (1.2)	1	3.0	5	
		Week 10	CR845	267	232 (86.9)	2.6 (1.2)	1	2.0	5	
			Placebo	262	238 (90.8)	2.7 (1.1)	1	3.0	5	
		Week 12	CR845	267	234 (87.6)	2.5 (1.2)	1	2.0	5	
			Placebo	262	241 (92.0)	2.8 (1.2)	1	3.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	267	245 (91.8)	-0.4 (1.0)	-3	0.0	3	-0.26 [-0.44, -0.08]
			Placebo	262	240 (91.6)	-0.2 (1.1)	-4	0.0	3	
		Week 8	CR845	267	236 (88.4)	-0.5 (1.1)	-4	0.0	3	-0.23 [-0.41, -0.05]
			Placebo	262	242 (92.4)	-0.3 (1.2)	-4	0.0	4	
		Week 10	CR845	267	229 (85.8)	-0.5 (1.2)	-4	0.0	3	-0.15 [-0.33, 0.03]
			Placebo	262	238 (90.8)	-0.3 (1.1)	-4	0.0	3	
		Week 12	CR845	267	232 (86.9)	-0.6 (1.2)	-4	0.0	4	-0.25 [-0.43, -0.07]
			Placebo	262	241 (92.0)	-0.3 (1.1)	-4	0.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DVC_ISHF: Change from baseline in 5-D distribution score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	5-D distribution score	Baseline	CR845	159	158 (99.4)	3.3 (1.2)	1	3.0	5	
			Placebo	163	163 (100.0)	3.3 (1.1)	1	3.0	5	
		Week 4	CR845	159	136 (85.5)	2.8 (1.2)	1	3.0	5	
			Placebo	163	150 (92.0)	3.0 (1.3)	1	3.0	5	
		Week 8	CR845	159	130 (81.8)	2.7 (1.3)	1	3.0	5	
			Placebo	163	150 (92.0)	2.9 (1.2)	1	3.0	5	
		Week 10	CR845	159	131 (82.4)	2.7 (1.2)	1	3.0	5	
			Placebo	163	146 (89.6)	2.9 (1.2)	1	3.0	5	
		Week 12	CR845	159	131 (82.4)	2.6 (1.2)	1	3.0	5	
			Placebo	163	144 (88.3)	2.9 (1.2)	1	3.0	5	
	Change from baseline in 5-D distribution score	Week 4	CR845	159	135 (84.9)	-0.5 (1.1)	-4	0.0	3	-0.20 [-0.44, 0.03]
			Placebo	163	150 (92.0)	-0.3 (1.0)	-4	0.0	2	
		Week 8	CR845	159	129 (81.1)	-0.6 (1.3)	-4	0.0	4	-0.18 [-0.41, 0.06]
			Placebo	163	150 (92.0)	-0.4 (1.2)	-4	0.0	3	
		Week 10	CR845	159	130 (81.8)	-0.7 (1.4)	-4	0.0	2	-0.26 [-0.49, -0.02]
			Placebo	163	146 (89.6)	-0.3 (1.1)	-4	0.0	3	
		Week 12	CR845	159	130 (81.8)	-0.7 (1.3)	-4	0.0	2	-0.30 [-0.54, -0.06]
			Placebo	163	144 (88.3)	-0.4 (1.0)	-3	0.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: afived_i, created on: 17FEB2022

Table IT2DTC_ISCA: Change from baseline in 5-D total score - MMRM results by age
ITT

Change from baseline in 5-D total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
A: Age									0.325
< 65 years	Week 4	CR845	282	247 (87.6)	-3.7 (0.3)	(-4.2, -3.2)	-1.7 (0.3)	(-2.2, -1.1)	<0.001 *
		Placebo	290	261 (90.0)	-2.1 (0.2)	(-2.6, -1.6)			
>= 65 years	Week 4	CR845	144	129 (89.6)	-3.5 (0.3)	(-4.2, -2.8)	-1.0 (0.4)	(-1.9, -0.2)	0.014 *
		Placebo	135	129 (95.6)	-2.5 (0.3)	(-3.1, -1.8)			
< 65 years	Week 8	CR845	282	236 (83.7)	-4.6 (0.3)	(-5.1, -4.0)	-1.2 (0.3)	(-1.9, -0.6)	<0.001 *
		Placebo	290	264 (91.0)	-3.3 (0.3)	(-3.8, -2.8)			
>= 65 years	Week 8	CR845	144	126 (87.5)	-4.0 (0.4)	(-4.7, -3.3)	-1.0 (0.4)	(-1.9, -0.1)	0.024 *
		Placebo	135	128 (94.8)	-3.0 (0.3)	(-3.7, -2.3)			
< 65 years	Week 10	CR845	282	237 (84.0)	-4.8 (0.3)	(-5.3, -4.3)	-1.3 (0.3)	(-1.9, -0.6)	<0.001 *
		Placebo	290	259 (89.3)	-3.5 (0.3)	(-4.0, -3.0)			
>= 65 years	Week 10	CR845	144	120 (83.3)	-4.3 (0.4)	(-5.0, -3.6)	-1.2 (0.4)	(-2.1, -0.3)	0.009 *
		Placebo	135	125 (92.6)	-3.1 (0.3)	(-3.8, -2.5)			
< 65 years	Week 12	CR845	282	239 (84.8)	-5.0 (0.3)	(-5.6, -4.5)	-1.5 (0.3)	(-2.1, -0.8)	<0.001 *
		Placebo	290	260 (89.7)	-3.5 (0.3)	(-4.1, -3.0)			
>= 65 years	Week 12	CR845	144	120 (83.3)	-4.4 (0.4)	(-5.1, -3.7)	-0.7 (0.5)	(-1.6, 0.2)	0.128
		Placebo	135	125 (92.6)	-3.7 (0.4)	(-4.4, -3.0)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DTC_ISCB: Change from baseline in 5-D total score - MMRM results by sex
ITT

Change from baseline in 5-D total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
B: Sex									0.003 i
Male	Week 4	CR845	249	220 (88.4)	-3.0 (0.3)	(-3.5, -2.5)	-1.0 (0.3)	(-1.5, -0.4)	0.002 *
		Placebo	258	231 (89.5)	-2.0 (0.3)	(-2.5, -1.5)			
Female	Week 4	CR845	177	156 (88.1)	-4.6 (0.3)	(-5.2, -4.0)	-2.1 (0.4)	(-2.9, -1.4)	<0.001 *
		Placebo	167	159 (95.2)	-2.4 (0.3)	(-3.0, -1.8)			
Male	Week 8	CR845	249	211 (84.7)	-3.6 (0.3)	(-4.2, -3.1)	-0.7 (0.3)	(-1.3, -0.0)	0.041 *
		Placebo	258	238 (92.2)	-3.0 (0.3)	(-3.5, -2.5)			
Female	Week 8	CR845	177	151 (85.3)	-5.4 (0.3)	(-6.0, -4.7)	-1.8 (0.4)	(-2.7, -1.0)	<0.001 *
		Placebo	167	154 (92.2)	-3.5 (0.3)	(-4.2, -2.9)			
Male	Week 10	CR845	249	207 (83.1)	-3.8 (0.3)	(-4.3, -3.2)	-0.5 (0.3)	(-1.1, 0.1)	0.121
		Placebo	258	233 (90.3)	-3.3 (0.3)	(-3.8, -2.8)			
Female	Week 10	CR845	177	150 (84.7)	-5.8 (0.3)	(-6.4, -5.1)	-2.3 (0.4)	(-3.2, -1.4)	<0.001 *
		Placebo	167	151 (90.4)	-3.5 (0.3)	(-4.2, -2.8)			
Male	Week 12	CR845	249	207 (83.1)	-4.1 (0.3)	(-4.6, -3.5)	-0.8 (0.3)	(-1.4, -0.1)	0.025 *
		Placebo	258	232 (89.9)	-3.3 (0.3)	(-3.8, -2.8)			
Female	Week 12	CR845	177	152 (85.9)	-5.8 (0.4)	(-6.5, -5.1)	-1.8 (0.5)	(-2.7, -0.9)	<0.001 *
		Placebo	167	153 (91.6)	-3.9 (0.4)	(-4.6, -3.2)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DTC_ISCC: Change from baseline in 5-D total score - MMRM results by race
ITT

Change from baseline in 5-D total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
C: Race									0.764
Black/African American	Week 4	CR845	135	113 (83.7)	-3.7 (0.4)	(-4.4, -2.9)	-1.6 (0.5)	(-2.5, -0.6)	0.001 *
		Placebo	114	101 (88.6)	-2.1 (0.4)	(-2.8, -1.3)			
White	Week 4	CR845	255	231 (90.6)	-3.7 (0.3)	(-4.2, -3.2)	-1.4 (0.3)	(-2.0, -0.9)	<0.001 *
		Placebo	262	243 (92.7)	-2.3 (0.2)	(-2.8, -1.8)			
Other	Week 4	CR845	35	31 (88.6)	-4.2 (0.8)	(-5.7, -2.7)	-1.6 (0.8)	(-3.1, -0.0)	0.044 *
		Placebo	47	44 (93.6)	-2.6 (0.7)	(-4.0, -1.3)			
Black/African American	Week 8	CR845	135	110 (81.5)	-4.7 (0.4)	(-5.4, -3.9)	-1.2 (0.5)	(-2.2, -0.3)	0.014 *
		Placebo	114	105 (92.1)	-3.4 (0.4)	(-4.2, -2.6)			
White	Week 8	CR845	255	220 (86.3)	-4.3 (0.3)	(-4.9, -3.8)	-1.2 (0.3)	(-1.8, -0.5)	<0.001 *
		Placebo	262	242 (92.4)	-3.2 (0.3)	(-3.7, -2.7)			
Other	Week 8	CR845	35	31 (88.6)	-4.6 (0.8)	(-6.2, -3.1)	-1.0 (0.8)	(-2.6, 0.6)	0.208
		Placebo	47	43 (91.5)	-3.6 (0.7)	(-5.0, -2.2)			
Black/African American	Week 10	CR845	135	105 (77.8)	-5.2 (0.4)	(-6.0, -4.4)	-1.6 (0.5)	(-2.6, -0.6)	0.002 *
		Placebo	114	102 (89.5)	-3.6 (0.4)	(-4.4, -2.8)			
White	Week 10	CR845	255	222 (87.1)	-4.5 (0.3)	(-5.0, -3.9)	-1.2 (0.3)	(-1.8, -0.5)	<0.001 *
		Placebo	262	238 (90.8)	-3.3 (0.3)	(-3.8, -2.8)			
Other	Week 10	CR845	35	29 (82.9)	-5.0 (0.8)	(-6.7, -3.4)	-1.1 (0.9)	(-2.8, 0.7)	0.217
		Placebo	47	42 (89.4)	-3.9 (0.7)	(-5.4, -2.5)			
Black/African American	Week 12	CR845	135	107 (79.3)	-5.4 (0.4)	(-6.2, -4.6)	-1.8 (0.5)	(-2.9, -0.8)	<0.001 *
		Placebo	114	103 (90.4)	-3.6 (0.4)	(-4.4, -2.8)			
White	Week 12	CR845	255	222 (87.1)	-4.8 (0.3)	(-5.4, -4.3)	-1.3 (0.3)	(-2.0, -0.7)	<0.001 *
		Placebo	262	239 (91.2)	-3.5 (0.3)	(-4.0, -3.0)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DTC_ISCC: Change from baseline in 5-D total score - MMRM results by race
ITT

Change from baseline in 5-D total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Other	Week 12	CR845	35	29 (82.9)	-3.7 (0.9)	(-5.5, -1.9)	0.9 (1.0)	(-1.1, 2.9)	0.378
		Placebo	47	41 (87.2)	-4.6 (0.8)	(-6.2, -3.0)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DTC_ISCD: Change from baseline in 5-D total score - MMRM results by baseline WI-NRS
ITT

Change from baseline in 5-D total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
D: Baseline worst itching NRS score (WI-NRS)									0.491
>= 4 to < 7	Week 4	CR845	185	166 (89.7)	-3.4 (0.3)	(-3.9, -2.8)	-1.7 (0.3)	(-2.3, -1.0)	<0.001 *
		Placebo	193	179 (92.7)	-1.7 (0.3)	(-2.3, -1.2)			
>= 7	Week 4	CR845	241	210 (87.1)	-4.1 (0.3)	(-4.6, -3.5)	-1.3 (0.3)	(-2.0, -0.7)	<0.001 *
		Placebo	232	211 (90.9)	-2.7 (0.3)	(-3.3, -2.2)			
>= 4 to < 7	Week 8	CR845	185	162 (87.6)	-3.8 (0.3)	(-4.4, -3.3)	-1.4 (0.3)	(-2.0, -0.7)	<0.001 *
		Placebo	193	177 (91.7)	-2.5 (0.3)	(-3.0, -1.9)			
>= 7	Week 8	CR845	241	200 (83.0)	-5.0 (0.3)	(-5.6, -4.4)	-1.0 (0.4)	(-1.8, -0.2)	0.011 *
		Placebo	232	215 (92.7)	-4.0 (0.3)	(-4.6, -3.4)			
>= 4 to < 7	Week 10	CR845	185	159 (85.9)	-4.1 (0.3)	(-4.7, -3.6)	-1.6 (0.3)	(-2.2, -0.9)	<0.001 *
		Placebo	193	173 (89.6)	-2.6 (0.3)	(-3.1, -2.0)			
>= 7	Week 10	CR845	241	198 (82.2)	-5.2 (0.3)	(-5.8, -4.6)	-1.0 (0.4)	(-1.8, -0.3)	0.008 *
		Placebo	232	211 (90.9)	-4.2 (0.3)	(-4.8, -3.6)			
>= 4 to < 7	Week 12	CR845	185	157 (84.9)	-4.3 (0.3)	(-4.9, -3.7)	-1.2 (0.4)	(-1.9, -0.5)	<0.001 *
		Placebo	193	175 (90.7)	-3.1 (0.3)	(-3.7, -2.5)			
>= 7	Week 12	CR845	241	202 (83.8)	-5.4 (0.3)	(-6.0, -4.8)	-1.3 (0.4)	(-2.1, -0.5)	0.002 *
		Placebo	232	210 (90.5)	-4.1 (0.3)	(-4.7, -3.5)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DTC_ISCE: Change from baseline in 5-D total score - MMRM results by specific medical condition
ITT

Change from baseline in 5-D total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
E: Presence of specific medical conditions									0.825
No	Week 4	CR845	359	314 (87.5)	-3.7 (0.2)	(-4.1, -3.3)	-1.5 (0.3)	(-2.0, -1.0)	<0.001 *
		Placebo	360	330 (91.7)	-2.2 (0.2)	(-2.6, -1.8)			
Yes	Week 4	CR845	67	62 (92.5)	-3.8 (0.4)	(-4.7, -3.0)	-1.3 (0.6)	(-2.5, -0.1)	0.032 *
		Placebo	65	60 (92.3)	-2.5 (0.4)	(-3.4, -1.7)			
No	Week 8	CR845	359	303 (84.4)	-4.3 (0.2)	(-4.7, -3.9)	-1.1 (0.3)	(-1.6, -0.5)	<0.001 *
		Placebo	360	328 (91.1)	-3.2 (0.2)	(-3.6, -2.9)			
Yes	Week 8	CR845	67	59 (88.1)	-4.9 (0.5)	(-5.8, -4.0)	-1.5 (0.6)	(-2.7, -0.2)	0.021 *
		Placebo	65	64 (98.5)	-3.5 (0.4)	(-4.3, -2.6)			
No	Week 10	CR845	359	300 (83.6)	-4.6 (0.2)	(-5.0, -4.2)	-1.2 (0.3)	(-1.8, -0.7)	<0.001 *
		Placebo	360	322 (89.4)	-3.4 (0.2)	(-3.8, -3.0)			
Yes	Week 10	CR845	67	57 (85.1)	-4.9 (0.5)	(-5.9, -3.9)	-1.2 (0.7)	(-2.6, 0.2)	0.087
		Placebo	65	62 (95.4)	-3.7 (0.5)	(-4.7, -2.7)			
No	Week 12	CR845	359	301 (83.8)	-4.7 (0.2)	(-5.1, -4.3)	-1.1 (0.3)	(-1.7, -0.5)	<0.001 *
		Placebo	360	322 (89.4)	-3.6 (0.2)	(-4.0, -3.2)			
Yes	Week 12	CR845	67	58 (86.6)	-5.7 (0.5)	(-6.7, -4.8)	-1.8 (0.7)	(-3.1, -0.4)	0.010 *
		Placebo	65	63 (96.9)	-4.0 (0.5)	(-4.9, -3.0)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor previous use of anti-itch medication is also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DTC_ISCF: Change from baseline in 5-D total score - MMRM results by use of concomitant itch medication
ITT

Change from baseline in 5-D total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
F: Use of concomitant itch medication									0.840
No	Week 4	CR845	267	242 (90.6)	-3.4 (0.2)	(-3.9, -2.9)	-1.5 (0.3)	(-2.1, -0.9)	<0.001 *
		Placebo	262	240 (91.6)	-1.9 (0.2)	(-2.4, -1.4)			
Yes	Week 4	CR845	159	134 (84.3)	-4.1 (0.3)	(-4.7, -3.4)	-1.4 (0.4)	(-2.2, -0.5)	0.001 *
		Placebo	163	150 (92.0)	-2.7 (0.3)	(-3.3, -2.0)			
No	Week 8	CR845	267	234 (87.6)	-4.2 (0.3)	(-4.7, -3.7)	-1.2 (0.3)	(-1.8, -0.6)	<0.001 *
		Placebo	262	242 (92.4)	-3.0 (0.3)	(-3.5, -2.5)			
Yes	Week 8	CR845	159	128 (80.5)	-4.7 (0.4)	(-5.4, -4.0)	-1.1 (0.5)	(-2.0, -0.2)	0.018 *
		Placebo	163	150 (92.0)	-3.6 (0.3)	(-4.3, -2.9)			
No	Week 10	CR845	267	228 (85.4)	-4.3 (0.3)	(-4.8, -3.8)	-1.1 (0.3)	(-1.7, -0.5)	<0.001 *
		Placebo	262	238 (90.8)	-3.2 (0.3)	(-3.8, -2.7)			
Yes	Week 10	CR845	159	129 (81.1)	-5.2 (0.4)	(-5.9, -4.5)	-1.5 (0.5)	(-2.4, -0.6)	<0.001 *
		Placebo	163	146 (89.6)	-3.7 (0.3)	(-4.3, -3.0)			
No	Week 12	CR845	267	231 (86.5)	-4.5 (0.3)	(-5.0, -3.9)	-1.0 (0.3)	(-1.7, -0.4)	0.002 *
		Placebo	262	241 (92.0)	-3.4 (0.3)	(-3.9, -2.9)			
Yes	Week 12	CR845	159	128 (80.5)	-5.4 (0.4)	(-6.1, -4.7)	-1.5 (0.5)	(-2.4, -0.6)	0.001 *
		Placebo	163	144 (88.3)	-3.9 (0.4)	(-4.6, -3.2)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor presence of medical condition is also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DDC_ISCA: Change from baseline in 5-D degree score - MMRM results by age
ITT

Change from baseline in 5-D degree score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
A: Age									0.888
< 65 years	Week 4	CR845	282	249 (88.3)	-0.7 (0.1)	(-0.8, -0.6)	-0.3 (0.1)	(-0.4, -0.2)	<0.001 *
		Placebo	290	261 (90.0)	-0.4 (0.1)	(-0.5, -0.3)			
>= 65 years	Week 4	CR845	144	130 (90.3)	-0.7 (0.1)	(-0.9, -0.6)	-0.3 (0.1)	(-0.5, -0.1)	0.001 *
		Placebo	135	129 (95.6)	-0.4 (0.1)	(-0.6, -0.3)			
< 65 years	Week 8	CR845	282	239 (84.8)	-0.8 (0.1)	(-0.9, -0.7)	-0.2 (0.1)	(-0.3, -0.0)	0.027 *
		Placebo	290	264 (91.0)	-0.7 (0.1)	(-0.8, -0.6)			
>= 65 years	Week 8	CR845	144	126 (87.5)	-0.7 (0.1)	(-0.9, -0.6)	-0.2 (0.1)	(-0.4, -0.0)	0.036 *
		Placebo	135	128 (94.8)	-0.5 (0.1)	(-0.7, -0.4)			
< 65 years	Week 10	CR845	282	239 (84.8)	-0.9 (0.1)	(-1.0, -0.8)	-0.3 (0.1)	(-0.4, -0.1)	<0.001 *
		Placebo	290	259 (89.3)	-0.6 (0.1)	(-0.8, -0.5)			
>= 65 years	Week 10	CR845	144	120 (83.3)	-0.8 (0.1)	(-1.0, -0.7)	-0.3 (0.1)	(-0.4, -0.1)	0.008 *
		Placebo	135	125 (92.6)	-0.6 (0.1)	(-0.7, -0.4)			
< 65 years	Week 12	CR845	282	241 (85.5)	-1.0 (0.1)	(-1.1, -0.8)	-0.2 (0.1)	(-0.4, -0.1)	0.004 *
		Placebo	290	260 (89.7)	-0.8 (0.1)	(-0.9, -0.6)			
>= 65 years	Week 12	CR845	144	121 (84.0)	-0.9 (0.1)	(-1.0, -0.7)	-0.2 (0.1)	(-0.4, 0.0)	0.092
		Placebo	135	125 (92.6)	-0.7 (0.1)	(-0.8, -0.5)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DDC_ISCB: Change from baseline in 5-D degree score - MMRM results by sex
ITT

Change from baseline in 5-D degree score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
B: Sex									0.002 i
Male	Week 4	CR845	249	220 (88.4)	-0.5 (0.1)	(-0.7, -0.4)	-0.2 (0.1)	(-0.3, -0.0)	0.026 *
		Placebo	258	231 (89.5)	-0.4 (0.1)	(-0.5, -0.3)			
Female	Week 4	CR845	177	159 (89.8)	-0.9 (0.1)	(-1.0, -0.7)	-0.5 (0.1)	(-0.6, -0.3)	<0.001 *
		Placebo	167	159 (95.2)	-0.4 (0.1)	(-0.5, -0.3)			
Male	Week 8	CR845	249	212 (85.1)	-0.6 (0.1)	(-0.7, -0.5)	-0.1 (0.1)	(-0.2, 0.1)	0.236
		Placebo	258	238 (92.2)	-0.5 (0.1)	(-0.6, -0.4)			
Female	Week 8	CR845	177	153 (86.4)	-1.0 (0.1)	(-1.2, -0.9)	-0.3 (0.1)	(-0.5, -0.1)	0.003 *
		Placebo	167	154 (92.2)	-0.7 (0.1)	(-0.9, -0.6)			
Male	Week 10	CR845	249	207 (83.1)	-0.7 (0.1)	(-0.8, -0.6)	-0.1 (0.1)	(-0.3, 0.0)	0.111
		Placebo	258	233 (90.3)	-0.6 (0.1)	(-0.7, -0.4)			
Female	Week 10	CR845	177	152 (85.9)	-1.1 (0.1)	(-1.2, -1.0)	-0.4 (0.1)	(-0.6, -0.3)	<0.001 *
		Placebo	167	151 (90.4)	-0.7 (0.1)	(-0.8, -0.5)			
Male	Week 12	CR845	249	207 (83.1)	-0.7 (0.1)	(-0.9, -0.6)	-0.1 (0.1)	(-0.2, 0.1)	0.275
		Placebo	258	232 (89.9)	-0.7 (0.1)	(-0.8, -0.5)			
Female	Week 12	CR845	177	155 (87.6)	-1.1 (0.1)	(-1.3, -1.0)	-0.3 (0.1)	(-0.5, -0.2)	<0.001 *
		Placebo	167	153 (91.6)	-0.8 (0.1)	(-0.9, -0.7)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DDC_ISCC: Change from baseline in 5-D degree score - MMRM results by race
ITT

Change from baseline in 5-D degree score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
C: Race									0.744
Black/African American	Week 4	CR845	135	114 (84.4)	-0.6 (0.1)	(-0.8, -0.5)	-0.4 (0.1)	(-0.6, -0.1)	0.001 *
		Placebo	114	101 (88.6)	-0.3 (0.1)	(-0.5, -0.1)			
White	Week 4	CR845	255	233 (91.4)	-0.7 (0.1)	(-0.8, -0.6)	-0.3 (0.1)	(-0.4, -0.1)	<0.001 *
		Placebo	262	243 (92.7)	-0.5 (0.1)	(-0.6, -0.4)			
Other	Week 4	CR845	35	31 (88.6)	-0.8 (0.2)	(-1.2, -0.5)	-0.4 (0.2)	(-0.7, -0.0)	0.039 *
		Placebo	47	44 (93.6)	-0.5 (0.2)	(-0.8, -0.2)			
Black/African American	Week 8	CR845	135	111 (82.2)	-0.8 (0.1)	(-1.0, -0.6)	-0.2 (0.1)	(-0.4, 0.1)	0.182
		Placebo	114	105 (92.1)	-0.6 (0.1)	(-0.8, -0.5)			
White	Week 8	CR845	255	222 (87.1)	-0.8 (0.1)	(-0.9, -0.7)	-0.2 (0.1)	(-0.3, -0.0)	0.015 *
		Placebo	262	242 (92.4)	-0.6 (0.1)	(-0.7, -0.5)			
Other	Week 8	CR845	35	31 (88.6)	-1.0 (0.2)	(-1.3, -0.6)	-0.3 (0.2)	(-0.6, 0.1)	0.112
		Placebo	47	43 (91.5)	-0.7 (0.1)	(-1.0, -0.4)			
Black/African American	Week 10	CR845	135	106 (78.5)	-0.9 (0.1)	(-1.1, -0.7)	-0.3 (0.1)	(-0.5, -0.1)	0.011 *
		Placebo	114	102 (89.5)	-0.6 (0.1)	(-0.8, -0.4)			
White	Week 10	CR845	255	223 (87.5)	-0.9 (0.1)	(-1.0, -0.8)	-0.3 (0.1)	(-0.4, -0.1)	<0.001 *
		Placebo	262	238 (90.8)	-0.6 (0.1)	(-0.7, -0.5)			
Other	Week 10	CR845	35	29 (82.9)	-0.9 (0.2)	(-1.3, -0.5)	-0.2 (0.2)	(-0.6, 0.2)	0.396
		Placebo	47	42 (89.4)	-0.7 (0.2)	(-1.0, -0.4)			
Black/African American	Week 12	CR845	135	109 (80.7)	-1.0 (0.1)	(-1.2, -0.9)	-0.3 (0.1)	(-0.5, -0.1)	0.002 *
		Placebo	114	103 (90.4)	-0.7 (0.1)	(-0.9, -0.5)			
White	Week 12	CR845	255	223 (87.5)	-0.9 (0.1)	(-1.0, -0.8)	-0.2 (0.1)	(-0.4, -0.1)	0.005 *
		Placebo	262	239 (91.2)	-0.7 (0.1)	(-0.8, -0.6)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DDC_ISCC: Change from baseline in 5-D degree score - MMRM results by race
ITT

Change from baseline in 5-D degree score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Other	Week 12	CR845	35	29 (82.9)	-0.7 (0.2)	(-1.1, -0.3)	0.2 (0.2)	(-0.2, 0.7)	0.360
		Placebo	47	41 (87.2)	-0.9 (0.2)	(-1.3, -0.6)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DDC_ISCD: Change from baseline in 5-D degree score - MMRM results by baseline WI-NRS
ITT

Change from baseline in 5-D degree score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
D: Baseline worst itching NRS score (WI-NRS)									0.247
>= 4 to < 7	Week 4	CR845	185	167 (90.3)	-0.5 (0.1)	(-0.7, -0.4)	-0.2 (0.1)	(-0.3, -0.0)	0.010 *
		Placebo	193	179 (92.7)	-0.3 (0.1)	(-0.5, -0.2)			
>= 7	Week 4	CR845	241	212 (88.0)	-0.9 (0.1)	(-1.0, -0.7)	-0.4 (0.1)	(-0.5, -0.2)	<0.001 *
		Placebo	232	211 (90.9)	-0.5 (0.1)	(-0.6, -0.4)			
>= 4 to < 7	Week 8	CR845	185	163 (88.1)	-0.6 (0.1)	(-0.7, -0.5)	-0.2 (0.1)	(-0.3, -0.0)	0.041 *
		Placebo	193	177 (91.7)	-0.5 (0.1)	(-0.6, -0.3)			
>= 7	Week 8	CR845	241	202 (83.8)	-1.0 (0.1)	(-1.1, -0.8)	-0.2 (0.1)	(-0.4, -0.0)	0.014 *
		Placebo	232	215 (92.7)	-0.8 (0.1)	(-0.9, -0.6)			
>= 4 to < 7	Week 10	CR845	185	160 (86.5)	-0.7 (0.1)	(-0.8, -0.6)	-0.3 (0.1)	(-0.4, -0.1)	<0.001 *
		Placebo	193	173 (89.6)	-0.4 (0.1)	(-0.6, -0.3)			
>= 7	Week 10	CR845	241	199 (82.6)	-1.0 (0.1)	(-1.2, -0.9)	-0.3 (0.1)	(-0.4, -0.1)	0.002 *
		Placebo	232	211 (90.9)	-0.8 (0.1)	(-0.9, -0.6)			
>= 4 to < 7	Week 12	CR845	185	158 (85.4)	-0.8 (0.1)	(-0.9, -0.6)	-0.2 (0.1)	(-0.4, -0.0)	0.014 *
		Placebo	193	175 (90.7)	-0.6 (0.1)	(-0.7, -0.5)			
>= 7	Week 12	CR845	241	204 (84.6)	-1.1 (0.1)	(-1.2, -0.9)	-0.2 (0.1)	(-0.4, -0.1)	0.008 *
		Placebo	232	210 (90.5)	-0.9 (0.1)	(-1.0, -0.7)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DDC_ISCE: Change from baseline in 5-D degree score - MMRM results by specific medical condition
ITT

Change from baseline in 5-D degree score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
E: Presence of specific medical conditions									0.136
No	Week 4	CR845	359	317 (88.3)	-0.7 (0.0)	(-0.7, -0.6)	-0.3 (0.1)	(-0.4, -0.2)	<0.001 *
		Placebo	360	330 (91.7)	-0.4 (0.0)	(-0.5, -0.3)			
Yes	Week 4	CR845	67	62 (92.5)	-0.9 (0.1)	(-1.1, -0.7)	-0.4 (0.1)	(-0.7, -0.1)	0.004 *
		Placebo	65	60 (92.3)	-0.4 (0.1)	(-0.6, -0.2)			
No	Week 8	CR845	359	306 (85.2)	-0.8 (0.0)	(-0.8, -0.7)	-0.1 (0.1)	(-0.3, -0.0)	0.025 *
		Placebo	360	328 (91.1)	-0.6 (0.0)	(-0.7, -0.5)			
Yes	Week 8	CR845	67	59 (88.1)	-0.9 (0.1)	(-1.2, -0.7)	-0.4 (0.2)	(-0.7, -0.1)	0.022 *
		Placebo	65	64 (98.5)	-0.6 (0.1)	(-0.8, -0.4)			
No	Week 10	CR845	359	302 (84.1)	-0.8 (0.0)	(-0.9, -0.7)	-0.2 (0.1)	(-0.4, -0.1)	<0.001 *
		Placebo	360	322 (89.4)	-0.6 (0.0)	(-0.7, -0.5)			
Yes	Week 10	CR845	67	57 (85.1)	-1.1 (0.1)	(-1.2, -0.9)	-0.4 (0.1)	(-0.7, -0.1)	0.003 *
		Placebo	65	62 (95.4)	-0.6 (0.1)	(-0.8, -0.4)			
No	Week 12	CR845	359	303 (84.4)	-0.9 (0.0)	(-1.0, -0.8)	-0.2 (0.1)	(-0.3, -0.0)	0.012 *
		Placebo	360	322 (89.4)	-0.7 (0.0)	(-0.8, -0.6)			
Yes	Week 12	CR845	67	59 (88.1)	-1.1 (0.1)	(-1.3, -0.9)	-0.4 (0.1)	(-0.7, -0.1)	0.010 *
		Placebo	65	63 (96.9)	-0.7 (0.1)	(-0.9, -0.5)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor previous use of anti-itch medication is also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DDC_ISCF: Change from baseline in 5-D degree score - MMRM results by use of concomitant itch medication
ITT

Change from baseline in 5-D degree score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
F: Use of concomitant itch medication									0.331
No	Week 4	CR845	267	244 (91.4)	-0.6 (0.1)	(-0.7, -0.5)	-0.3 (0.1)	(-0.4, -0.2)	<0.001 *
		Placebo	262	240 (91.6)	-0.4 (0.1)	(-0.5, -0.2)			
Yes	Week 4	CR845	159	135 (84.9)	-0.8 (0.1)	(-0.9, -0.7)	-0.3 (0.1)	(-0.5, -0.1)	<0.001 *
		Placebo	163	150 (92.0)	-0.5 (0.1)	(-0.6, -0.3)			
No	Week 8	CR845	267	236 (88.4)	-0.7 (0.1)	(-0.8, -0.6)	-0.2 (0.1)	(-0.3, -0.0)	0.025 *
		Placebo	262	242 (92.4)	-0.6 (0.1)	(-0.7, -0.5)			
Yes	Week 8	CR845	159	129 (81.1)	-0.9 (0.1)	(-1.0, -0.7)	-0.2 (0.1)	(-0.4, -0.0)	0.042 *
		Placebo	163	150 (92.0)	-0.7 (0.1)	(-0.8, -0.5)			
No	Week 10	CR845	267	229 (85.8)	-0.8 (0.1)	(-0.9, -0.7)	-0.2 (0.1)	(-0.4, -0.1)	0.003 *
		Placebo	262	238 (90.8)	-0.6 (0.1)	(-0.7, -0.5)			
Yes	Week 10	CR845	159	130 (81.8)	-1.0 (0.1)	(-1.1, -0.8)	-0.3 (0.1)	(-0.5, -0.1)	0.001 *
		Placebo	163	146 (89.6)	-0.7 (0.1)	(-0.8, -0.5)			
No	Week 12	CR845	267	232 (86.9)	-0.8 (0.1)	(-1.0, -0.7)	-0.1 (0.1)	(-0.3, 0.0)	0.065
		Placebo	262	241 (92.0)	-0.7 (0.1)	(-0.8, -0.6)			
Yes	Week 12	CR845	159	130 (81.8)	-1.1 (0.1)	(-1.2, -0.9)	-0.3 (0.1)	(-0.5, -0.1)	0.002 *
		Placebo	163	144 (88.3)	-0.8 (0.1)	(-0.9, -0.6)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor presence of medical condition is also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DLC_ISCA: Change from baseline in 5-D duration score - MMRM results by age
ITT

Change from baseline in 5-D duration score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
A: Age									0.943
< 65 years	Week 4	CR845	282	248 (87.9)	-0.7 (0.1)	(-0.8, -0.5)	-0.4 (0.1)	(-0.6, -0.2)	<0.001 *
		Placebo	290	261 (90.0)	-0.3 (0.1)	(-0.5, -0.1)			
>= 65 years	Week 4	CR845	144	129 (89.6)	-0.7 (0.1)	(-1.0, -0.5)	-0.2 (0.1)	(-0.5, 0.0)	0.098
		Placebo	135	129 (95.6)	-0.5 (0.1)	(-0.7, -0.3)			
< 65 years	Week 8	CR845	282	237 (84.0)	-0.9 (0.1)	(-1.1, -0.7)	-0.2 (0.1)	(-0.4, -0.1)	0.012 *
		Placebo	290	264 (91.0)	-0.7 (0.1)	(-0.8, -0.5)			
>= 65 years	Week 8	CR845	144	126 (87.5)	-1.0 (0.1)	(-1.2, -0.7)	-0.3 (0.1)	(-0.6, -0.1)	0.013 *
		Placebo	135	128 (94.8)	-0.6 (0.1)	(-0.8, -0.4)			
< 65 years	Week 10	CR845	282	237 (84.0)	-0.9 (0.1)	(-1.1, -0.7)	-0.2 (0.1)	(-0.4, -0.0)	0.030 *
		Placebo	290	259 (89.3)	-0.7 (0.1)	(-0.8, -0.5)			
>= 65 years	Week 10	CR845	144	120 (83.3)	-0.9 (0.1)	(-1.1, -0.7)	-0.2 (0.1)	(-0.5, 0.0)	0.078
		Placebo	135	125 (92.6)	-0.6 (0.1)	(-0.9, -0.4)			
< 65 years	Week 12	CR845	282	239 (84.8)	-0.9 (0.1)	(-1.1, -0.7)	-0.3 (0.1)	(-0.5, -0.1)	0.005 *
		Placebo	290	260 (89.7)	-0.6 (0.1)	(-0.8, -0.4)			
>= 65 years	Week 12	CR845	144	121 (84.0)	-1.0 (0.1)	(-1.2, -0.8)	-0.3 (0.1)	(-0.5, 0.0)	0.050
		Placebo	135	125 (92.6)	-0.8 (0.1)	(-1.0, -0.6)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DLC_ISCB: Change from baseline in 5-D duration score - MMRM results by sex
ITT

Change from baseline in 5-D duration score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
B: Sex									0.029 i
Male	Week 4	CR845	249	221 (88.8)	-0.5 (0.1)	(-0.7, -0.3)	-0.3 (0.1)	(-0.5, -0.1)	0.015 *
		Placebo	258	231 (89.5)	-0.2 (0.1)	(-0.4, -0.1)			
Female	Week 4	CR845	177	156 (88.1)	-1.0 (0.1)	(-1.1, -0.8)	-0.4 (0.1)	(-0.7, -0.2)	0.001 *
		Placebo	167	159 (95.2)	-0.5 (0.1)	(-0.7, -0.3)			
Male	Week 8	CR845	249	212 (85.1)	-0.7 (0.1)	(-0.9, -0.6)	-0.2 (0.1)	(-0.4, 0.0)	0.115
		Placebo	258	238 (92.2)	-0.6 (0.1)	(-0.7, -0.4)			
Female	Week 8	CR845	177	151 (85.3)	-1.2 (0.1)	(-1.4, -1.0)	-0.4 (0.1)	(-0.7, -0.2)	0.001 *
		Placebo	167	154 (92.2)	-0.7 (0.1)	(-0.9, -0.5)			
Male	Week 10	CR845	249	207 (83.1)	-0.6 (0.1)	(-0.8, -0.5)	0.0 (0.1)	(-0.2, 0.2)	0.947
		Placebo	258	233 (90.3)	-0.7 (0.1)	(-0.8, -0.5)			
Female	Week 10	CR845	177	150 (84.7)	-1.2 (0.1)	(-1.4, -1.0)	-0.5 (0.1)	(-0.8, -0.3)	<0.001 *
		Placebo	167	151 (90.4)	-0.7 (0.1)	(-0.9, -0.5)			
Male	Week 12	CR845	249	207 (83.1)	-0.8 (0.1)	(-0.9, -0.6)	-0.2 (0.1)	(-0.4, 0.0)	0.096
		Placebo	258	232 (89.9)	-0.6 (0.1)	(-0.7, -0.4)			
Female	Week 12	CR845	177	153 (86.4)	-1.2 (0.1)	(-1.4, -1.0)	-0.4 (0.1)	(-0.6, -0.2)	0.001 *
		Placebo	167	153 (91.6)	-0.8 (0.1)	(-1.0, -0.6)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DLC_ISCC: Change from baseline in 5-D duration score - MMRM results by race
ITT

Change from baseline in 5-D duration score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
C: Race									0.321
Black/African American	Week 4	CR845	135	113 (83.7)	-0.7 (0.1)	(-1.0, -0.5)	-0.3 (0.2)	(-0.6, 0.0)	0.054
		Placebo	114	101 (88.6)	-0.4 (0.1)	(-0.7, -0.2)			
White	Week 4	CR845	255	232 (91.0)	-0.7 (0.1)	(-0.9, -0.5)	-0.4 (0.1)	(-0.6, -0.2)	<0.001 *
		Placebo	262	243 (92.7)	-0.3 (0.1)	(-0.5, -0.2)			
Other	Week 4	CR845	35	31 (88.6)	-0.7 (0.2)	(-1.2, -0.2)	-0.2 (0.2)	(-0.7, 0.3)	0.371
		Placebo	47	44 (93.6)	-0.5 (0.2)	(-0.9, -0.1)			
Black/African American	Week 8	CR845	135	110 (81.5)	-1.0 (0.1)	(-1.3, -0.8)	-0.4 (0.2)	(-0.7, -0.1)	0.020 *
		Placebo	114	105 (92.1)	-0.7 (0.1)	(-0.9, -0.4)			
White	Week 8	CR845	255	221 (86.7)	-0.9 (0.1)	(-1.0, -0.7)	-0.2 (0.1)	(-0.4, -0.0)	0.019 *
		Placebo	262	242 (92.4)	-0.6 (0.1)	(-0.8, -0.5)			
Other	Week 8	CR845	35	31 (88.6)	-1.1 (0.2)	(-1.6, -0.6)	-0.4 (0.3)	(-0.9, 0.1)	0.151
		Placebo	47	43 (91.5)	-0.7 (0.2)	(-1.1, -0.3)			
Black/African American	Week 10	CR845	135	105 (77.8)	-1.2 (0.1)	(-1.4, -0.9)	-0.6 (0.2)	(-0.9, -0.3)	<0.001 *
		Placebo	114	102 (89.5)	-0.6 (0.1)	(-0.8, -0.4)			
White	Week 10	CR845	255	222 (87.1)	-0.8 (0.1)	(-1.0, -0.6)	-0.1 (0.1)	(-0.3, 0.1)	0.290
		Placebo	262	238 (90.8)	-0.7 (0.1)	(-0.9, -0.5)			
Other	Week 10	CR845	35	29 (82.9)	-0.9 (0.2)	(-1.4, -0.5)	-0.1 (0.2)	(-0.6, 0.4)	0.656
		Placebo	47	42 (89.4)	-0.8 (0.2)	(-1.2, -0.4)			
Black/African American	Week 12	CR845	135	108 (80.0)	-1.2 (0.1)	(-1.4, -1.0)	-0.5 (0.1)	(-0.8, -0.2)	<0.001 *
		Placebo	114	103 (90.4)	-0.7 (0.1)	(-0.9, -0.5)			
White	Week 12	CR845	255	222 (87.1)	-0.9 (0.1)	(-1.1, -0.7)	-0.3 (0.1)	(-0.5, -0.1)	0.005 *
		Placebo	262	239 (91.2)	-0.6 (0.1)	(-0.8, -0.5)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DLC_ISCC: Change from baseline in 5-D duration score - MMRM results by race
ITT

Change from baseline in 5-D duration score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Other	Week 12	CR845	35	29 (82.9)	-0.5 (0.3)	(-1.0, 0.0)	0.3 (0.3)	(-0.3, 0.9)	0.309
		Placebo	47	41 (87.2)	-0.8 (0.2)	(-1.3, -0.4)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DLC_ISCD: Change from baseline in 5-D duration score - MMRM results by baseline WI-NRS
ITT

Change from baseline in 5-D duration score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
D: Baseline worst itching NRS score (WI-NRS)									0.959
>= 4 to < 7	Week 4	CR845	185	167 (90.3)	-0.5 (0.1)	(-0.7, -0.3)	-0.3 (0.1)	(-0.6, -0.1)	0.004 *
		Placebo	193	179 (92.7)	-0.1 (0.1)	(-0.3, 0.0)			
>= 7	Week 4	CR845	241	210 (87.1)	-0.9 (0.1)	(-1.1, -0.7)	-0.3 (0.1)	(-0.6, -0.1)	0.005 *
		Placebo	232	211 (90.9)	-0.6 (0.1)	(-0.8, -0.4)			
>= 4 to < 7	Week 8	CR845	185	162 (87.6)	-0.7 (0.1)	(-0.9, -0.5)	-0.3 (0.1)	(-0.5, -0.1)	0.001 *
		Placebo	193	177 (91.7)	-0.4 (0.1)	(-0.5, -0.2)			
>= 7	Week 8	CR845	241	201 (83.4)	-1.2 (0.1)	(-1.3, -1.0)	-0.2 (0.1)	(-0.5, -0.0)	0.042 *
		Placebo	232	215 (92.7)	-0.9 (0.1)	(-1.1, -0.7)			
>= 4 to < 7	Week 10	CR845	185	159 (85.9)	-0.6 (0.1)	(-0.8, -0.5)	-0.2 (0.1)	(-0.5, -0.0)	0.021 *
		Placebo	193	173 (89.6)	-0.4 (0.1)	(-0.6, -0.2)			
>= 7	Week 10	CR845	241	198 (82.2)	-1.1 (0.1)	(-1.3, -1.0)	-0.2 (0.1)	(-0.4, 0.0)	0.075
		Placebo	232	211 (90.9)	-0.9 (0.1)	(-1.1, -0.8)			
>= 4 to < 7	Week 12	CR845	185	157 (84.9)	-0.7 (0.1)	(-0.8, -0.5)	-0.2 (0.1)	(-0.5, -0.0)	0.037 *
		Placebo	193	175 (90.7)	-0.4 (0.1)	(-0.6, -0.2)			
>= 7	Week 12	CR845	241	203 (84.2)	-1.2 (0.1)	(-1.4, -1.0)	-0.3 (0.1)	(-0.6, -0.1)	0.005 *
		Placebo	232	210 (90.5)	-0.9 (0.1)	(-1.1, -0.7)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DLC_ISCE: Change from baseline in 5-D duration score - MMRM results by specific medical condition
ITT

Change from baseline in 5-D duration score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
E: Presence of specific medical conditions									0.995
No	Week 4	CR845	359	315 (87.7)	-0.7 (0.1)	(-0.9, -0.6)	-0.4 (0.1)	(-0.5, -0.2)	<0.001 *
		Placebo	360	330 (91.7)	-0.4 (0.1)	(-0.5, -0.2)			
Yes	Week 4	CR845	67	62 (92.5)	-0.7 (0.1)	(-1.0, -0.4)	-0.2 (0.2)	(-0.6, 0.3)	0.461
		Placebo	65	60 (92.3)	-0.6 (0.1)	(-0.9, -0.3)			
No	Week 8	CR845	359	304 (84.7)	-0.9 (0.1)	(-1.1, -0.8)	-0.3 (0.1)	(-0.4, -0.1)	0.003 *
		Placebo	360	328 (91.1)	-0.7 (0.1)	(-0.8, -0.6)			
Yes	Week 8	CR845	67	59 (88.1)	-1.0 (0.1)	(-1.3, -0.7)	-0.4 (0.2)	(-0.8, 0.0)	0.080
		Placebo	65	64 (98.5)	-0.7 (0.1)	(-0.9, -0.4)			
No	Week 10	CR845	359	300 (83.6)	-0.9 (0.1)	(-1.1, -0.8)	-0.2 (0.1)	(-0.4, -0.1)	0.009 *
		Placebo	360	322 (89.4)	-0.7 (0.1)	(-0.8, -0.6)			
Yes	Week 10	CR845	67	57 (85.1)	-0.9 (0.2)	(-1.2, -0.6)	-0.2 (0.2)	(-0.6, 0.2)	0.369
		Placebo	65	62 (95.4)	-0.7 (0.2)	(-1.0, -0.4)			
No	Week 12	CR845	359	301 (83.8)	-0.9 (0.1)	(-1.1, -0.8)	-0.3 (0.1)	(-0.4, -0.1)	0.004 *
		Placebo	360	322 (89.4)	-0.7 (0.1)	(-0.8, -0.5)			
Yes	Week 12	CR845	67	59 (88.1)	-1.1 (0.1)	(-1.4, -0.9)	-0.4 (0.2)	(-0.7, -0.0)	0.050 *
		Placebo	65	63 (96.9)	-0.8 (0.1)	(-1.0, -0.5)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor previous use of anti-itch medication is also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DLC_ISCF: Change from baseline in 5-D duration score - MMRM results by use of concomitant itch medication
ITT

Change from baseline in 5-D duration score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
F: Use of concomitant itch medication									0.863
No	Week 4	CR845	267	243 (91.0)	-0.6 (0.1)	(-0.8, -0.4)	-0.3 (0.1)	(-0.5, -0.1)	0.002 *
		Placebo	262	240 (91.6)	-0.3 (0.1)	(-0.5, -0.1)			
Yes	Week 4	CR845	159	134 (84.3)	-0.8 (0.1)	(-1.0, -0.6)	-0.3 (0.1)	(-0.6, -0.1)	0.019 *
		Placebo	163	150 (92.0)	-0.5 (0.1)	(-0.7, -0.3)			
No	Week 8	CR845	267	235 (88.0)	-0.9 (0.1)	(-1.0, -0.7)	-0.3 (0.1)	(-0.5, -0.1)	<0.001 *
		Placebo	262	242 (92.4)	-0.6 (0.1)	(-0.7, -0.4)			
Yes	Week 8	CR845	159	128 (80.5)	-1.0 (0.1)	(-1.2, -0.7)	-0.2 (0.1)	(-0.4, 0.1)	0.265
		Placebo	163	150 (92.0)	-0.8 (0.1)	(-1.0, -0.6)			
No	Week 10	CR845	267	228 (85.4)	-0.8 (0.1)	(-1.0, -0.7)	-0.2 (0.1)	(-0.4, -0.0)	0.031 *
		Placebo	262	238 (90.8)	-0.6 (0.1)	(-0.8, -0.5)			
Yes	Week 10	CR845	159	129 (81.1)	-1.0 (0.1)	(-1.2, -0.8)	-0.2 (0.1)	(-0.5, 0.1)	0.132
		Placebo	163	146 (89.6)	-0.8 (0.1)	(-1.0, -0.6)			
No	Week 12	CR845	267	231 (86.5)	-0.9 (0.1)	(-1.0, -0.7)	-0.3 (0.1)	(-0.5, -0.1)	0.007 *
		Placebo	262	241 (92.0)	-0.6 (0.1)	(-0.7, -0.4)			
Yes	Week 12	CR845	159	129 (81.1)	-1.1 (0.1)	(-1.3, -0.8)	-0.3 (0.1)	(-0.5, -0.0)	0.043 *
		Placebo	163	144 (88.3)	-0.8 (0.1)	(-1.0, -0.6)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor presence of medical condition is also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DWC_ISCA: Change from baseline in 5-D direction score - MMRM results by age
ITT

Change from baseline in 5-D direction score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
A: Age									0.027 i
< 65 years	Week 4	CR845	282	250 (88.7)	-1.2 (0.1)	(-1.4, -1.1)	-0.5 (0.1)	(-0.7, -0.4)	<0.001 *
		Placebo	290	261 (90.0)	-0.7 (0.1)	(-0.8, -0.6)			
>= 65 years	Week 4	CR845	144	130 (90.3)	-1.1 (0.1)	(-1.2, -0.9)	-0.3 (0.1)	(-0.5, -0.1)	0.005 *
		Placebo	135	129 (95.6)	-0.8 (0.1)	(-0.9, -0.6)			
< 65 years	Week 8	CR845	282	238 (84.4)	-1.4 (0.1)	(-1.5, -1.2)	-0.5 (0.1)	(-0.6, -0.3)	<0.001 *
		Placebo	290	264 (91.0)	-0.9 (0.1)	(-1.0, -0.8)			
>= 65 years	Week 8	CR845	144	126 (87.5)	-1.0 (0.1)	(-1.2, -0.8)	-0.0 (0.1)	(-0.2, 0.2)	0.781
		Placebo	135	128 (94.8)	-1.0 (0.1)	(-1.1, -0.8)			
< 65 years	Week 10	CR845	282	239 (84.8)	-1.4 (0.1)	(-1.5, -1.2)	-0.4 (0.1)	(-0.5, -0.2)	<0.001 *
		Placebo	290	259 (89.3)	-1.0 (0.1)	(-1.1, -0.8)			
>= 65 years	Week 10	CR845	144	120 (83.3)	-1.2 (0.1)	(-1.4, -1.1)	-0.4 (0.1)	(-0.6, -0.2)	<0.001 *
		Placebo	135	125 (92.6)	-0.8 (0.1)	(-1.0, -0.7)			
< 65 years	Week 12	CR845	282	241 (85.5)	-1.4 (0.1)	(-1.5, -1.2)	-0.4 (0.1)	(-0.6, -0.3)	<0.001 *
		Placebo	290	260 (89.7)	-0.9 (0.1)	(-1.1, -0.8)			
>= 65 years	Week 12	CR845	144	120 (83.3)	-1.1 (0.1)	(-1.3, -1.0)	-0.1 (0.1)	(-0.4, 0.1)	0.225
		Placebo	135	125 (92.6)	-1.0 (0.1)	(-1.2, -0.8)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DWC_ISCB: Change from baseline in 5-D direction score - MMRM results by sex
ITT

Change from baseline in 5-D direction score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
B: Sex									0.010 i
Male	Week 4	CR845	249	221 (88.8)	-1.1 (0.1)	(-1.2, -1.0)	-0.4 (0.1)	(-0.5, -0.2)	<0.001 *
		Placebo	258	231 (89.5)	-0.7 (0.1)	(-0.9, -0.6)			
Female	Week 4	CR845	177	159 (89.8)	-1.3 (0.1)	(-1.4, -1.2)	-0.5 (0.1)	(-0.7, -0.4)	<0.001 *
		Placebo	167	159 (95.2)	-0.8 (0.1)	(-0.9, -0.6)			
Male	Week 8	CR845	249	211 (84.7)	-1.1 (0.1)	(-1.2, -0.9)	-0.2 (0.1)	(-0.3, -0.0)	0.018 *
		Placebo	258	238 (92.2)	-0.9 (0.1)	(-1.0, -0.7)			
Female	Week 8	CR845	177	153 (86.4)	-1.5 (0.1)	(-1.6, -1.4)	-0.5 (0.1)	(-0.7, -0.3)	<0.001 *
		Placebo	167	154 (92.2)	-1.0 (0.1)	(-1.2, -0.9)			
Male	Week 10	CR845	249	207 (83.1)	-1.2 (0.1)	(-1.3, -1.0)	-0.2 (0.1)	(-0.4, -0.1)	0.002 *
		Placebo	258	233 (90.3)	-0.9 (0.1)	(-1.0, -0.8)			
Female	Week 10	CR845	177	152 (85.9)	-1.5 (0.1)	(-1.7, -1.4)	-0.6 (0.1)	(-0.8, -0.4)	<0.001 *
		Placebo	167	151 (90.4)	-0.9 (0.1)	(-1.1, -0.8)			
Male	Week 12	CR845	249	207 (83.1)	-1.2 (0.1)	(-1.3, -1.0)	-0.3 (0.1)	(-0.4, -0.1)	0.004 *
		Placebo	258	232 (89.9)	-0.9 (0.1)	(-1.0, -0.8)			
Female	Week 12	CR845	177	154 (87.0)	-1.5 (0.1)	(-1.6, -1.3)	-0.4 (0.1)	(-0.6, -0.2)	<0.001 *
		Placebo	167	153 (91.6)	-1.0 (0.1)	(-1.2, -0.9)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DWC_ISCC: Change from baseline in 5-D direction score - MMRM results by race
ITT

Change from baseline in 5-D direction score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
C: Race									0.704
Black/African American	Week 4	CR845	135	114 (84.4)	-1.2 (0.1)	(-1.3, -1.0)	-0.5 (0.1)	(-0.7, -0.2)	<0.001 *
		Placebo	114	101 (88.6)	-0.7 (0.1)	(-0.9, -0.5)			
White	Week 4	CR845	255	234 (91.8)	-1.2 (0.1)	(-1.3, -1.0)	-0.4 (0.1)	(-0.6, -0.2)	<0.001 *
		Placebo	262	243 (92.7)	-0.8 (0.1)	(-0.9, -0.6)			
Other	Week 4	CR845	35	31 (88.6)	-1.3 (0.2)	(-1.7, -1.0)	-0.5 (0.2)	(-0.9, -0.1)	0.010 *
		Placebo	47	44 (93.6)	-0.8 (0.2)	(-1.1, -0.5)			
Black/African American	Week 8	CR845	135	111 (82.2)	-1.3 (0.1)	(-1.5, -1.2)	-0.3 (0.1)	(-0.5, -0.1)	0.011 *
		Placebo	114	105 (92.1)	-1.0 (0.1)	(-1.2, -0.9)			
White	Week 8	CR845	255	221 (86.7)	-1.2 (0.1)	(-1.3, -1.1)	-0.3 (0.1)	(-0.5, -0.2)	<0.001 *
		Placebo	262	242 (92.4)	-0.9 (0.1)	(-1.0, -0.7)			
Other	Week 8	CR845	35	31 (88.6)	-1.3 (0.2)	(-1.6, -0.9)	-0.2 (0.2)	(-0.6, 0.1)	0.196
		Placebo	47	43 (91.5)	-1.0 (0.2)	(-1.3, -0.7)			
Black/African American	Week 10	CR845	135	106 (78.5)	-1.5 (0.1)	(-1.7, -1.3)	-0.4 (0.1)	(-0.7, -0.2)	<0.001 *
		Placebo	114	102 (89.5)	-1.0 (0.1)	(-1.2, -0.9)			
White	Week 10	CR845	255	223 (87.5)	-1.2 (0.1)	(-1.4, -1.1)	-0.4 (0.1)	(-0.6, -0.2)	<0.001 *
		Placebo	262	238 (90.8)	-0.8 (0.1)	(-1.0, -0.7)			
Other	Week 10	CR845	35	29 (82.9)	-1.3 (0.2)	(-1.7, -1.0)	-0.2 (0.2)	(-0.6, 0.1)	0.204
		Placebo	47	42 (89.4)	-1.1 (0.2)	(-1.4, -0.8)			
Black/African American	Week 12	CR845	135	108 (80.0)	-1.5 (0.1)	(-1.6, -1.3)	-0.4 (0.1)	(-0.7, -0.2)	<0.001 *
		Placebo	114	103 (90.4)	-1.0 (0.1)	(-1.2, -0.8)			
White	Week 12	CR845	255	223 (87.5)	-1.2 (0.1)	(-1.4, -1.1)	-0.3 (0.1)	(-0.5, -0.2)	<0.001 *
		Placebo	262	239 (91.2)	-0.9 (0.1)	(-1.0, -0.8)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DWC_ISCC: Change from baseline in 5-D direction score - MMRM results by race
ITT

Change from baseline in 5-D direction score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Other	Week 12	CR845	35	29 (82.9)	-1.2 (0.2)	(-1.6, -0.8)	-0.0 (0.2)	(-0.5, 0.4)	0.835
		Placebo	47	41 (87.2)	-1.1 (0.2)	(-1.5, -0.8)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DWC_ISCD: Change from baseline in 5-D direction score - MMRM results by baseline WI-NRS
ITT

Change from baseline in 5-D direction score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
D: Baseline worst itching NRS score (WI-NRS)									0.765
>= 4 to < 7	Week 4	CR845	185	168 (90.8)	-1.2 (0.1)	(-1.3, -1.0)	-0.5 (0.1)	(-0.6, -0.3)	<0.001 *
		Placebo	193	179 (92.7)	-0.7 (0.1)	(-0.9, -0.6)			
>= 7	Week 4	CR845	241	212 (88.0)	-1.2 (0.1)	(-1.3, -1.1)	-0.4 (0.1)	(-0.6, -0.3)	<0.001 *
		Placebo	232	211 (90.9)	-0.8 (0.1)	(-0.9, -0.7)			
>= 4 to < 7	Week 8	CR845	185	163 (88.1)	-1.2 (0.1)	(-1.3, -1.1)	-0.4 (0.1)	(-0.5, -0.2)	<0.001 *
		Placebo	193	177 (91.7)	-0.8 (0.1)	(-1.0, -0.7)			
>= 7	Week 8	CR845	241	201 (83.4)	-1.3 (0.1)	(-1.4, -1.2)	-0.3 (0.1)	(-0.5, -0.1)	0.001 *
		Placebo	232	215 (92.7)	-1.0 (0.1)	(-1.2, -0.9)			
>= 4 to < 7	Week 10	CR845	185	160 (86.5)	-1.3 (0.1)	(-1.4, -1.1)	-0.4 (0.1)	(-0.6, -0.3)	<0.001 *
		Placebo	193	173 (89.6)	-0.9 (0.1)	(-1.0, -0.7)			
>= 7	Week 10	CR845	241	199 (82.6)	-1.4 (0.1)	(-1.5, -1.2)	-0.4 (0.1)	(-0.6, -0.2)	<0.001 *
		Placebo	232	211 (90.9)	-1.0 (0.1)	(-1.1, -0.9)			
>= 4 to < 7	Week 12	CR845	185	158 (85.4)	-1.2 (0.1)	(-1.4, -1.1)	-0.3 (0.1)	(-0.5, -0.1)	0.003 *
		Placebo	193	175 (90.7)	-0.9 (0.1)	(-1.1, -0.8)			
>= 7	Week 12	CR845	241	203 (84.2)	-1.4 (0.1)	(-1.5, -1.2)	-0.4 (0.1)	(-0.6, -0.2)	<0.001 *
		Placebo	232	210 (90.5)	-1.0 (0.1)	(-1.1, -0.8)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DWC_ISCE: Change from baseline in 5-D direction score - MMRM results by specific medical condition
ITT

Change from baseline in 5-D direction score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
E: Presence of specific medical conditions									0.338
No	Week 4	CR845	359	318 (88.6)	-1.2 (0.0)	(-1.3, -1.1)	-0.4 (0.1)	(-0.6, -0.3)	<0.001 *
		Placebo	360	330 (91.7)	-0.8 (0.0)	(-0.8, -0.7)			
Yes	Week 4	CR845	67	62 (92.5)	-1.2 (0.1)	(-1.4, -1.0)	-0.5 (0.2)	(-0.8, -0.2)	<0.001 *
		Placebo	65	60 (92.3)	-0.7 (0.1)	(-0.9, -0.5)			
No	Week 8	CR845	359	305 (85.0)	-1.2 (0.0)	(-1.3, -1.1)	-0.3 (0.1)	(-0.4, -0.2)	<0.001 *
		Placebo	360	328 (91.1)	-0.9 (0.0)	(-1.0, -0.8)			
Yes	Week 8	CR845	67	59 (88.1)	-1.6 (0.1)	(-1.8, -1.4)	-0.5 (0.1)	(-0.8, -0.2)	<0.001 *
		Placebo	65	64 (98.5)	-1.1 (0.1)	(-1.3, -0.9)			
No	Week 10	CR845	359	302 (84.1)	-1.3 (0.0)	(-1.4, -1.2)	-0.4 (0.1)	(-0.5, -0.3)	<0.001 *
		Placebo	360	322 (89.4)	-0.9 (0.0)	(-1.0, -0.8)			
Yes	Week 10	CR845	67	57 (85.1)	-1.4 (0.1)	(-1.7, -1.2)	-0.4 (0.2)	(-0.8, -0.1)	0.007 *
		Placebo	65	62 (95.4)	-1.0 (0.1)	(-1.2, -0.8)			
No	Week 12	CR845	359	303 (84.4)	-1.2 (0.1)	(-1.3, -1.1)	-0.3 (0.1)	(-0.4, -0.2)	<0.001 *
		Placebo	360	322 (89.4)	-0.9 (0.1)	(-1.0, -0.8)			
Yes	Week 12	CR845	67	58 (86.6)	-1.5 (0.1)	(-1.8, -1.3)	-0.5 (0.2)	(-0.9, -0.2)	0.004 *
		Placebo	65	63 (96.9)	-1.0 (0.1)	(-1.3, -0.8)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor previous use of anti-itch medication is also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DWC_ISCF: Change from baseline in 5-D direction score - MMRM results by use of concomitant itch medication
ITT

Change from baseline in 5-D direction score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
F: Use of concomitant itch medication									0.141
No	Week 4	CR845	267	245 (91.8)	-1.1 (0.1)	(-1.3, -1.0)	-0.4 (0.1)	(-0.6, -0.3)	<0.001 *
		Placebo	262	240 (91.6)	-0.7 (0.1)	(-0.8, -0.6)			
Yes	Week 4	CR845	159	135 (84.9)	-1.2 (0.1)	(-1.4, -1.1)	-0.5 (0.1)	(-0.7, -0.3)	<0.001 *
		Placebo	163	150 (92.0)	-0.8 (0.1)	(-0.9, -0.6)			
No	Week 8	CR845	267	235 (88.0)	-1.2 (0.1)	(-1.3, -1.1)	-0.3 (0.1)	(-0.4, -0.1)	<0.001 *
		Placebo	262	242 (92.4)	-0.9 (0.1)	(-1.1, -0.8)			
Yes	Week 8	CR845	159	129 (81.1)	-1.3 (0.1)	(-1.5, -1.1)	-0.4 (0.1)	(-0.6, -0.2)	<0.001 *
		Placebo	163	150 (92.0)	-0.9 (0.1)	(-1.1, -0.7)			
No	Week 10	CR845	267	229 (85.8)	-1.2 (0.1)	(-1.4, -1.1)	-0.3 (0.1)	(-0.4, -0.1)	<0.001 *
		Placebo	262	238 (90.8)	-1.0 (0.1)	(-1.1, -0.8)			
Yes	Week 10	CR845	159	130 (81.8)	-1.5 (0.1)	(-1.6, -1.3)	-0.6 (0.1)	(-0.8, -0.4)	<0.001 *
		Placebo	163	146 (89.6)	-0.8 (0.1)	(-1.0, -0.7)			
No	Week 12	CR845	267	232 (86.9)	-1.2 (0.1)	(-1.4, -1.1)	-0.3 (0.1)	(-0.5, -0.1)	<0.001 *
		Placebo	262	241 (92.0)	-0.9 (0.1)	(-1.1, -0.8)			
Yes	Week 12	CR845	159	129 (81.1)	-1.4 (0.1)	(-1.6, -1.2)	-0.4 (0.1)	(-0.6, -0.2)	<0.001 *
		Placebo	163	144 (88.3)	-1.0 (0.1)	(-1.2, -0.8)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor presence of medical condition is also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DNC_ISCA: Change from baseline in 5-D disability score - MMRM results by age
ITT

Change from baseline in 5-D disability score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
A: Age									0.442
< 65 years	Week 4	CR845	282	250 (88.7)	-0.7 (0.1)	(-0.8, -0.5)	-0.2 (0.1)	(-0.4, -0.1)	0.011 *
		Placebo	290	261 (90.0)	-0.4 (0.1)	(-0.6, -0.3)			
>= 65 years	Week 4	CR845	144	130 (90.3)	-0.6 (0.1)	(-0.8, -0.4)	-0.0 (0.1)	(-0.3, 0.2)	0.855
		Placebo	135	129 (95.6)	-0.5 (0.1)	(-0.7, -0.3)			
< 65 years	Week 8	CR845	282	239 (84.8)	-0.9 (0.1)	(-1.1, -0.7)	-0.2 (0.1)	(-0.4, 0.0)	0.115
		Placebo	290	264 (91.0)	-0.7 (0.1)	(-0.9, -0.6)			
>= 65 years	Week 8	CR845	144	126 (87.5)	-0.8 (0.1)	(-1.0, -0.6)	-0.2 (0.1)	(-0.5, 0.1)	0.110
		Placebo	135	128 (94.8)	-0.6 (0.1)	(-0.8, -0.4)			
< 65 years	Week 10	CR845	282	239 (84.8)	-1.1 (0.1)	(-1.2, -0.9)	-0.2 (0.1)	(-0.4, 0.0)	0.060
		Placebo	290	259 (89.3)	-0.9 (0.1)	(-1.0, -0.7)			
>= 65 years	Week 10	CR845	144	120 (83.3)	-0.9 (0.1)	(-1.1, -0.7)	-0.2 (0.1)	(-0.5, 0.1)	0.111
		Placebo	135	125 (92.6)	-0.7 (0.1)	(-0.9, -0.4)			
< 65 years	Week 12	CR845	282	241 (85.5)	-1.1 (0.1)	(-1.3, -1.0)	-0.2 (0.1)	(-0.4, -0.0)	0.044 *
		Placebo	290	260 (89.7)	-0.9 (0.1)	(-1.1, -0.7)			
>= 65 years	Week 12	CR845	144	121 (84.0)	-0.9 (0.1)	(-1.1, -0.7)	0.0 (0.1)	(-0.2, 0.3)	0.803
		Placebo	135	125 (92.6)	-0.9 (0.1)	(-1.1, -0.7)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DNC_ISCB: Change from baseline in 5-D disability score - MMRM results by sex
ITT

Change from baseline in 5-D disability score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
B: Sex									0.018 i
Male	Week 4	CR845	249	221 (88.8)	-0.5 (0.1)	(-0.7, -0.4)	-0.1 (0.1)	(-0.3, 0.1)	0.394
		Placebo	258	231 (89.5)	-0.4 (0.1)	(-0.6, -0.3)			
Female	Week 4	CR845	177	159 (89.8)	-0.8 (0.1)	(-1.0, -0.6)	-0.3 (0.1)	(-0.5, -0.1)	0.017 *
		Placebo	167	159 (95.2)	-0.5 (0.1)	(-0.7, -0.3)			
Male	Week 8	CR845	249	212 (85.1)	-0.7 (0.1)	(-0.9, -0.6)	-0.0 (0.1)	(-0.2, 0.2)	0.687
		Placebo	258	238 (92.2)	-0.7 (0.1)	(-0.9, -0.5)			
Female	Week 8	CR845	177	153 (86.4)	-1.1 (0.1)	(-1.2, -0.9)	-0.4 (0.1)	(-0.6, -0.1)	0.003 *
		Placebo	167	154 (92.2)	-0.7 (0.1)	(-0.9, -0.5)			
Male	Week 10	CR845	249	207 (83.1)	-0.8 (0.1)	(-1.0, -0.7)	-0.0 (0.1)	(-0.2, 0.2)	0.897
		Placebo	258	233 (90.3)	-0.8 (0.1)	(-1.0, -0.7)			
Female	Week 10	CR845	177	152 (85.9)	-1.2 (0.1)	(-1.4, -1.0)	-0.5 (0.1)	(-0.7, -0.2)	<0.001 *
		Placebo	167	151 (90.4)	-0.8 (0.1)	(-1.0, -0.6)			
Male	Week 12	CR845	249	207 (83.1)	-0.9 (0.1)	(-1.1, -0.7)	-0.0 (0.1)	(-0.2, 0.2)	0.865
		Placebo	258	232 (89.9)	-0.9 (0.1)	(-1.1, -0.7)			
Female	Week 12	CR845	177	155 (87.6)	-1.2 (0.1)	(-1.4, -1.0)	-0.3 (0.1)	(-0.6, -0.0)	0.036 *
		Placebo	167	153 (91.6)	-0.9 (0.1)	(-1.1, -0.7)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DNC_ISCC: Change from baseline in 5-D disability score - MMRM results by race
ITT

Change from baseline in 5-D disability score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
C: Race									0.932
Black/African American	Week 4	CR845	135	114 (84.4)	-0.7 (0.1)	(-0.9, -0.4)	-0.1 (0.1)	(-0.4, 0.2)	0.397
		Placebo	114	101 (88.6)	-0.5 (0.1)	(-0.8, -0.3)			
White	Week 4	CR845	255	234 (91.8)	-0.6 (0.1)	(-0.8, -0.5)	-0.2 (0.1)	(-0.4, 0.0)	0.054
		Placebo	262	243 (92.7)	-0.5 (0.1)	(-0.6, -0.3)			
Other	Week 4	CR845	35	31 (88.6)	-0.8 (0.2)	(-1.3, -0.4)	-0.2 (0.2)	(-0.7, 0.3)	0.446
		Placebo	47	44 (93.6)	-0.6 (0.2)	(-1.0, -0.2)			
Black/African American	Week 8	CR845	135	111 (82.2)	-0.9 (0.1)	(-1.2, -0.7)	-0.2 (0.2)	(-0.5, 0.1)	0.273
		Placebo	114	105 (92.1)	-0.8 (0.1)	(-1.0, -0.5)			
White	Week 8	CR845	255	222 (87.1)	-0.9 (0.1)	(-1.0, -0.7)	-0.2 (0.1)	(-0.4, 0.0)	0.082
		Placebo	262	242 (92.4)	-0.7 (0.1)	(-0.8, -0.5)			
Other	Week 8	CR845	35	31 (88.6)	-0.9 (0.2)	(-1.3, -0.4)	-0.2 (0.2)	(-0.6, 0.3)	0.500
		Placebo	47	43 (91.5)	-0.7 (0.2)	(-1.1, -0.3)			
Black/African American	Week 10	CR845	135	106 (78.5)	-1.1 (0.1)	(-1.3, -0.8)	-0.1 (0.2)	(-0.4, 0.2)	0.536
		Placebo	114	102 (89.5)	-1.0 (0.1)	(-1.2, -0.7)			
White	Week 10	CR845	255	223 (87.5)	-0.9 (0.1)	(-1.1, -0.8)	-0.2 (0.1)	(-0.4, -0.0)	0.037 *
		Placebo	262	238 (90.8)	-0.7 (0.1)	(-0.9, -0.6)			
Other	Week 10	CR845	35	29 (82.9)	-1.4 (0.2)	(-1.9, -1.0)	-0.5 (0.3)	(-1.1, -0.0)	0.044 *
		Placebo	47	42 (89.4)	-0.9 (0.2)	(-1.3, -0.5)			
Black/African American	Week 12	CR845	135	109 (80.7)	-1.1 (0.1)	(-1.4, -0.9)	-0.1 (0.2)	(-0.5, 0.2)	0.394
		Placebo	114	103 (90.4)	-1.0 (0.1)	(-1.2, -0.7)			
White	Week 12	CR845	255	223 (87.5)	-1.0 (0.1)	(-1.2, -0.9)	-0.2 (0.1)	(-0.4, 0.0)	0.098
		Placebo	262	239 (91.2)	-0.9 (0.1)	(-1.0, -0.7)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DNC_ISCC: Change from baseline in 5-D disability score - MMRM results by race
ITT

Change from baseline in 5-D disability score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Other	Week 12	CR845	35	29 (82.9)	-1.1 (0.3)	(-1.6, -0.5)	0.1 (0.3)	(-0.5, 0.7)	0.778
		Placebo	47	41 (87.2)	-1.2 (0.2)	(-1.6, -0.7)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DNC_ISCD: Change from baseline in 5-D disability score - MMRM results by baseline WI-NRS
ITT

Change from baseline in 5-D disability score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
D: Baseline worst itching NRS score (WI-NRS)									0.306
>= 4 to < 7	Week 4	CR845	185	168 (90.8)	-0.7 (0.1)	(-0.9, -0.5)	-0.3 (0.1)	(-0.5, -0.0)	0.019 *
		Placebo	193	179 (92.7)	-0.4 (0.1)	(-0.6, -0.2)			
>= 7	Week 4	CR845	241	212 (88.0)	-0.7 (0.1)	(-0.8, -0.5)	-0.1 (0.1)	(-0.3, 0.1)	0.261
		Placebo	232	211 (90.9)	-0.6 (0.1)	(-0.7, -0.4)			
>= 4 to < 7	Week 8	CR845	185	163 (88.1)	-0.8 (0.1)	(-1.0, -0.6)	-0.3 (0.1)	(-0.5, -0.0)	0.030 *
		Placebo	193	177 (91.7)	-0.6 (0.1)	(-0.7, -0.4)			
>= 7	Week 8	CR845	241	202 (83.8)	-1.0 (0.1)	(-1.1, -0.8)	-0.1 (0.1)	(-0.3, 0.1)	0.241
		Placebo	232	215 (92.7)	-0.8 (0.1)	(-1.0, -0.7)			
>= 4 to < 7	Week 10	CR845	185	160 (86.5)	-0.9 (0.1)	(-1.1, -0.7)	-0.3 (0.1)	(-0.5, -0.1)	0.010 *
		Placebo	193	173 (89.6)	-0.6 (0.1)	(-0.8, -0.4)			
>= 7	Week 10	CR845	241	199 (82.6)	-1.1 (0.1)	(-1.3, -0.9)	-0.1 (0.1)	(-0.4, 0.1)	0.226
		Placebo	232	211 (90.9)	-1.0 (0.1)	(-1.1, -0.8)			
>= 4 to < 7	Week 12	CR845	185	158 (85.4)	-1.0 (0.1)	(-1.2, -0.8)	-0.2 (0.1)	(-0.4, 0.0)	0.122
		Placebo	193	175 (90.7)	-0.8 (0.1)	(-1.0, -0.6)			
>= 7	Week 12	CR845	241	204 (84.6)	-1.1 (0.1)	(-1.3, -0.9)	-0.1 (0.1)	(-0.3, 0.1)	0.392
		Placebo	232	210 (90.5)	-1.0 (0.1)	(-1.2, -0.8)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DNC_ISCE: Change from baseline in 5-D disability score - MMRM results by specific medical condition
ITT

Change from baseline in 5-D disability score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
E: Presence of specific medical conditions									0.946
No	Week 4	CR845	359	318 (88.6)	-0.7 (0.1)	(-0.8, -0.6)	-0.2 (0.1)	(-0.3, -0.0)	0.026 *
		Placebo	360	330 (91.7)	-0.5 (0.1)	(-0.6, -0.4)			
Yes	Week 4	CR845	67	62 (92.5)	-0.6 (0.1)	(-0.9, -0.3)	-0.1 (0.2)	(-0.5, 0.3)	0.689
		Placebo	65	60 (92.3)	-0.5 (0.1)	(-0.8, -0.3)			
No	Week 8	CR845	359	306 (85.2)	-0.9 (0.1)	(-1.0, -0.7)	-0.2 (0.1)	(-0.3, 0.0)	0.083
		Placebo	360	328 (91.1)	-0.7 (0.1)	(-0.8, -0.6)			
Yes	Week 8	CR845	67	59 (88.1)	-1.0 (0.1)	(-1.3, -0.7)	-0.3 (0.2)	(-0.7, 0.1)	0.133
		Placebo	65	64 (98.5)	-0.7 (0.1)	(-1.0, -0.4)			
No	Week 10	CR845	359	302 (84.1)	-1.0 (0.1)	(-1.2, -0.9)	-0.2 (0.1)	(-0.4, -0.0)	0.015 *
		Placebo	360	322 (89.4)	-0.8 (0.1)	(-0.9, -0.7)			
Yes	Week 10	CR845	67	57 (85.1)	-1.1 (0.2)	(-1.4, -0.7)	-0.1 (0.2)	(-0.5, 0.3)	0.585
		Placebo	65	62 (95.4)	-0.9 (0.1)	(-1.2, -0.6)			
No	Week 12	CR845	359	303 (84.4)	-1.0 (0.1)	(-1.2, -0.9)	-0.1 (0.1)	(-0.3, 0.1)	0.223
		Placebo	360	322 (89.4)	-0.9 (0.1)	(-1.0, -0.8)			
Yes	Week 12	CR845	67	59 (88.1)	-1.3 (0.1)	(-1.6, -1.0)	-0.2 (0.2)	(-0.6, 0.2)	0.348
		Placebo	65	63 (96.9)	-1.1 (0.1)	(-1.4, -0.8)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor previous use of anti-itch medication is also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DNC_ISCF: Change from baseline in 5-D disability score - MMRM results by use of concomitant itch medication
ITT

Change from baseline in 5-D disability score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
F: Use of concomitant itch medication									0.913
No	Week 4	CR845	267	245 (91.8)	-0.6 (0.1)	(-0.7, -0.4)	-0.2 (0.1)	(-0.4, -0.0)	0.028 *
		Placebo	262	240 (91.6)	-0.4 (0.1)	(-0.5, -0.2)			
Yes	Week 4	CR845	159	135 (84.9)	-0.7 (0.1)	(-0.9, -0.5)	-0.1 (0.1)	(-0.4, 0.2)	0.391
		Placebo	163	150 (92.0)	-0.6 (0.1)	(-0.8, -0.4)			
No	Week 8	CR845	267	236 (88.4)	-0.8 (0.1)	(-1.0, -0.7)	-0.2 (0.1)	(-0.3, 0.0)	0.116
		Placebo	262	242 (92.4)	-0.7 (0.1)	(-0.8, -0.5)			
Yes	Week 8	CR845	159	129 (81.1)	-1.0 (0.1)	(-1.2, -0.7)	-0.2 (0.1)	(-0.5, 0.1)	0.118
		Placebo	163	150 (92.0)	-0.7 (0.1)	(-0.9, -0.5)			
No	Week 10	CR845	267	229 (85.8)	-1.0 (0.1)	(-1.1, -0.8)	-0.2 (0.1)	(-0.4, -0.0)	0.041 *
		Placebo	262	238 (90.8)	-0.8 (0.1)	(-0.9, -0.6)			
Yes	Week 10	CR845	159	130 (81.8)	-1.1 (0.1)	(-1.3, -0.9)	-0.2 (0.1)	(-0.5, 0.1)	0.168
		Placebo	163	146 (89.6)	-0.9 (0.1)	(-1.1, -0.7)			
No	Week 12	CR845	267	232 (86.9)	-1.0 (0.1)	(-1.1, -0.8)	-0.1 (0.1)	(-0.3, 0.1)	0.574
		Placebo	262	241 (92.0)	-0.9 (0.1)	(-1.1, -0.7)			
Yes	Week 12	CR845	159	130 (81.8)	-1.2 (0.1)	(-1.4, -1.0)	-0.2 (0.1)	(-0.5, 0.0)	0.074
		Placebo	163	144 (88.3)	-0.9 (0.1)	(-1.1, -0.7)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor presence of medical condition is also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DVC_ISCA: Change from baseline in 5-D distribution score - MMRM results by age
ITT

Change from baseline in 5-D distribution score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
A: Age									0.383
< 65 years	Week 4	CR845	282	250 (88.7)	-0.4 (0.1)	(-0.6, -0.3)	-0.3 (0.1)	(-0.4, -0.1)	0.002 *
		Placebo	290	261 (90.0)	-0.2 (0.1)	(-0.3, -0.1)			
>= 65 years	Week 4	CR845	144	130 (90.3)	-0.4 (0.1)	(-0.6, -0.2)	-0.2 (0.1)	(-0.4, 0.1)	0.138
		Placebo	135	129 (95.6)	-0.2 (0.1)	(-0.4, 0.0)			
< 65 years	Week 8	CR845	282	239 (84.8)	-0.6 (0.1)	(-0.7, -0.4)	-0.2 (0.1)	(-0.4, -0.1)	0.011 *
		Placebo	290	264 (91.0)	-0.3 (0.1)	(-0.5, -0.2)			
>= 65 years	Week 8	CR845	144	126 (87.5)	-0.4 (0.1)	(-0.6, -0.2)	-0.2 (0.1)	(-0.4, 0.1)	0.134
		Placebo	135	128 (94.8)	-0.3 (0.1)	(-0.4, -0.1)			
< 65 years	Week 10	CR845	282	239 (84.8)	-0.6 (0.1)	(-0.7, -0.5)	-0.3 (0.1)	(-0.5, -0.1)	0.003 *
		Placebo	290	259 (89.3)	-0.3 (0.1)	(-0.5, -0.2)			
>= 65 years	Week 10	CR845	144	120 (83.3)	-0.4 (0.1)	(-0.6, -0.2)	-0.0 (0.1)	(-0.3, 0.2)	0.731
		Placebo	135	125 (92.6)	-0.4 (0.1)	(-0.6, -0.2)			
< 65 years	Week 12	CR845	282	241 (85.5)	-0.7 (0.1)	(-0.8, -0.5)	-0.4 (0.1)	(-0.6, -0.2)	<0.001 *
		Placebo	290	260 (89.7)	-0.3 (0.1)	(-0.5, -0.2)			
>= 65 years	Week 12	CR845	144	121 (84.0)	-0.4 (0.1)	(-0.6, -0.2)	-0.2 (0.1)	(-0.4, 0.1)	0.186
		Placebo	135	125 (92.6)	-0.3 (0.1)	(-0.5, -0.1)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DVC_ISCB: Change from baseline in 5-D distribution score - MMRM results by sex
ITT

Change from baseline in 5-D distribution score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
B: Sex									0.185
Male	Week 4	CR845	249	221 (88.8)	-0.3 (0.1)	(-0.4, -0.1)	-0.1 (0.1)	(-0.3, 0.1)	0.218
		Placebo	258	231 (89.5)	-0.2 (0.1)	(-0.3, -0.0)			
Female	Week 4	CR845	177	159 (89.8)	-0.6 (0.1)	(-0.8, -0.4)	-0.4 (0.1)	(-0.6, -0.2)	<0.001 *
		Placebo	167	159 (95.2)	-0.2 (0.1)	(-0.4, -0.0)			
Male	Week 8	CR845	249	212 (85.1)	-0.5 (0.1)	(-0.6, -0.3)	-0.2 (0.1)	(-0.4, -0.0)	0.019 *
		Placebo	258	238 (92.2)	-0.3 (0.1)	(-0.4, -0.1)			
Female	Week 8	CR845	177	153 (86.4)	-0.6 (0.1)	(-0.8, -0.4)	-0.2 (0.1)	(-0.5, 0.0)	0.070
		Placebo	167	154 (92.2)	-0.4 (0.1)	(-0.6, -0.2)			
Male	Week 10	CR845	249	207 (83.1)	-0.4 (0.1)	(-0.6, -0.3)	-0.2 (0.1)	(-0.4, 0.0)	0.088
		Placebo	258	233 (90.3)	-0.3 (0.1)	(-0.4, -0.1)			
Female	Week 10	CR845	177	152 (85.9)	-0.7 (0.1)	(-0.9, -0.5)	-0.2 (0.1)	(-0.5, -0.0)	0.046 *
		Placebo	167	151 (90.4)	-0.4 (0.1)	(-0.6, -0.3)			
Male	Week 12	CR845	249	207 (83.1)	-0.5 (0.1)	(-0.6, -0.3)	-0.3 (0.1)	(-0.5, -0.1)	0.005 *
		Placebo	258	232 (89.9)	-0.2 (0.1)	(-0.4, -0.1)			
Female	Week 12	CR845	177	155 (87.6)	-0.8 (0.1)	(-0.9, -0.6)	-0.3 (0.1)	(-0.6, -0.1)	0.006 *
		Placebo	167	153 (91.6)	-0.4 (0.1)	(-0.6, -0.2)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DVC_ISCC: Change from baseline in 5-D distribution score - MMRM results by race
ITT

Change from baseline in 5-D distribution score					Repeated measures analysis					
					Change from Baseline		Treatment Difference			
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value	
C: Race									0.868	
Black/African American	Week 4	CR845	135	114 (84.4)	-0.4 (0.1)	(-0.6, -0.2)	-0.3 (0.1)	(-0.6, -0.0)	0.019	*
		Placebo	114	101 (88.6)	-0.1 (0.1)	(-0.3, 0.1)				
White	Week 4	CR845	255	234 (91.8)	-0.4 (0.1)	(-0.6, -0.3)	-0.2 (0.1)	(-0.4, -0.0)	0.027	*
		Placebo	262	243 (92.7)	-0.2 (0.1)	(-0.4, -0.1)				
Other	Week 4	CR845	35	31 (88.6)	-0.5 (0.2)	(-0.9, -0.1)	-0.4 (0.2)	(-0.9, 0.1)	0.097	
		Placebo	47	44 (93.6)	-0.1 (0.2)	(-0.5, 0.3)				
Black/African American	Week 8	CR845	135	111 (82.2)	-0.5 (0.1)	(-0.7, -0.3)	-0.2 (0.1)	(-0.5, 0.1)	0.113	
		Placebo	114	105 (92.1)	-0.3 (0.1)	(-0.5, -0.1)				
White	Week 8	CR845	255	222 (87.1)	-0.6 (0.1)	(-0.7, -0.4)	-0.2 (0.1)	(-0.4, -0.1)	0.010	*
		Placebo	262	242 (92.4)	-0.3 (0.1)	(-0.5, -0.2)				
Other	Week 8	CR845	35	31 (88.6)	-0.4 (0.2)	(-0.8, 0.0)	-0.1 (0.2)	(-0.6, 0.3)	0.619	
		Placebo	47	43 (91.5)	-0.3 (0.2)	(-0.7, 0.1)				
Black/African American	Week 10	CR845	135	106 (78.5)	-0.5 (0.1)	(-0.7, -0.3)	-0.2 (0.1)	(-0.5, 0.1)	0.201	
		Placebo	114	102 (89.5)	-0.3 (0.1)	(-0.6, -0.1)				
White	Week 10	CR845	255	223 (87.5)	-0.6 (0.1)	(-0.7, -0.4)	-0.2 (0.1)	(-0.4, -0.0)	0.030	*
		Placebo	262	238 (90.8)	-0.4 (0.1)	(-0.5, -0.2)				
Other	Week 10	CR845	35	29 (82.9)	-0.5 (0.2)	(-0.9, -0.1)	-0.3 (0.2)	(-0.7, 0.2)	0.247	
		Placebo	47	42 (89.4)	-0.2 (0.2)	(-0.6, 0.1)				
Black/African American	Week 12	CR845	135	109 (80.7)	-0.6 (0.1)	(-0.8, -0.4)	-0.4 (0.1)	(-0.7, -0.1)	0.005	*
		Placebo	114	103 (90.4)	-0.2 (0.1)	(-0.4, 0.0)				
White	Week 12	CR845	255	223 (87.5)	-0.7 (0.1)	(-0.8, -0.5)	-0.3 (0.1)	(-0.5, -0.2)	<0.001	*
		Placebo	262	239 (91.2)	-0.3 (0.1)	(-0.5, -0.2)				

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DVC_ISCC: Change from baseline in 5-D distribution score - MMRM results by race
ITT

Change from baseline in 5-D distribution score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Other	Week 12	CR845	35	29 (82.9)	-0.3 (0.2)	(-0.7, 0.2)	0.1 (0.2)	(-0.3, 0.6)	0.547
		Placebo	47	41 (87.2)	-0.4 (0.2)	(-0.8, -0.0)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DVC_ISCD: Change from baseline in 5-D distribution score - MMRM results by baseline WI-NRS
ITT

Change from baseline in 5-D distribution score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
D: Baseline worst itching NRS score (WI-NRS)									0.367
>= 4 to < 7	Week 4	CR845	185	168 (90.8)	-0.4 (0.1)	(-0.6, -0.2)	-0.3 (0.1)	(-0.5, -0.2)	<0.001 *
		Placebo	193	179 (92.7)	-0.1 (0.1)	(-0.2, 0.1)			
>= 7	Week 4	CR845	241	212 (88.0)	-0.5 (0.1)	(-0.6, -0.3)	-0.1 (0.1)	(-0.3, 0.0)	0.122
		Placebo	232	211 (90.9)	-0.3 (0.1)	(-0.5, -0.2)			
>= 4 to < 7	Week 8	CR845	185	163 (88.1)	-0.4 (0.1)	(-0.6, -0.3)	-0.2 (0.1)	(-0.4, -0.0)	0.018 *
		Placebo	193	177 (91.7)	-0.2 (0.1)	(-0.4, -0.0)			
>= 7	Week 8	CR845	241	202 (83.8)	-0.6 (0.1)	(-0.8, -0.5)	-0.2 (0.1)	(-0.4, 0.0)	0.050
		Placebo	232	215 (92.7)	-0.4 (0.1)	(-0.6, -0.2)			
>= 4 to < 7	Week 10	CR845	185	160 (86.5)	-0.5 (0.1)	(-0.7, -0.3)	-0.3 (0.1)	(-0.5, -0.1)	0.005 *
		Placebo	193	173 (89.6)	-0.2 (0.1)	(-0.4, -0.0)			
>= 7	Week 10	CR845	241	199 (82.6)	-0.6 (0.1)	(-0.8, -0.4)	-0.1 (0.1)	(-0.3, 0.1)	0.234
		Placebo	232	211 (90.9)	-0.5 (0.1)	(-0.6, -0.3)			
>= 4 to < 7	Week 12	CR845	185	158 (85.4)	-0.5 (0.1)	(-0.7, -0.4)	-0.3 (0.1)	(-0.5, -0.1)	0.008 *
		Placebo	193	175 (90.7)	-0.3 (0.1)	(-0.4, -0.1)			
>= 7	Week 12	CR845	241	204 (84.6)	-0.7 (0.1)	(-0.8, -0.5)	-0.3 (0.1)	(-0.5, -0.1)	0.002 *
		Placebo	232	210 (90.5)	-0.3 (0.1)	(-0.5, -0.2)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DVC_ISCE: Change from baseline in 5-D distribution score - MMRM results by specific medical condition
ITT

Change from baseline in 5-D distribution score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
E: Presence of specific medical conditions									0.790
No	Week 4	CR845	359	318 (88.6)	-0.4 (0.1)	(-0.5, -0.3)	-0.2 (0.1)	(-0.4, -0.1)	0.001 *
		Placebo	360	330 (91.7)	-0.2 (0.1)	(-0.3, -0.1)			
Yes	Week 4	CR845	67	62 (92.5)	-0.4 (0.1)	(-0.7, -0.2)	-0.2 (0.2)	(-0.5, 0.2)	0.270
		Placebo	65	60 (92.3)	-0.2 (0.1)	(-0.5, -0.0)			
No	Week 8	CR845	359	306 (85.2)	-0.6 (0.1)	(-0.7, -0.4)	-0.3 (0.1)	(-0.4, -0.1)	0.002 *
		Placebo	360	328 (91.1)	-0.3 (0.1)	(-0.4, -0.2)			
Yes	Week 8	CR845	67	59 (88.1)	-0.5 (0.1)	(-0.7, -0.2)	-0.0 (0.2)	(-0.4, 0.3)	0.819
		Placebo	65	64 (98.5)	-0.4 (0.1)	(-0.7, -0.2)			
No	Week 10	CR845	359	302 (84.1)	-0.6 (0.1)	(-0.7, -0.4)	-0.2 (0.1)	(-0.4, -0.0)	0.014 *
		Placebo	360	322 (89.4)	-0.4 (0.1)	(-0.5, -0.2)			
Yes	Week 10	CR845	67	57 (85.1)	-0.6 (0.1)	(-0.8, -0.3)	-0.2 (0.2)	(-0.6, 0.2)	0.316
		Placebo	65	62 (95.4)	-0.4 (0.1)	(-0.6, -0.1)			
No	Week 12	CR845	359	303 (84.4)	-0.6 (0.1)	(-0.7, -0.5)	-0.3 (0.1)	(-0.4, -0.1)	0.001 *
		Placebo	360	322 (89.4)	-0.3 (0.1)	(-0.4, -0.2)			
Yes	Week 12	CR845	67	59 (88.1)	-0.7 (0.1)	(-1.0, -0.5)	-0.4 (0.2)	(-0.8, -0.1)	0.010 *
		Placebo	65	63 (96.9)	-0.3 (0.1)	(-0.5, -0.1)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor previous use of anti-itch medication is also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DVC_ISCF: Change from baseline in 5-D distribution score - MMRM results by use of concomitant itch medication
ITT

Change from baseline in 5-D distribution score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
F: Use of concomitant itch medication									0.879
No	Week 4	CR845	267	245 (91.8)	-0.4 (0.1)	(-0.5, -0.2)	-0.3 (0.1)	(-0.4, -0.1)	0.002 *
		Placebo	262	240 (91.6)	-0.1 (0.1)	(-0.3, 0.0)			
Yes	Week 4	CR845	159	135 (84.9)	-0.5 (0.1)	(-0.7, -0.3)	-0.2 (0.1)	(-0.4, 0.0)	0.125
		Placebo	163	150 (92.0)	-0.3 (0.1)	(-0.5, -0.1)			
No	Week 8	CR845	267	236 (88.4)	-0.5 (0.1)	(-0.6, -0.3)	-0.2 (0.1)	(-0.4, -0.1)	0.009 *
		Placebo	262	242 (92.4)	-0.2 (0.1)	(-0.4, -0.1)			
Yes	Week 8	CR845	159	129 (81.1)	-0.6 (0.1)	(-0.8, -0.4)	-0.2 (0.1)	(-0.4, 0.1)	0.139
		Placebo	163	150 (92.0)	-0.4 (0.1)	(-0.6, -0.2)			
No	Week 10	CR845	267	229 (85.8)	-0.5 (0.1)	(-0.6, -0.3)	-0.2 (0.1)	(-0.4, 0.0)	0.069
		Placebo	262	238 (90.8)	-0.3 (0.1)	(-0.4, -0.1)			
Yes	Week 10	CR845	159	130 (81.8)	-0.7 (0.1)	(-0.9, -0.5)	-0.2 (0.1)	(-0.5, 0.0)	0.053
		Placebo	163	146 (89.6)	-0.4 (0.1)	(-0.6, -0.2)			
No	Week 12	CR845	267	232 (86.9)	-0.5 (0.1)	(-0.7, -0.3)	-0.3 (0.1)	(-0.5, -0.1)	0.004 *
		Placebo	262	241 (92.0)	-0.2 (0.1)	(-0.4, -0.1)			
Yes	Week 12	CR845	159	130 (81.8)	-0.7 (0.1)	(-0.9, -0.6)	-0.4 (0.1)	(-0.6, -0.1)	0.004 *
		Placebo	163	144 (88.3)	-0.4 (0.1)	(-0.6, -0.2)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor presence of medical condition is also included in the model.
Source Data: afived_i, created on: 17FEB2022

Table IT2DTCD5_ISPA: Decrease of 5-D total score of at least 5 points by age
ITT

Decrease of 5-D total score of at least 5 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	A: Age										0.253
	< 65 years	282	239 (84.8)	123 (43.6) [37.7, 49.6]	290	260 (89.7)	107 (36.9) [31.3, 42.7]	1.182 [0.967, 1.445]	1.323 [0.946, 1.850]	6.7 [-1.7, 15.1]	0.102
	>= 65 years	144	120 (83.3)	60 (41.7) [33.5, 50.2]	135	125 (92.6)	58 (43.0) [34.5, 51.8]	0.970 [0.737, 1.276]	0.948 [0.590, 1.525]	-1.3 [-13.6, 11.0]	0.827

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived_i, created on: 17FEB2022

Table IT2DTCD5_ISPB: Decrease of 5-D total score of at least 5 points by sex
ITT

Decrease of 5-D total score of at least 5 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	B: Sex										0.580
	Male	249	207 (83.1)	97 (39.0) [32.9, 45.3]	258	232 (89.9)	95 (36.8) [30.9, 43.0]	1.058 [0.847, 1.322]	1.095 [0.765, 1.568]	2.1 [-6.7, 11.0]	0.621
	Female	177	152 (85.9)	86 (48.6) [41.0, 56.2]	167	153 (91.6)	70 (41.9) [34.3, 49.8]	1.159 [0.917, 1.465]	1.310 [0.855, 2.005]	6.7 [-4.4, 17.8]	0.215

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived_i, created on: 17FEB2022

Table IT2DTCD5_ISPC: Decrease of 5-D total score of at least 5 points by race
ITT

Decrease of 5-D total score of at least 5 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	C: Race										0.145
	Black/African American	135	107 (79.3)	57 (42.2) [33.8, 51.0]	114	103 (90.4)	40 (35.1) [26.4, 44.6]	1.203 [0.875, 1.654]	1.352 [0.808, 2.261]	7.1 [-5.8, 20.0]	0.251
	White	255	222 (87.1)	114 (44.7) [38.5, 51.0]	262	239 (91.2)	100 (38.2) [32.3, 44.3]	1.171 [0.953, 1.439]	1.310 [0.922, 1.860]	6.5 [-2.3, 15.4]	0.132
	Other	35	29 (82.9)	12 (34.3) [19.1, 52.2]	47	41 (87.2)	24 (51.1) [36.1, 65.9]	0.671 [0.392, 1.149]	0.500 [0.203, 1.233]	-16.8 [-40.5, 7.0]	0.132

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived_i, created on: 17FEB2022

Table IT2DTCD5_ISPD: Decrease of 5-D total score of at least 5 points by baseline WI-NRS
ITT

Decrease of 5-D total score of at least 5 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.504
	>= 4 to < 7	185	157 (84.9)	67 (36.2) [29.3, 43.6]	193	175 (90.7)	59 (30.6) [24.2, 37.6]	1.185 [0.890, 1.577]	1.290 [0.840, 1.980]	5.6 [-4.4, 15.7]	0.245
	>= 7	241	202 (83.8)	116 (48.1) [41.7, 54.6]	232	210 (90.5)	106 (45.7) [39.2, 52.3]	1.053 [0.869, 1.276]	1.103 [0.769, 1.583]	2.4 [-7.0, 11.9]	0.595

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived_i, created on: 17FEB2022

Table IT2DTCD5_ISPE: Decrease of 5-D total score of at least 5 points by specific medical condition
ITT

Decrease of 5-D total score of at least 5 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	E: Presence of specific medical conditions										0.833
	No	359	301 (83.8)	150 (41.8) [36.6, 47.1]	360	322 (89.4)	135 (37.5) [32.5, 42.7]	1.114 [0.930, 1.335]	1.196 [0.887, 1.613]	4.3 [-3.1, 11.7]	0.241
	Yes	67	58 (86.6)	33 (49.3) [36.8, 61.8]	65	63 (96.9)	30 (46.2) [33.7, 59.0]	1.067 [0.746, 1.526]	1.132 [0.572, 2.243]	3.1 [-15.5, 21.7]	0.722

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived_i, created on: 17FEB2022

Table IT2DTCD5_ISPF: Decrease of 5-D total score of at least 5 points by use of concomitant itch medication
ITT

Decrease of 5-D total score of at least 5 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	F: Use of concomitant itch medication										0.651
	No	267	231 (86.5)	115 (43.1) [37.1, 49.2]	262	241 (92.0)	105 (40.1) [34.1, 46.3]	1.075 [0.878, 1.316]	1.131 [0.800, 1.599]	3.0 [-5.8, 11.8]	0.485
	Yes	159	128 (80.5)	68 (42.8) [35.0, 50.8]	163	144 (88.3)	60 (36.8) [29.4, 44.7]	1.162 [0.887, 1.522]	1.283 [0.820, 2.006]	6.0 [-5.3, 17.3]	0.276

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived_i, created on: 17FEB2022

Table IT2DDCD1_ISPA: Decrease of 5-D degree score of at least 1 point by age
ITT

Decrease of 5-D degree score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	A: Age										0.802
	< 65 years	282	241 (85.5)	166 (58.9) [52.9, 64.7]	290	260 (89.7)	158 (54.5) [48.6, 60.3]	1.080 [0.936, 1.247]	1.196 [0.859, 1.665]	4.4 [-4.1, 12.8]	0.291
	>= 65 years	144	121 (84.0)	78 (54.2) [45.7, 62.5]	135	125 (92.6)	70 (51.9) [43.1, 60.5]	1.045 [0.837, 1.303]	1.097 [0.685, 1.757]	2.3 [-10.1, 14.7]	0.699

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived_i, created on: 17FEB2022

Table IT2DDCD1_ISPB: Decrease of 5-D degree score of at least 1 point by sex
ITT

Decrease of 5-D degree score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	B: Sex										0.102	
	Male	249	207 (83.1)	130 (52.2) [45.8, 58.6]	258	232 (89.9)	138 (53.5) [47.2, 59.7]	0.976 [0.828, 1.151]	0.950 [0.670, 1.346]	-1.3 [-10.4, 7.8]	0.773	
	Female	177	155 (87.6)	114 (64.4) [56.9, 71.4]	167	153 (91.6)	90 (53.9) [46.0, 61.6]	1.195 [1.000, 1.428]	1.548 [1.004, 2.386]	10.5 [-0.4, 21.4]	0.048	*

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived_i, created on: 17FEB2022

Table IT2DDCD1_ISPC: Decrease of 5-D degree score of at least 1 point by race
ITT

Decrease of 5-D degree score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	C: Race										0.378
	Black/African American	135	109 (80.7)	79 (58.5) [49.7, 66.9]	114	103 (90.4)	58 (50.9) [41.3, 60.4]	1.150 [0.914, 1.447]	1.362 [0.824, 2.250]	7.6 [-5.5, 20.8]	0.228
	White	255	223 (87.5)	146 (57.3) [50.9, 63.4]	262	239 (91.2)	139 (53.1) [46.8, 59.2]	1.079 [0.924, 1.261]	1.185 [0.838, 1.677]	4.2 [-4.8, 13.2]	0.337
	Other	35	29 (82.9)	18 (51.4) [34.0, 68.6]	47	41 (87.2)	29 (61.7) [46.4, 75.5]	0.833 [0.563, 1.235]	0.657 [0.271, 1.594]	-10.3 [-34.4, 13.8]	0.355

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived_i, created on: 17FEB2022

Table IT2DDCD1_ISPD: Decrease of 5-D degree score of at least 1 point by baseline WI-NRS
ITT

Decrease of 5-D degree score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.259
	>= 4 to < 7	185	158 (85.4)	99 (53.5) [46.0, 60.9]	193	175 (90.7)	89 (46.1) [38.9, 53.4]	1.160 [0.947, 1.422]	1.345 [0.898, 2.016]	7.4 [-3.2, 18.0]	0.151
	>= 7	241	204 (84.6)	145 (60.2) [53.7, 66.4]	232	210 (90.5)	139 (59.9) [53.3, 66.3]	1.004 [0.867, 1.163]	1.011 [0.699, 1.460]	0.3 [-9.0, 9.5]	0.955

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived_i, created on: 17FEB2022

Table IT2DDCD1_ISPE: Decrease of 5-D degree score of at least 1 point by specific medical condition
ITT

Decrease of 5-D degree score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	E: Presence of specific medical conditions										0.869
	No	359	303 (84.4)	202 (56.3) [51.0, 61.5]	360	322 (89.4)	189 (52.5) [47.2, 57.8]	1.072 [0.937, 1.226]	1.164 [0.868, 1.562]	3.8 [-3.8, 11.3]	0.311
	Yes	67	59 (88.1)	42 (62.7) [50.0, 74.2]	65	63 (96.9)	39 (60.0) [47.1, 72.0]	1.045 [0.797, 1.370]	1.120 [0.556, 2.258]	2.7 [-15.4, 20.8]	0.752

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived_i, created on: 17FEB2022

Table IT2DDCD1_ISPF: Decrease of 5-D degree score of at least 1 point by use of concomitant itch medication
ITT

Decrease of 5-D degree score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	F: Use of concomitant itch medication										0.360
	No	267	232 (86.9)	151 (56.6) [50.4, 62.6]	262	241 (92.0)	145 (55.3) [49.1, 61.5]	1.022 [0.878, 1.189]	1.050 [0.745, 1.481]	1.2 [-7.6, 10.0]	0.779
	Yes	159	130 (81.8)	93 (58.5) [50.4, 66.2]	163	144 (88.3)	83 (50.9) [43.0, 58.8]	1.149 [0.941, 1.403]	1.358 [0.874, 2.109]	7.6 [-3.9, 19.0]	0.173

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived_i, created on: 17FEB2022

Table IT2DLCD1_ISPA: Decrease of 5-D duration score of at least 1 point by age
ITT

Decrease of 5-D duration score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	A: Age										0.378
	< 65 years	282	239 (84.8)	135 (47.9) [41.9, 53.9]	290	260 (89.7)	140 (48.3) [42.4, 54.2]	0.992 [0.836, 1.176]	0.984 [0.709, 1.366]	-0.4 [-8.9, 8.1]	0.923
	>= 65 years	144	121 (84.0)	76 (52.8) [44.3, 61.1]	135	125 (92.6)	63 (46.7) [38.0, 55.4]	1.131 [0.892, 1.434]	1.277 [0.798, 2.045]	6.1 [-6.3, 18.5]	0.308

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived_i, created on: 17FEB2022

Table IT2DLCD1_ISPB: Decrease of 5-D duration score of at least 1 point by sex
ITT

Decrease of 5-D duration score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	B: Sex										0.174
	Male	249	207 (83.1)	112 (45.0) [38.7, 51.4]	258	232 (89.9)	122 (47.3) [41.1, 53.6]	0.951 [0.788, 1.148]	0.911 [0.643, 1.292]	-2.3 [-11.4, 6.8]	0.603
	Female	177	153 (86.4)	99 (55.9) [48.3, 63.4]	167	153 (91.6)	81 (48.5) [40.7, 56.3]	1.153 [0.941, 1.414]	1.348 [0.882, 2.060]	7.4 [-3.7, 18.5]	0.169

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived_i, created on: 17FEB2022

Table IT2DLCD1_ISPC: Decrease of 5-D duration score of at least 1 point by race
ITT

Decrease of 5-D duration score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	C: Race										0.148
	Black/African American	135	108 (80.0)	69 (51.1) [42.4, 59.8]	114	103 (90.4)	57 (50.0) [40.5, 59.5]	1.022 [0.799, 1.308]	1.045 [0.635, 1.721]	1.1 [-12.2, 14.4]	0.862
	White	255	222 (87.1)	130 (51.0) [44.7, 57.3]	262	239 (91.2)	119 (45.4) [39.3, 51.7]	1.122 [0.938, 1.343]	1.250 [0.885, 1.766]	5.6 [-3.4, 14.5]	0.206
	Other	35	29 (82.9)	12 (34.3) [19.1, 52.2]	47	41 (87.2)	25 (53.2) [38.1, 67.9]	0.645 [0.379, 1.097]	0.459 [0.186, 1.133]	-18.9 [-42.6, 4.8]	0.091

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived_i, created on: 17FEB2022

Table IT2DLCD1_ISPD: Decrease of 5-D duration score of at least 1 point by baseline WI-NRS
ITT

Decrease of 5-D duration score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.572
	>= 4 to < 7	185	157 (84.9)	74 (40.0) [32.9, 47.4]	193	175 (90.7)	79 (40.9) [33.9, 48.2]	0.977 [0.765, 1.248]	0.962 [0.638, 1.451]	-0.9 [-11.4, 9.5]	0.854
	>= 7	241	203 (84.2)	137 (56.8) [50.3, 63.2]	232	210 (90.5)	124 (53.4) [46.8, 60.0]	1.064 [0.904, 1.252]	1.147 [0.798, 1.649]	3.4 [-6.0, 12.8]	0.458

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived_i, created on: 17FEB2022

Table IT2DLCD1_ISPE: Decrease of 5-D duration score of at least 1 point by specific medical condition
ITT

Decrease of 5-D duration score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	E: Presence of specific medical conditions										0.421
	No	359	301 (83.8)	178 (49.6) [44.3, 54.9]	360	322 (89.4)	168 (46.7) [41.4, 52.0]	1.062 [0.913, 1.237]	1.124 [0.839, 1.506]	2.9 [-4.7, 10.5]	0.434
	Yes	67	59 (88.1)	33 (49.3) [36.8, 61.8]	65	63 (96.9)	35 (53.8) [41.0, 66.3]	0.915 [0.657, 1.274]	0.832 [0.420, 1.648]	-4.6 [-23.1, 14.0]	0.599

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived_i, created on: 17FEB2022

Table IT2DLCD1_ISPF: Decrease of 5-D duration score of at least 1 point by use of concomitant itch medication
ITT

Decrease of 5-D duration score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	F: Use of concomitant itch medication										0.160
	No	267	231 (86.5)	135 (50.6) [44.4, 56.7]	262	241 (92.0)	118 (45.0) [38.9, 51.3]	1.123 [0.939, 1.342]	1.248 [0.887, 1.757]	5.5 [-3.4, 14.4]	0.204
	Yes	159	129 (81.1)	76 (47.8) [39.8, 55.9]	163	144 (88.3)	85 (52.1) [44.2, 60.0]	0.917 [0.736, 1.141]	0.840 [0.543, 1.301]	-4.3 [-15.9, 7.2]	0.436

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived_i, created on: 17FEB2022

Table IT2DNCD1_ISPA: Decrease of 5-D disability score of at least 1 point by age
ITT

Decrease of 5-D disability score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	A: Age										0.233
	< 65 years	282	241 (85.5)	163 (57.8) [51.8, 63.6]	290	260 (89.7)	159 (54.8) [48.9, 60.7]	1.054 [0.912, 1.218]	1.129 [0.811, 1.571]	3.0 [-5.5, 11.4]	0.474
	>= 65 years	144	121 (84.0)	75 (52.1) [43.6, 60.5]	135	125 (92.6)	78 (57.8) [49.0, 66.2]	0.901 [0.729, 1.115]	0.794 [0.495, 1.274]	-5.7 [-18.1, 6.7]	0.340

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived_i, created on: 17FEB2022

Table IT2DNCD1_ISPB: Decrease of 5-D disability score of at least 1 point by sex
ITT

Decrease of 5-D disability score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	B: Sex										0.907
	Male	249	207 (83.1)	136 (54.6) [48.2, 60.9]	258	232 (89.9)	140 (54.3) [48.0, 60.5]	1.007 [0.858, 1.180]	1.014 [0.715, 1.439]	0.4 [-8.7, 9.4]	0.936
	Female	177	155 (87.6)	102 (57.6) [50.0, 65.0]	167	153 (91.6)	97 (58.1) [50.2, 65.7]	0.992 [0.828, 1.188]	0.981 [0.640, 1.506]	-0.5 [-11.5, 10.6]	0.932

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived_i, created on: 17FEB2022

Table IT2DNCD1_ISPC: Decrease of 5-D disability score of at least 1 point by race
ITT

Decrease of 5-D disability score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	C: Race										0.584
	Black/African American	135	109 (80.7)	69 (51.1) [42.4, 59.8]	114	103 (90.4)	64 (56.1) [46.5, 65.4]	0.910 [0.722, 1.147]	0.817 [0.495, 1.348]	-5.0 [-18.3, 8.2]	0.429
	White	255	223 (87.5)	148 (58.0) [51.7, 64.2]	262	239 (91.2)	146 (55.7) [49.5, 61.8]	1.042 [0.896, 1.210]	1.099 [0.776, 1.557]	2.3 [-6.6, 11.2]	0.596
	Other	35	29 (82.9)	21 (60.0) [42.1, 76.1]	47	41 (87.2)	26 (55.3) [40.1, 69.8]	1.085 [0.747, 1.575]	1.212 [0.499, 2.943]	4.7 [-19.4, 28.7]	0.674

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived_i, created on: 17FEB2022

Table IT2DNCD1_ISPD: Decrease of 5-D disability score of at least 1 point by baseline WI-NRS
ITT

Decrease of 5-D disability score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.315
	>= 4 to < 7	185	158 (85.4)	102 (55.1) [47.7, 62.4]	193	175 (90.7)	99 (51.3) [44.0, 58.5]	1.075 [0.890, 1.299]	1.167 [0.779, 1.749]	3.8 [-6.7, 14.4]	0.455
	>= 7	241	204 (84.6)	136 (56.4) [49.9, 62.8]	232	210 (90.5)	138 (59.5) [52.9, 65.9]	0.949 [0.814, 1.106]	0.882 [0.612, 1.271]	-3.1 [-12.4, 6.3]	0.502

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived_i, created on: 17FEB2022

Table IT2DNCD1_ISPE: Decrease of 5-D disability score of at least 1 point by specific medical condition
ITT

Decrease of 5-D disability score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	E: Presence of specific medical conditions										0.523
	No	359	303 (84.4)	198 (55.2) [49.8, 60.4]	360	322 (89.4)	195 (54.2) [48.9, 59.4]	1.018 [0.891, 1.163]	1.041 [0.776, 1.396]	1.0 [-6.6, 8.5]	0.791
	Yes	67	59 (88.1)	40 (59.7) [47.0, 71.5]	65	63 (96.9)	42 (64.6) [51.8, 76.1]	0.924 [0.708, 1.206]	0.811 [0.401, 1.642]	-4.9 [-23.0, 13.1]	0.562

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived_i, created on: 17FEB2022

Table IT2DNCD1_ISPF: Decrease of 5-D disability score of at least 1 point by use of concomitant itch medication
ITT

Decrease of 5-D disability score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	F: Use of concomitant itch medication										0.152
	No	267	232 (86.9)	143 (53.6) [47.4, 59.7]	262	241 (92.0)	150 (57.3) [51.0, 63.3]	0.935 [0.803, 1.090]	0.861 [0.611, 1.214]	-3.7 [-12.5, 5.2]	0.393
	Yes	159	130 (81.8)	95 (59.7) [51.7, 67.4]	163	144 (88.3)	87 (53.4) [45.4, 61.2]	1.119 [0.924, 1.356]	1.297 [0.834, 2.017]	6.4 [-5.1, 17.8]	0.249

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived_i, created on: 17FEB2022

Table IT2DVCD1_ISPA: Decrease of 5-D distribution score of at least 1 point by age
ITT

Decrease of 5-D distribution score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	A: Age										0.700
	< 65 years	282	241 (85.5)	116 (41.1) [35.3, 47.1]	290	260 (89.7)	101 (34.8) [29.4, 40.6]	1.181 [0.957, 1.458]	1.308 [0.932, 1.835]	6.3 [-2.0, 14.6]	0.120
	>= 65 years	144	121 (84.0)	55 (38.2) [30.2, 46.7]	135	125 (92.6)	47 (34.8) [26.8, 43.5]	1.097 [0.804, 1.497]	1.157 [0.710, 1.885]	3.4 [-8.6, 15.4]	0.559

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived_i, created on: 17FEB2022

Table IT2DVCD1_ISPB: Decrease of 5-D distribution score of at least 1 point by sex
ITT

Decrease of 5-D distribution score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	B: Sex										0.905
	Male	249	207 (83.1)	94 (37.8) [31.7, 44.1]	258	232 (89.9)	84 (32.6) [26.9, 38.6]	1.159 [0.915, 1.470]	1.256 [0.872, 1.810]	5.2 [-3.5, 13.9]	0.221
	Female	177	155 (87.6)	77 (43.5) [36.1, 51.1]	167	153 (91.6)	64 (38.3) [30.9, 46.2]	1.135 [0.879, 1.465]	1.239 [0.805, 1.907]	5.2 [-5.8, 16.1]	0.330

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived_i, created on: 17FEB2022

Table IT2DVCD1_ISPC: Decrease of 5-D distribution score of at least 1 point by race
ITT

Decrease of 5-D distribution score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	C: Race										0.378
	Black/African American	135	109 (80.7)	46 (34.1) [26.1, 42.7]	114	103 (90.4)	34 (29.8) [21.6, 39.1]	1.142 [0.792, 1.648]	1.216 [0.711, 2.079]	4.2 [-8.2, 16.7]	0.475
	White	255	223 (87.5)	112 (43.9) [37.7, 50.2]	262	239 (91.2)	93 (35.5) [29.7, 41.6]	1.237 [0.999, 1.533]	1.423 [0.999, 2.027]	8.4 [-0.4, 17.2]	0.050
	Other	35	29 (82.9)	12 (34.3) [19.1, 52.2]	47	41 (87.2)	20 (42.6) [28.3, 57.8]	0.806 [0.457, 1.419]	0.704 [0.285, 1.743]	-8.3 [-31.9, 15.4]	0.451

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived_i, created on: 17FEB2022

Table IT2DVCD1_ISPD: Decrease of 5-D distribution score of at least 1 point by baseline WI-NRS
ITT

Decrease of 5-D distribution score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.987
	>= 4 to < 7	185	158 (85.4)	73 (39.5) [32.4, 46.9]	193	175 (90.7)	66 (34.2) [27.5, 41.4]	1.154 [0.885, 1.504]	1.254 [0.825, 1.906]	5.3 [-5.0, 15.5]	0.289
	>= 7	241	204 (84.6)	98 (40.7) [34.4, 47.2]	232	210 (90.5)	82 (35.3) [29.2, 41.9]	1.150 [0.913, 1.450]	1.254 [0.864, 1.819]	5.3 [-3.8, 14.5]	0.234

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived_i, created on: 17FEB2022

Table IT2DVCD1_ISPE: Decrease of 5-D distribution score of at least 1 point by specific medical condition
ITT

Decrease of 5-D distribution score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	E: Presence of specific medical conditions										0.953
	No	359	303 (84.4)	144 (40.1) [35.0, 45.4]	360	322 (89.4)	125 (34.7) [29.8, 39.9]	1.155 [0.955, 1.397]	1.259 [0.930, 1.704]	5.4 [-2.0, 12.7]	0.136
	Yes	67	59 (88.1)	27 (40.3) [28.5, 53.0]	65	63 (96.9)	23 (35.4) [23.9, 48.2]	1.139 [0.734, 1.767]	1.233 [0.609, 2.494]	4.9 [-13.1, 23.0]	0.562

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived_i, created on: 17FEB2022

Table IT2DVCD1_ISPF: Decrease of 5-D distribution score of at least 1 point by use of concomitant itch medication
ITT

Decrease of 5-D distribution score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	F: Use of concomitant itch medication										0.659
	No	267	232 (86.9)	109 (40.8) [34.9, 47.0]	262	241 (92.0)	90 (34.4) [28.6, 40.4]	1.188 [0.953, 1.482]	1.318 [0.926, 1.876]	6.5 [-2.1, 15.1]	0.125
	Yes	159	130 (81.8)	62 (39.0) [31.4, 47.0]	163	144 (88.3)	58 (35.6) [28.3, 43.4]	1.096 [0.825, 1.455]	1.157 [0.736, 1.819]	3.4 [-7.8, 14.6]	0.527

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived_i, created on: 17FEB2022

Table IT2DWCD1_ISPA: Decrease of 5-D direction score of at least 1 point by age
ITT

Decrease of 5-D direction score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	A: Age										0.011	i
	< 65 years	282	241 (85.5)	201 (71.3) [65.6, 76.5]	290	260 (89.7)	165 (56.9) [51.0, 62.7]	1.253 [1.106, 1.419]	1.880 [1.328, 2.660]	14.4 [6.3, 22.5]	<0.001	*
	>= 65 years	144	120 (83.3)	86 (59.7) [51.2, 67.8]	135	125 (92.6)	86 (63.7) [55.0, 71.8]	0.938 [0.779, 1.128]	0.845 [0.521, 1.370]	-4.0 [-16.1, 8.1]	0.495	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived_i, created on: 17FEB2022

Table IT2DWCD1_ISPB: Decrease of 5-D direction score of at least 1 point by sex
ITT

Decrease of 5-D direction score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	B: Sex										0.409	
	Male	249	207 (83.1)	160 (64.3) [58.0, 70.2]	258	232 (89.9)	151 (58.5) [52.3, 64.6]	1.098 [0.956, 1.261]	1.274 [0.890, 1.823]	5.7 [-3.1, 14.6]	0.186	
	Female	177	154 (87.0)	127 (71.8) [64.5, 78.3]	167	153 (91.6)	100 (59.9) [52.0, 67.4]	1.198 [1.026, 1.399]	1.702 [1.085, 2.670]	11.9 [1.3, 22.4]	0.020	*

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived_i, created on: 17FEB2022

Table IT2DWCD1_ISPC: Decrease of 5-D direction score of at least 1 point by race
ITT

Decrease of 5-D direction score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	C: Race										0.371	
	Black/African American	135	108 (80.0)	92 (68.1) [59.6, 75.9]	114	103 (90.4)	67 (58.8) [49.2, 67.9]	1.160 [0.957, 1.405]	1.501 [0.893, 2.524]	9.4 [-3.4, 22.2]	0.126	
	White	255	223 (87.5)	174 (68.2) [62.1, 73.9]	262	239 (91.2)	152 (58.0) [51.8, 64.1]	1.176 [1.030, 1.343]	1.555 [1.084, 2.229]	10.2 [1.6, 18.9]	0.016	*
	Other	35	29 (82.9)	20 (57.1) [39.4, 73.7]	47	41 (87.2)	30 (63.8) [48.5, 77.3]	0.895 [0.625, 1.281]	0.756 [0.309, 1.850]	-6.7 [-30.6, 17.2]	0.542	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived_i, created on: 17FEB2022

Table IT2DWCD1_ISPD: Decrease of 5-D direction score of at least 1 point by baseline WI-NRS
ITT

Decrease of 5-D direction score of at least 1 point		CR845 N	CR845 nval (%) n (%) [95 % CI]	Placebo N	Placebo nval (%) n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	D: Baseline worst itching NRS score (WI-NRS)								0.525	
	>= 4 to < 7	185	158 (85.4) 126 (68.1) [60.9, 74.8]	193	175 (90.7) 111 (57.5) [50.2, 64.6]	1.184 [1.013, 1.385]	1.578 [1.036, 2.403]	10.6 [0.4, 20.8]	0.033	*
	>= 7	241	203 (84.2) 161 (66.8) [60.5, 72.7]	232	210 (90.5) 140 (60.3) [53.7, 66.7]	1.107 [0.965, 1.270]	1.323 [0.908, 1.925]	6.5 [-2.6, 15.5]	0.145	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived_i, created on: 17FEB2022

Table IT2DWCD1_ISPE: Decrease of 5-D direction score of at least 1 point by specific medical condition
ITT

Decrease of 5-D direction score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	E: Presence of specific medical conditions										0.800	
	No	359	303 (84.4)	239 (66.6) [61.4, 71.4]	360	322 (89.4)	209 (58.1) [52.8, 63.2]	1.147 [1.023, 1.286]	1.439 [1.063, 1.949]	8.5 [1.2, 15.9]	0.019	*
	Yes	67	58 (86.6)	48 (71.6) [59.3, 82.0]	65	63 (96.9)	42 (64.6) [51.8, 76.1]	1.109 [0.877, 1.402]	1.383 [0.663, 2.886]	7.0 [-10.4, 24.4]	0.388	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived_i, created on: 17FEB2022

Table IT2DWCD1_ISPF: Decrease of 5-D direction score of at least 1 point by use of concomitant itch medication
ITT

Decrease of 5-D direction score of at least 1 point		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	F: Use of concomitant itch medication										0.713	
	No	267	232 (86.9)	184 (68.9) [63.0, 74.4]	262	241 (92.0)	156 (59.5) [53.3, 65.5]	1.157 [1.018, 1.316]	1.506 [1.053, 2.154]	9.4 [0.9, 17.9]	0.025	*
	Yes	159	129 (81.1)	103 (64.8) [56.8, 72.2]	163	144 (88.3)	95 (58.3) [50.3, 65.9]	1.111 [0.935, 1.322]	1.317 [0.839, 2.065]	6.5 [-4.7, 17.7]	0.232	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: afived_i, created on: 17FEB2022

Table IT2PGI_ISPA: Relevant improvement in PGIC by age
ITT

		CR845			Placebo						
Relevant improvement in PGIC		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	A: Age										0.355
	< 65 years	282	263 (93.3)	151 (53.5) [47.5, 59.5]	290	275 (94.8)	106 (36.6) [31.0, 42.4]	1.465 [1.216, 1.765]	2.001 [1.432, 2.796]	17.0 [8.6, 25.4]	<0.001 *
	>= 65 years	144	134 (93.1)	71 (49.3) [40.9, 57.8]	135	128 (94.8)	53 (39.3) [31.0, 48.0]	1.256 [0.961, 1.641]	1.505 [0.935, 2.421]	10.0 [-2.3, 22.4]	0.092

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. PGIC = patient global impression of change.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: apgic_i, created on: 24FEB2022

Table IT2PGI_ISPB: Relevant improvement in PGIC by sex
ITT

		CR845			Placebo							
Relevant improvement in PGIC		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	B: Sex										0.913	
	Male	249	231 (92.8)	121 (48.6) [42.2, 55.0]	258	245 (95.0)	91 (35.3) [29.4, 41.4]	1.378 [1.118, 1.698]	1.735 [1.215, 2.477]	13.3 [4.4, 22.2]	0.002	*
	Female	177	166 (93.8)	101 (57.1) [49.4, 64.5]	167	158 (94.6)	68 (40.7) [33.2, 48.6]	1.401 [1.121, 1.752]	1.935 [1.260, 2.971]	16.3 [5.3, 27.4]	0.002	*

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. PGIC = patient global impression of change.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: apgic_i, created on: 24FEB2022

Table IT2PGI_ISPC: Relevant improvement in PGIC by race
ITT

		CR845			Placebo						
Relevant improvement in PGIC		N	nval	n (%) [95 % CI]	N	nval	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	C: Race										0.031 i
	Black/African American	135	124 (91.9)	76 (56.3) [47.5, 64.8]	114	106 (93.0)	43 (37.7) [28.8, 47.3]	1.493 [1.129, 1.972]	2.127 [1.278, 3.538]	18.6 [5.6, 31.6]	0.004 *
	White	255	239 (93.7)	131 (51.4) [45.1, 57.7]	262	251 (95.8)	90 (34.4) [28.6, 40.4]	1.496 [1.218, 1.837]	2.019 [1.417, 2.877]	17.0 [8.2, 25.8]	<0.001 *
	Other	35	33 (94.3)	15 (42.9) [26.3, 60.6]	47	44 (93.6)	26 (55.3) [40.1, 69.8]	0.775 [0.489, 1.228]	0.606 [0.251, 1.464]	-12.5 [-36.7, 11.7]	0.267

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. PGIC = patient global impression of change.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: apgic_i, created on: 24FEB2022

Table IT2PGI_ISPD: Relevant improvement in PGIC by baseline WI-NRS
ITT

Relevant improvement in PGIC		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.249	
	>= 4 to < 7	185	174 (94.1)	113 (61.1) [53.7, 68.1]	193	183 (94.8)	77 (39.9) [32.9, 47.2]	1.531 [1.244, 1.885]	2.364 [1.565, 3.572]	21.2 [10.8, 31.6]	<0.001	*
	>= 7	241	223 (92.5)	109 (45.2) [38.8, 51.7]	232	220 (94.8)	82 (35.3) [29.2, 41.9]	1.280 [1.024, 1.599]	1.511 [1.044, 2.187]	9.9 [0.7, 19.1]	0.029	*

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. PGIC = patient global impression of change.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: apgic_i, created on: 24FEB2022

Table IT2PGI_ISPE: Relevant improvement in PGIC by specific medical condition
ITT

		CR845			Placebo						
Relevant improvement in PGIC		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	E: Presence of specific medical conditions										0.133
	No	359	336 (93.6)	182 (50.7) [45.4, 56.0]	360	340 (94.4)	138 (38.3) [33.3, 43.6]	1.323 [1.120, 1.561]	1.654 [1.230, 2.225]	12.4 [4.9, 19.9]	<0.001 *
	Yes	67	61 (91.0)	40 (59.7) [47.0, 71.5]	65	63 (96.9)	21 (32.3) [21.2, 45.1]	1.848 [1.235, 2.765]	3.104 [1.521, 6.333]	27.4 [9.5, 45.3]	0.002 *

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. PGIC = patient global impression of change.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: apgic_i, created on: 24FEB2022

Table IT2PGI_ISPF: Relevant improvement in PGIC by use of concomitant itch medication
ITT

		CR845			Placebo						
Relevant improvement in PGIC		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	F: Use of concomitant itch medication										0.512
	No	267	250 (93.6)	135 (50.6) [44.4, 56.7]	262	248 (94.7)	99 (37.8) [31.9, 44.0]	1.338 [1.101, 1.627]	1.684 [1.191, 2.381]	12.8 [4.0, 21.5]	0.003 *
	Yes	159	147 (92.5)	87 (54.7) [46.6, 62.6]	163	155 (95.1)	60 (36.8) [29.4, 44.7]	1.486 [1.162, 1.901]	2.074 [1.328, 3.240]	17.9 [6.6, 29.2]	0.001 *

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values. PGIC = patient global impression of change.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: apgic_i, created on: 24FEB2022

Table IT2STC_ISHA: Change from baseline in Skindex-10 total score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
< 65 years	Skindex-10 total score	Baseline	CR845	282	273 (96.8)	35.8 (14.3)	0	37.0	60	
			Placebo	290	282 (97.2)	36.1 (15.1)	3	36.0	60	
		Week 4	CR845	282	252 (89.4)	25.4 (15.4)	0	23.0	60	
			Placebo	290	254 (87.6)	28.7 (15.8)	0	26.0	60	
		Week 8	CR845	282	236 (83.7)	22.5 (16.7)	0	20.0	60	
			Placebo	290	261 (90.0)	25.2 (16.8)	0	22.0	60	
		Week 10	CR845	282	240 (85.1)	20.1 (16.0)	0	17.0	60	
			Placebo	290	255 (87.9)	24.7 (17.0)	0	21.0	60	
		Week 12	CR845	282	240 (85.1)	19.0 (15.9)	0	15.0	60	
			Placebo	290	255 (87.9)	23.1 (17.0)	0	18.0	60	
	Change from baseline in Skindex-10 total score	Week 4	CR845	282	245 (86.9)	-10.3 (13.6)	-51	-10.0	29	-0.21 [-0.39, -0.03]
			Placebo	290	247 (85.2)	-7.3 (15.4)	-55	-6.0	52	
		Week 8	CR845	282	229 (81.2)	-13.0 (15.0)	-51	-12.0	30	-0.14 [-0.31, 0.04]
			Placebo	290	254 (87.6)	-11.0 (15.6)	-60	-9.0	40	
		Week 10	CR845	282	235 (83.3)	-15.5 (15.0)	-55	-14.0	31	-0.25 [-0.43, -0.07]
			Placebo	290	248 (85.5)	-11.5 (17.0)	-60	-9.0	41	
		Week 12	CR845	282	235 (83.3)	-16.5 (15.5)	-58	-17.0	39	-0.22 [-0.40, -0.04]
			Placebo	290	250 (86.2)	-13.0 (16.8)	-60	-11.0	41	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2STC_ISHA: Change from baseline in Skindex-10 total score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 65 years	Skindex-10 total score	Baseline	CR845	144	141 (97.9)	35.7 (15.5)	1	36.0	60	
			Placebo	135	133 (98.5)	35.9 (15.3)	0	36.0	60	
		Week 4	CR845	144	126 (87.5)	24.8 (17.0)	0	22.5	60	
			Placebo	135	123 (91.1)	25.9 (16.7)	0	24.0	60	
		Week 8	CR845	144	122 (84.7)	21.6 (16.5)	0	18.0	60	
			Placebo	135	122 (90.4)	23.9 (15.9)	0	24.0	60	
		Week 10	CR845	144	118 (81.9)	19.1 (16.6)	0	14.5	60	
			Placebo	135	121 (89.6)	21.9 (15.6)	0	21.0	60	
		Week 12	CR845	144	120 (83.3)	19.4 (16.4)	0	15.0	60	
			Placebo	135	120 (88.9)	21.5 (15.3)	0	20.0	60	
	Change from baseline in Skindex-10 total score	Week 4	CR845	144	124 (86.1)	-11.4 (17.0)	-59	-7.0	40	-0.09 [-0.34, 0.16]
			Placebo	135	122 (90.4)	-10.1 (13.7)	-49	-8.0	23	
		Week 8	CR845	144	120 (83.3)	-14.5 (16.0)	-54	-13.0	43	-0.14 [-0.40, 0.11]
			Placebo	135	121 (89.6)	-12.3 (14.4)	-60	-11.0	44	
		Week 10	CR845	144	117 (81.3)	-16.2 (16.2)	-57	-14.0	24	-0.18 [-0.44, 0.07]
			Placebo	135	119 (88.1)	-13.4 (13.8)	-42	-13.0	32	
		Week 12	CR845	144	118 (81.9)	-16.7 (16.9)	-57	-15.0	30	-0.15 [-0.41, 0.10]
			Placebo	135	118 (87.4)	-14.3 (14.4)	-51	-12.5	26	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2STC_ISHB: Change from baseline in Skindex-10 total score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Male	Skindex-10 total score	Baseline	CR845	249	243 (97.6)	35.3 (14.6)	0	36.0	60	
			Placebo	258	251 (97.3)	34.7 (15.4)	0	35.0	60	
		Week 4	CR845	249	220 (88.4)	25.2 (15.0)	0	23.5	60	
			Placebo	258	223 (86.4)	26.4 (16.1)	0	24.0	60	
		Week 8	CR845	249	209 (83.9)	23.5 (16.6)	0	22.0	60	
			Placebo	258	234 (90.7)	24.2 (16.2)	0	20.5	60	
		Week 10	CR845	249	208 (83.5)	21.6 (16.2)	0	18.0	60	
			Placebo	258	228 (88.4)	22.9 (16.3)	0	20.0	60	
		Week 12	CR845	249	207 (83.1)	20.2 (16.1)	0	16.0	60	
			Placebo	258	228 (88.4)	21.8 (15.7)	0	18.0	60	
	Change from baseline in Skindex-10 total score	Week 4	CR845	249	216 (86.7)	-9.8 (13.5)	-59	-9.0	40	-0.09 [-0.28, 0.10]
			Placebo	258	216 (83.7)	-8.5 (15.5)	-55	-6.5	52	
		Week 8	CR845	249	205 (82.3)	-11.7 (14.6)	-54	-12.0	43	-0.04 [-0.23, 0.15]
			Placebo	258	228 (88.4)	-11.1 (15.2)	-60	-10.0	40	
		Week 10	CR845	249	205 (82.3)	-13.5 (13.7)	-55	-12.0	24	-0.12 [-0.31, 0.07]
			Placebo	258	222 (86.0)	-11.7 (16.5)	-60	-9.5	41	
		Week 12	CR845	249	203 (81.5)	-14.9 (14.4)	-57	-15.0	26	-0.13 [-0.32, 0.06]
			Placebo	258	223 (86.4)	-12.9 (16.2)	-60	-11.0	41	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2STC_ISHB: Change from baseline in Skindex-10 total score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Female	Skindex-10 total score	Baseline	CR845	177	171 (96.6)	36.5 (14.9)	1	38.0	60	
			Placebo	167	164 (98.2)	38.1 (14.5)	5	39.5	60	
		Week 4	CR845	177	158 (89.3)	25.1 (17.2)	0	22.5	60	
			Placebo	167	154 (92.2)	29.9 (16.0)	0	27.0	60	
		Week 8	CR845	177	149 (84.2)	20.4 (16.7)	0	16.0	60	
			Placebo	167	149 (89.2)	25.8 (17.1)	0	26.0	60	
		Week 10	CR845	177	150 (84.7)	17.2 (15.8)	0	12.0	60	
			Placebo	167	148 (88.6)	25.2 (16.9)	0	23.0	60	
		Week 12	CR845	177	153 (86.4)	17.7 (15.9)	0	14.0	60	
			Placebo	167	147 (88.0)	23.8 (17.6)	0	22.0	60	
	Change from baseline in Skindex-10 total score	Week 4	CR845	177	153 (86.4)	-11.8 (16.4)	-56	-10.0	29	-0.27 [-0.50, -0.05]
			Placebo	167	153 (91.6)	-7.7 (14.0)	-50	-6.0	30	
		Week 8	CR845	177	144 (81.4)	-16.2 (16.0)	-53	-14.0	30	-0.27 [-0.51, -0.04]
			Placebo	167	147 (88.0)	-11.9 (15.3)	-60	-11.0	44	
		Week 10	CR845	177	147 (83.1)	-18.8 (17.1)	-57	-16.0	31	-0.37 [-0.60, -0.14]
			Placebo	167	145 (86.8)	-12.8 (15.3)	-58	-10.0	32	
		Week 12	CR845	177	150 (84.7)	-18.9 (17.6)	-58	-18.0	39	-0.28 [-0.51, -0.05]
			Placebo	167	145 (86.8)	-14.2 (15.8)	-59	-12.0	32	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2STC_ISHC: Change from baseline in Skindex-10 total score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Black/African American	Skindex-10 total score	Baseline	CR845	135	131 (97.0)	34.4 (14.2)	4	33.0	60	
			Placebo	114	112 (98.2)	37.0 (15.3)	4	37.0	60	
		Week 4	CR845	135	114 (84.4)	25.0 (15.7)	0	21.0	60	
			Placebo	114	97 (85.1)	27.9 (14.6)	2	26.0	60	
		Week 8	CR845	135	111 (82.2)	22.1 (16.5)	0	19.0	60	
			Placebo	114	102 (89.5)	25.7 (17.1)	0	22.5	60	
		Week 10	CR845	135	107 (79.3)	19.4 (16.0)	0	15.0	60	
			Placebo	114	98 (86.0)	24.6 (17.4)	0	21.0	60	
		Week 12	CR845	135	107 (79.3)	18.1 (15.9)	0	14.0	60	
			Placebo	114	101 (88.6)	22.7 (17.1)	0	18.0	60	
	Change from baseline in Skindex-10 total score	Week 4	CR845	135	111 (82.2)	-9.8 (14.6)	-59	-8.0	29	-0.08 [-0.36, 0.19]
			Placebo	114	95 (83.3)	-8.7 (13.4)	-47	-7.0	21	
		Week 8	CR845	135	108 (80.0)	-13.5 (14.5)	-54	-13.0	30	-0.08 [-0.35, 0.19]
			Placebo	114	100 (87.7)	-12.3 (13.9)	-60	-11.0	30	
		Week 10	CR845	135	105 (77.8)	-15.3 (14.0)	-55	-13.0	13	-0.12 [-0.40, 0.16]
			Placebo	114	96 (84.2)	-13.5 (16.5)	-60	-12.5	25	
		Week 12	CR845	135	104 (77.0)	-16.7 (15.4)	-57	-17.5	30	-0.10 [-0.38, 0.18]
			Placebo	114	99 (86.8)	-15.2 (15.5)	-60	-13.0	15	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2STC_ISHC: Change from baseline in Skindex-10 total score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
White	Skindex-10 total score	Baseline	CR845	255	247 (96.9)	36.2 (15.2)	0	38.0	60	
			Placebo	262	258 (98.5)	35.4 (15.1)	0	36.0	60	
		Week 4	CR845	255	232 (91.0)	24.7 (16.1)	0	23.0	60	
			Placebo	262	236 (90.1)	27.8 (16.8)	0	26.0	60	
		Week 8	CR845	255	215 (84.3)	21.9 (17.0)	0	19.0	60	
			Placebo	262	238 (90.8)	24.2 (16.4)	0	23.0	60	
		Week 10	CR845	255	221 (86.7)	19.8 (16.1)	0	17.0	60	
			Placebo	262	235 (89.7)	23.2 (16.1)	0	20.0	60	
		Week 12	CR845	255	223 (87.5)	19.2 (15.8)	0	15.0	60	
			Placebo	262	232 (88.5)	22.8 (16.1)	0	20.0	60	
	Change from baseline in Skindex-10 total score	Week 4	CR845	255	226 (88.6)	-11.3 (15.0)	-56	-11.0	40	-0.24 [-0.42, -0.05]
			Placebo	262	232 (88.5)	-7.7 (15.6)	-55	-6.0	52	
		Week 8	CR845	255	209 (82.0)	-13.5 (15.8)	-53	-12.0	43	-0.18 [-0.36, 0.01]
			Placebo	262	234 (89.3)	-10.7 (15.7)	-60	-9.0	44	
		Week 10	CR845	255	217 (85.1)	-15.8 (15.7)	-56	-15.0	31	-0.26 [-0.45, -0.07]
			Placebo	262	231 (88.2)	-11.6 (16.1)	-57	-10.0	41	
		Week 12	CR845	255	219 (85.9)	-16.7 (16.1)	-58	-16.0	39	-0.28 [-0.46, -0.09]
			Placebo	262	228 (87.0)	-12.2 (16.2)	-59	-11.0	41	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2STC_ISHC: Change from baseline in Skindex-10 total score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Other	Skindex-10 total score	Baseline	CR845	35	35 (100.0)	38.3 (13.1)	13	37.0	60	
			Placebo	47	44 (93.6)	36.9 (14.9)	10	37.0	60	
		Week 4	CR845	35	31 (88.6)	28.9 (16.2)	0	28.0	60	
			Placebo	47	42 (89.4)	26.5 (15.4)	2	24.5	60	
		Week 8	CR845	35	31 (88.6)	24.8 (15.4)	0	25.0	48	
			Placebo	47	41 (87.2)	24.6 (15.7)	0	22.0	60	
		Week 10	CR845	35	29 (82.9)	20.3 (17.6)	0	16.0	54	
			Placebo	47	41 (87.2)	25.1 (17.6)	0	22.0	60	
		Week 12	CR845	35	29 (82.9)	22.3 (18.3)	0	21.0	60	
			Placebo	47	41 (87.2)	21.0 (17.6)	0	17.0	60	
	Change from baseline in Skindex-10 total score	Week 4	CR845	35	31 (88.6)	-9.2 (14.0)	-48	-6.0	22	0.07 [-0.39, 0.54]
			Placebo	47	41 (87.2)	-10.2 (14.2)	-50	-7.0	13	
		Week 8	CR845	35	31 (88.6)	-14.3 (15.8)	-53	-10.0	15	-0.09 [-0.56, 0.38]
			Placebo	47	40 (85.1)	-12.8 (15.5)	-44	-9.5	13	
		Week 10	CR845	35	29 (82.9)	-17.8 (17.3)	-57	-13.0	18	-0.39 [-0.87, 0.10]
			Placebo	47	39 (83.0)	-11.7 (14.4)	-43	-8.0	15	
		Week 12	CR845	35	29 (82.9)	-16.2 (17.5)	-56	-14.0	18	-0.04 [-0.52, 0.44]
			Placebo	47	40 (85.1)	-15.6 (16.1)	-51	-11.0	8	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2STC_ISHD: Change from baseline in Skindex-10 total score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 4 to < 7	Skindex-10 total score	Baseline	CR845	185	182 (98.4)	30.1 (14.1)	0	31.0	60	
			Placebo	193	190 (98.4)	29.5 (14.6)	0	28.0	60	
		Week 4	CR845	185	166 (89.7)	18.7 (12.6)	0	18.0	58	
			Placebo	193	173 (89.6)	22.1 (14.6)	0	19.0	60	
		Week 8	CR845	185	161 (87.0)	16.7 (13.4)	0	14.0	60	
			Placebo	193	173 (89.6)	19.7 (14.9)	0	15.0	60	
		Week 10	CR845	185	160 (86.5)	14.9 (12.6)	0	12.0	60	
			Placebo	193	171 (88.6)	18.7 (15.4)	0	14.0	60	
		Week 12	CR845	185	158 (85.4)	14.0 (12.2)	0	10.0	60	
			Placebo	193	171 (88.6)	18.7 (15.0)	0	15.0	60	
	Change from baseline in Skindex-10 total score	Week 4	CR845	185	164 (88.6)	-10.8 (13.7)	-59	-9.0	27	-0.27 [-0.49, -0.06]
			Placebo	193	170 (88.1)	-6.8 (15.3)	-49	-6.0	52	
		Week 8	CR845	185	159 (85.9)	-13.3 (14.7)	-54	-12.0	30	-0.27 [-0.48, -0.05]
			Placebo	193	171 (88.6)	-9.4 (14.4)	-51	-9.0	44	
		Week 10	CR845	185	158 (85.4)	-14.7 (14.2)	-55	-14.0	31	-0.29 [-0.51, -0.07]
			Placebo	193	169 (87.6)	-10.3 (16.2)	-54	-9.0	41	
		Week 12	CR845	185	156 (84.3)	-15.9 (14.6)	-57	-15.5	39	-0.38 [-0.60, -0.16]
			Placebo	193	169 (87.6)	-10.2 (15.5)	-56	-10.0	41	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2STC_ISHD: Change from baseline in Skindex-10 total score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 7	Skindex-10 total score	Baseline	CR845	241	232 (96.3)	40.2 (13.7)	0	42.0	60	
			Placebo	232	225 (97.0)	41.6 (13.2)	5	43.0	60	
		Week 4	CR845	241	212 (88.0)	30.2 (16.5)	0	30.0	60	
			Placebo	232	204 (87.9)	32.7 (15.8)	3	31.5	60	
		Week 8	CR845	241	197 (81.7)	26.7 (17.7)	0	26.0	60	
			Placebo	232	210 (90.5)	29.0 (16.7)	0	27.0	60	
		Week 10	CR845	241	198 (82.2)	23.7 (17.7)	0	20.0	60	
			Placebo	232	205 (88.4)	28.0 (16.4)	0	26.0	60	
		Week 12	CR845	241	202 (83.8)	23.1 (17.5)	0	22.0	60	
			Placebo	232	204 (87.9)	25.8 (17.0)	0	24.0	60	
	Change from baseline in Skindex-10 total score	Week 4	CR845	241	205 (85.1)	-10.6 (15.6)	-56	-9.0	40	-0.08 [-0.27, 0.12]
			Placebo	232	199 (85.8)	-9.4 (14.4)	-55	-6.0	30	
		Week 8	CR845	241	190 (78.8)	-13.7 (16.0)	-53	-12.5	43	-0.04 [-0.24, 0.15]
			Placebo	232	204 (87.9)	-13.0 (15.7)	-60	-11.0	30	
		Week 10	CR845	241	194 (80.5)	-16.6 (16.3)	-57	-14.0	25	-0.18 [-0.38, 0.02]
			Placebo	232	198 (85.3)	-13.7 (15.7)	-60	-11.0	19	
		Week 12	CR845	241	197 (81.7)	-17.2 (17.0)	-58	-17.0	30	-0.06 [-0.26, 0.14]
			Placebo	232	199 (85.8)	-16.2 (16.0)	-60	-15.0	17	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2STC_ISHE: Change from baseline in Skindex-10 total score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	Skindex-10 total score	Baseline	CR845	359	348 (96.9)	35.9 (14.7)	0	36.5	60	
			Placebo	360	353 (98.1)	35.0 (15.3)	0	35.0	60	
		Week 4	CR845	359	317 (88.3)	25.0 (15.7)	0	23.0	60	
			Placebo	360	323 (89.7)	27.2 (16.0)	0	25.0	60	
		Week 8	CR845	359	302 (84.1)	22.0 (16.5)	0	19.0	60	
			Placebo	360	322 (89.4)	24.0 (16.5)	0	21.0	60	
		Week 10	CR845	359	302 (84.1)	19.8 (16.0)	0	17.0	60	
			Placebo	360	318 (88.3)	23.2 (16.5)	0	20.0	60	
		Week 12	CR845	359	301 (83.8)	19.0 (16.0)	0	15.0	60	
			Placebo	360	314 (87.2)	22.0 (16.2)	0	18.0	60	
	Change from baseline in Skindex-10 total score	Week 4	CR845	359	309 (86.1)	-10.9 (14.5)	-59	-10.0	29	-0.22 [-0.38, -0.06]
			Placebo	360	318 (88.3)	-7.7 (14.8)	-55	-6.0	52	
		Week 8	CR845	359	294 (81.9)	-13.8 (14.9)	-54	-13.0	30	-0.19 [-0.35, -0.03]
			Placebo	360	317 (88.1)	-11.0 (15.4)	-60	-10.0	44	
		Week 10	CR845	359	296 (82.5)	-15.8 (14.9)	-57	-14.0	30	-0.27 [-0.43, -0.11]
			Placebo	360	312 (86.7)	-11.6 (16.2)	-60	-9.0	41	
		Week 12	CR845	359	295 (82.2)	-16.7 (15.6)	-58	-16.0	30	-0.25 [-0.41, -0.09]
			Placebo	360	310 (86.1)	-12.7 (16.0)	-60	-11.0	41	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2STC_ISHE: Change from baseline in Skindex-10 total score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	Skindex-10 total score	Baseline	CR845	67	66 (98.5)	35.2 (14.7)	5	35.0	60	
			Placebo	65	62 (95.4)	41.7 (12.9)	10	44.5	60	
		Week 4	CR845	67	61 (91.0)	26.1 (17.3)	0	23.0	60	
			Placebo	65	54 (83.1)	31.3 (16.4)	0	30.5	60	
		Week 8	CR845	67	56 (83.6)	23.6 (17.5)	0	22.5	60	
			Placebo	65	61 (93.8)	29.2 (16.3)	0	30.0	60	
		Week 10	CR845	67	56 (83.6)	19.3 (17.2)	0	15.0	60	
			Placebo	65	58 (89.2)	27.2 (16.6)	2	25.0	60	
		Week 12	CR845	67	59 (88.1)	19.9 (16.2)	0	18.0	60	
			Placebo	65	61 (93.8)	25.8 (17.5)	0	25.0	60	
	Change from baseline in Skindex-10 total score	Week 4	CR845	67	60 (89.6)	-9.4 (16.4)	-51	-8.0	40	0.12 [-0.26, 0.49]
			Placebo	65	51 (78.5)	-11.2 (15.5)	-49	-8.0	11	
		Week 8	CR845	67	55 (82.1)	-12.2 (17.8)	-51	-10.0	43	0.10 [-0.27, 0.46]
			Placebo	65	58 (89.2)	-13.7 (14.2)	-51	-12.0	18	
		Week 10	CR845	67	56 (83.6)	-15.5 (17.9)	-55	-14.0	31	-0.02 [-0.39, 0.36]
			Placebo	65	55 (84.6)	-15.2 (14.6)	-54	-15.0	12	
		Week 12	CR845	67	58 (86.6)	-16.0 (17.8)	-56	-15.0	39	0.08 [-0.29, 0.44]
			Placebo	65	58 (89.2)	-17.3 (15.8)	-56	-15.0	15	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2STC_ISHF: Change from baseline in Skindex-10 total score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	Skindex-10 total score	Baseline	CR845	267	258 (96.6)	34.8 (15.0)	0	36.0	60	
			Placebo	262	257 (98.1)	35.6 (15.2)	0	36.0	60	
		Week 4	CR845	267	243 (91.0)	24.4 (15.4)	0	22.0	60	
			Placebo	262	233 (88.9)	27.1 (16.1)	0	25.0	60	
		Week 8	CR845	267	236 (88.4)	21.1 (16.4)	0	17.0	60	
			Placebo	262	237 (90.5)	23.9 (15.7)	0	21.0	60	
		Week 10	CR845	267	229 (85.8)	19.5 (16.1)	0	16.0	60	
			Placebo	262	234 (89.3)	22.8 (16.0)	0	20.0	60	
		Week 12	CR845	267	232 (86.9)	18.7 (16.2)	0	14.0	60	
			Placebo	262	238 (90.8)	21.6 (15.7)	0	18.0	60	
	Change from baseline in Skindex-10 total score	Week 4	CR845	267	236 (88.4)	-10.3 (15.2)	-56	-9.0	40	-0.13 [-0.32, 0.05]
			Placebo	262	229 (87.4)	-8.2 (15.4)	-55	-6.0	52	
		Week 8	CR845	267	229 (85.8)	-13.6 (15.4)	-53	-13.0	43	-0.13 [-0.31, 0.05]
			Placebo	262	234 (89.3)	-11.6 (15.7)	-60	-10.0	44	
		Week 10	CR845	267	224 (83.9)	-15.0 (15.3)	-57	-13.0	31	-0.15 [-0.34, 0.03]
			Placebo	262	230 (87.8)	-12.5 (17.4)	-60	-10.0	41	
		Week 12	CR845	267	226 (84.6)	-16.0 (16.4)	-56	-15.5	39	-0.14 [-0.32, 0.05]
			Placebo	262	234 (89.3)	-13.8 (16.6)	-60	-11.0	41	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2STC_ISHF: Change from baseline in Skindex-10 total score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	Skindex-10 total score	Baseline	CR845	159	156 (98.1)	37.4 (14.2)	0	38.0	60	
			Placebo	163	158 (96.9)	36.8 (15.0)	3	38.0	60	
		Week 4	CR845	159	135 (84.9)	26.6 (16.9)	0	25.0	60	
			Placebo	163	144 (88.3)	29.0 (16.2)	0	26.0	60	
		Week 8	CR845	159	122 (76.7)	24.4 (17.1)	0	21.0	60	
			Placebo	163	146 (89.6)	26.3 (17.7)	0	24.0	60	
		Week 10	CR845	159	129 (81.1)	20.2 (16.4)	0	18.0	60	
			Placebo	163	142 (87.1)	25.4 (17.4)	0	22.0	60	
		Week 12	CR845	159	128 (80.5)	20.0 (15.8)	0	16.5	60	
			Placebo	163	137 (84.0)	24.4 (17.6)	0	21.0	60	
	Change from baseline in Skindex-10 total score	Week 4	CR845	159	133 (83.6)	-11.3 (14.0)	-59	-10.0	22	-0.23 [-0.47, 0.01]
			Placebo	163	140 (85.9)	-8.1 (14.1)	-49	-7.0	39	
		Week 8	CR845	159	120 (75.5)	-13.5 (15.4)	-54	-12.0	30	-0.16 [-0.41, 0.08]
			Placebo	163	141 (86.5)	-11.1 (14.4)	-60	-10.0	30	
		Week 10	CR845	159	128 (80.5)	-17.1 (15.6)	-55	-15.0	24	-0.38 [-0.62, -0.13]
			Placebo	163	137 (84.0)	-11.6 (13.4)	-51	-10.0	19	
		Week 12	CR845	159	127 (79.9)	-17.6 (15.2)	-58	-18.0	18	-0.32 [-0.57, -0.08]
			Placebo	163	134 (82.2)	-12.8 (15.0)	-57	-12.0	41	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SDC_ISHA: Change from baseline in Skindex-10 disease score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
< 65 years	Skindex-10 disease score	Baseline	CR845	282	276 (97.9)	13.0 (4.0)	0	14.0	18	
			Placebo	290	286 (98.6)	13.0 (3.9)	2	13.5	18	
		Week 4	CR845	282	253 (89.7)	9.4 (4.8)	0	9.0	18	
			Placebo	290	256 (88.3)	10.7 (4.6)	0	11.0	18	
		Week 8	CR845	282	242 (85.8)	8.4 (5.1)	0	8.0	18	
			Placebo	290	263 (90.7)	9.3 (4.9)	0	9.0	18	
		Week 10	CR845	282	241 (85.5)	7.6 (5.0)	0	7.0	18	
			Placebo	290	255 (87.9)	9.0 (5.0)	0	9.0	18	
		Week 12	CR845	282	241 (85.5)	7.1 (5.0)	0	6.0	18	
			Placebo	290	256 (88.3)	8.7 (5.1)	0	8.0	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	282	249 (88.3)	-3.7 (4.5)	-16	-3.0	9	-0.34 [-0.52, -0.16]
			Placebo	290	253 (87.2)	-2.2 (4.6)	-17	-2.0	12	
		Week 8	CR845	282	238 (84.4)	-4.6 (4.9)	-16	-4.5	11	-0.21 [-0.39, -0.03]
			Placebo	290	260 (89.7)	-3.6 (4.7)	-18	-3.0	7	
		Week 10	CR845	282	237 (84.0)	-5.4 (5.0)	-18	-6.0	9	-0.31 [-0.49, -0.13]
			Placebo	290	252 (86.9)	-3.9 (4.9)	-18	-3.0	8	
		Week 12	CR845	282	238 (84.4)	-5.9 (5.2)	-18	-6.0	9	-0.33 [-0.51, -0.15]
			Placebo	290	254 (87.6)	-4.2 (5.0)	-18	-4.0	12	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SDC_ISHA: Change from baseline in Skindex-10 disease score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 65 years	Skindex-10 disease score	Baseline	CR845	144	143 (99.3)	13.1 (4.1)	1	14.0	18	
			Placebo	135	135 (100.0)	13.1 (4.0)	0	14.0	18	
		Week 4	CR845	144	127 (88.2)	9.4 (5.4)	0	10.0	18	
			Placebo	135	125 (92.6)	9.8 (5.2)	0	9.0	18	
		Week 8	CR845	144	125 (86.8)	8.5 (5.1)	0	8.0	18	
			Placebo	135	123 (91.1)	9.2 (4.8)	0	9.0	18	
		Week 10	CR845	144	120 (83.3)	7.6 (5.1)	0	6.0	18	
			Placebo	135	123 (91.1)	8.6 (4.8)	0	8.0	18	
		Week 12	CR845	144	120 (83.3)	7.7 (5.2)	0	8.0	18	
			Placebo	135	121 (89.6)	8.4 (4.8)	0	9.0	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	144	127 (88.2)	-3.7 (5.2)	-17	-3.0	10	-0.08 [-0.33, 0.16]
			Placebo	135	125 (92.6)	-3.3 (4.5)	-16	-3.0	6	
		Week 8	CR845	144	125 (86.8)	-4.5 (5.3)	-17	-5.0	11	-0.13 [-0.37, 0.12]
			Placebo	135	123 (91.1)	-3.9 (4.6)	-18	-3.0	9	
		Week 10	CR845	144	120 (83.3)	-5.5 (5.4)	-18	-5.0	8	-0.22 [-0.47, 0.04]
			Placebo	135	123 (91.1)	-4.4 (4.7)	-15	-4.0	8	
		Week 12	CR845	144	120 (83.3)	-5.5 (5.8)	-18	-6.0	9	-0.15 [-0.41, 0.10]
			Placebo	135	121 (89.6)	-4.7 (4.6)	-16	-4.0	7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SDC_ISHB: Change from baseline in Skindex-10 disease score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Male	Skindex-10 disease score	Baseline	CR845	249	245 (98.4)	12.7 (4.2)	0	13.0	18	
			Placebo	258	256 (99.2)	12.8 (4.0)	0	13.0	18	
		Week 4	CR845	249	221 (88.8)	9.5 (4.8)	0	9.0	18	
			Placebo	258	227 (88.0)	10.1 (5.0)	0	10.0	18	
		Week 8	CR845	249	212 (85.1)	8.8 (5.1)	0	8.0	18	
			Placebo	258	236 (91.5)	9.2 (4.7)	0	9.0	18	
		Week 10	CR845	249	209 (83.9)	8.2 (4.9)	0	8.0	18	
			Placebo	258	229 (88.8)	8.7 (4.8)	0	8.0	18	
		Week 12	CR845	249	207 (83.1)	7.6 (5.0)	0	7.0	18	
			Placebo	258	229 (88.8)	8.6 (4.8)	0	8.0	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	249	219 (88.0)	-3.1 (4.4)	-17	-3.0	8	-0.13 [-0.31, 0.06]
			Placebo	258	225 (87.2)	-2.5 (4.7)	-17	-2.0	12	
		Week 8	CR845	249	210 (84.3)	-3.8 (4.9)	-16	-4.0	11	-0.04 [-0.23, 0.15]
			Placebo	258	235 (91.1)	-3.6 (4.5)	-18	-3.0	7	
		Week 10	CR845	249	207 (83.1)	-4.4 (4.8)	-18	-4.0	9	-0.09 [-0.28, 0.10]
			Placebo	258	228 (88.4)	-4.0 (4.7)	-18	-3.0	8	
		Week 12	CR845	249	205 (82.3)	-5.0 (5.0)	-18	-5.0	7	-0.17 [-0.36, 0.02]
			Placebo	258	228 (88.4)	-4.1 (4.8)	-18	-4.0	12	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SDC_ISHB: Change from baseline in Skindex-10 disease score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Female	Skindex-10 disease score	Baseline	CR845	177	174 (98.3)	13.6 (3.8)	1	14.5	18	
			Placebo	167	165 (98.8)	13.4 (3.9)	2	14.0	18	
		Week 4	CR845	177	159 (89.8)	9.3 (5.3)	0	9.0	18	
			Placebo	167	154 (92.2)	10.8 (4.6)	0	11.0	18	
		Week 8	CR845	177	155 (87.6)	8.0 (5.2)	0	8.0	18	
			Placebo	167	150 (89.8)	9.4 (5.1)	0	9.0	18	
		Week 10	CR845	177	152 (85.9)	6.7 (5.0)	0	6.0	18	
			Placebo	167	149 (89.2)	9.2 (5.1)	0	9.0	18	
		Week 12	CR845	177	154 (87.0)	6.9 (5.1)	0	6.0	18	
			Placebo	167	148 (88.6)	8.7 (5.3)	0	9.0	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	177	157 (88.7)	-4.5 (5.1)	-17	-4.0	10	-0.42 [-0.65, -0.20]
			Placebo	167	153 (91.6)	-2.5 (4.4)	-15	-2.0	7	
		Week 8	CR845	177	153 (86.4)	-5.7 (5.0)	-17	-6.0	9	-0.36 [-0.59, -0.14]
			Placebo	167	148 (88.6)	-3.9 (5.0)	-18	-3.0	9	
		Week 10	CR845	177	150 (84.7)	-6.9 (5.3)	-18	-7.0	9	-0.52 [-0.76, -0.29]
			Placebo	167	147 (88.0)	-4.2 (5.1)	-18	-4.0	7	
		Week 12	CR845	177	153 (86.4)	-6.8 (5.7)	-18	-6.0	9	-0.38 [-0.61, -0.15]
			Placebo	167	147 (88.0)	-4.7 (5.1)	-18	-4.0	5	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SDC_ISHC: Change from baseline in Skindex-10 disease score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Black/African American	Skindex-10 disease score	Baseline	CR845	135	132 (97.8)	13.1 (4.0)	2	14.0	18	
			Placebo	114	113 (99.1)	13.3 (3.9)	2	14.0	18	
		Week 4	CR845	135	115 (85.2)	9.9 (4.9)	0	9.0	18	
			Placebo	114	98 (86.0)	10.9 (4.5)	0	10.0	18	
		Week 8	CR845	135	113 (83.7)	8.9 (4.9)	0	8.0	18	
			Placebo	114	104 (91.2)	9.6 (4.9)	0	9.0	18	
		Week 10	CR845	135	107 (79.3)	7.9 (4.8)	0	7.0	18	
			Placebo	114	99 (86.8)	9.4 (5.1)	0	9.0	18	
		Week 12	CR845	135	107 (79.3)	7.3 (5.2)	0	6.0	18	
			Placebo	114	102 (89.5)	9.0 (5.1)	0	9.0	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	135	113 (83.7)	-3.4 (4.8)	-17	-3.0	9	-0.24 [-0.51, 0.03]
			Placebo	114	97 (85.1)	-2.3 (4.3)	-13	-2.0	7	
		Week 8	CR845	135	111 (82.2)	-4.6 (4.9)	-16	-5.0	11	-0.18 [-0.44, 0.09]
			Placebo	114	103 (90.4)	-3.7 (4.7)	-18	-3.0	7	
		Week 10	CR845	135	105 (77.8)	-5.3 (5.3)	-18	-5.0	9	-0.25 [-0.52, 0.03]
			Placebo	114	98 (86.0)	-4.0 (5.3)	-18	-4.0	7	
		Week 12	CR845	135	105 (77.8)	-5.9 (5.5)	-18	-6.0	9	-0.26 [-0.54, 0.01]
			Placebo	114	101 (88.6)	-4.5 (5.0)	-18	-4.0	9	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SDC_ISHC: Change from baseline in Skindex-10 disease score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
White	Skindex-10 disease score	Baseline	CR845	255	251 (98.4)	13.1 (4.2)	0	14.0	18	
			Placebo	262	261 (99.6)	12.9 (4.0)	0	13.0	18	
		Week 4	CR845	255	233 (91.4)	9.1 (5.1)	0	9.0	18	
			Placebo	262	239 (91.2)	10.3 (5.0)	0	11.0	18	
		Week 8	CR845	255	222 (87.1)	8.2 (5.3)	0	8.0	18	
			Placebo	262	239 (91.2)	9.0 (4.9)	0	9.0	18	
		Week 10	CR845	255	224 (87.8)	7.4 (5.1)	0	7.0	18	
			Placebo	262	236 (90.1)	8.7 (4.8)	0	8.0	18	
		Week 12	CR845	255	224 (87.8)	7.2 (4.9)	0	6.0	18	
			Placebo	262	233 (88.9)	8.7 (5.0)	0	9.0	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	255	231 (90.6)	-4.0 (4.8)	-17	-4.0	10	-0.29 [-0.47, -0.11]
			Placebo	262	238 (90.8)	-2.6 (4.8)	-17	-2.0	12	
		Week 8	CR845	255	220 (86.3)	-4.6 (5.2)	-17	-5.0	11	-0.18 [-0.37, 0.00]
			Placebo	262	238 (90.8)	-3.7 (4.7)	-18	-3.0	9	
		Week 10	CR845	255	222 (87.1)	-5.5 (5.1)	-18	-6.0	9	-0.30 [-0.48, -0.11]
			Placebo	262	235 (89.7)	-4.1 (4.8)	-15	-3.0	8	
		Week 12	CR845	255	223 (87.5)	-5.8 (5.2)	-18	-6.0	9	-0.34 [-0.52, -0.15]
			Placebo	262	232 (88.5)	-4.1 (4.9)	-18	-3.0	12	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SDC_ISHC: Change from baseline in Skindex-10 disease score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Other	Skindex-10 disease score	Baseline	CR845	35	35 (100.0)	12.7 (3.6)	5	13.0	18	
			Placebo	47	45 (95.7)	13.0 (3.9)	6	12.0	18	
		Week 4	CR845	35	31 (88.6)	9.6 (4.6)	0	10.0	18	
			Placebo	47	42 (89.4)	9.9 (4.6)	1	9.5	18	
		Week 8	CR845	35	31 (88.6)	8.4 (4.4)	0	8.0	16	
			Placebo	47	41 (87.2)	9.4 (4.5)	0	9.0	18	
		Week 10	CR845	35	29 (82.9)	7.3 (5.0)	0	6.0	15	
			Placebo	47	41 (87.2)	8.9 (4.9)	0	9.0	18	
		Week 12	CR845	35	29 (82.9)	8.0 (5.4)	0	8.0	18	
			Placebo	47	41 (87.2)	7.4 (5.0)	0	7.0	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	35	31 (88.6)	-3.0 (4.2)	-11	-3.0	5	0.03 [-0.44, 0.50]
			Placebo	47	41 (87.2)	-3.1 (4.3)	-15	-3.0	5	
		Week 8	CR845	35	31 (88.6)	-4.6 (4.9)	-13	-4.0	7	-0.17 [-0.64, 0.30]
			Placebo	47	40 (85.1)	-3.8 (4.6)	-16	-4.0	7	
		Week 10	CR845	35	29 (82.9)	-5.5 (5.3)	-17	-5.0	8	-0.28 [-0.76, 0.20]
			Placebo	47	40 (85.1)	-4.2 (4.3)	-15	-4.0	3	
		Week 12	CR845	35	29 (82.9)	-5.0 (5.9)	-16	-5.0	7	0.13 [-0.34, 0.61]
			Placebo	47	41 (87.2)	-5.6 (4.2)	-16	-5.0	3	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SDC_ISHD: Change from baseline in Skindex-10 disease score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 4 to < 7	Skindex-10 disease score	Baseline	CR845	185	183 (98.9)	11.1 (4.0)	0	11.0	18	
			Placebo	193	191 (99.0)	11.1 (3.9)	0	11.0	18	
		Week 4	CR845	185	167 (90.3)	7.3 (4.2)	0	8.0	18	
			Placebo	193	175 (90.7)	8.9 (4.6)	0	8.0	18	
		Week 8	CR845	185	164 (88.6)	6.7 (4.5)	0	6.0	18	
			Placebo	193	175 (90.7)	8.0 (4.4)	0	7.0	18	
		Week 10	CR845	185	161 (87.0)	6.1 (4.2)	0	6.0	18	
			Placebo	193	171 (88.6)	7.5 (4.6)	0	7.0	18	
		Week 12	CR845	185	158 (85.4)	5.8 (4.0)	0	5.0	18	
			Placebo	193	172 (89.1)	7.4 (4.7)	0	7.0	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	185	166 (89.7)	-3.6 (4.7)	-17	-3.0	10	-0.30 [-0.51, -0.08]
			Placebo	193	173 (89.6)	-2.2 (4.7)	-16	-2.0	12	
		Week 8	CR845	185	163 (88.1)	-4.4 (5.1)	-16	-5.0	9	-0.28 [-0.49, -0.06]
			Placebo	193	174 (90.2)	-3.1 (4.3)	-14	-3.0	9	
		Week 10	CR845	185	160 (86.5)	-4.9 (4.8)	-16	-5.0	9	-0.26 [-0.48, -0.04]
			Placebo	193	170 (88.1)	-3.6 (4.7)	-14	-3.0	8	
		Week 12	CR845	185	157 (84.9)	-5.2 (5.0)	-17	-6.0	9	-0.30 [-0.52, -0.08]
			Placebo	193	171 (88.6)	-3.7 (4.8)	-16	-3.0	12	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SDC_ISHD: Change from baseline in Skindex-10 disease score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 7	Skindex-10 disease score	Baseline	CR845	241	236 (97.9)	14.6 (3.4)	0	15.0	18	
			Placebo	232	230 (99.1)	14.6 (3.3)	5	15.0	18	
		Week 4	CR845	241	213 (88.4)	11.0 (4.9)	0	11.0	18	
			Placebo	232	206 (88.8)	11.8 (4.6)	0	12.0	18	
		Week 8	CR845	241	203 (84.2)	9.9 (5.1)	0	10.0	18	
			Placebo	232	211 (90.9)	10.3 (5.0)	0	10.0	18	
		Week 10	CR845	241	200 (83.0)	8.8 (5.3)	0	9.0	18	
			Placebo	232	207 (89.2)	10.1 (4.8)	0	10.0	18	
		Week 12	CR845	241	203 (84.2)	8.5 (5.5)	0	9.0	18	
			Placebo	232	205 (88.4)	9.6 (5.0)	0	10.0	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	241	210 (87.1)	-3.8 (4.7)	-17	-3.5	9	-0.21 [-0.40, -0.02]
			Placebo	232	205 (88.4)	-2.8 (4.5)	-17	-2.0	7	
		Week 8	CR845	241	200 (83.0)	-4.8 (5.1)	-17	-4.5	11	-0.11 [-0.30, 0.08]
			Placebo	232	209 (90.1)	-4.2 (5.0)	-18	-4.0	7	
		Week 10	CR845	241	197 (81.7)	-5.9 (5.4)	-18	-5.0	9	-0.29 [-0.49, -0.10]
			Placebo	232	205 (88.4)	-4.4 (4.9)	-18	-4.0	7	
		Week 12	CR845	241	201 (83.4)	-6.2 (5.6)	-18	-6.0	9	-0.24 [-0.44, -0.05]
			Placebo	232	204 (87.9)	-4.9 (4.9)	-18	-4.5	7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SDC_ISHE: Change from baseline in Skindex-10 disease score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	Skindex-10 disease score	Baseline	CR845	359	352 (98.1)	13.0 (4.1)	0	14.0	18	
			Placebo	360	357 (99.2)	12.7 (4.0)	0	13.0	18	
		Week 4	CR845	359	319 (88.9)	9.3 (4.9)	0	9.0	18	
			Placebo	360	324 (90.0)	10.2 (4.7)	0	10.0	18	
		Week 8	CR845	359	309 (86.1)	8.4 (5.1)	0	8.0	18	
			Placebo	360	323 (89.7)	9.0 (4.8)	0	9.0	18	
		Week 10	CR845	359	304 (84.7)	7.6 (5.0)	0	7.0	18	
			Placebo	360	319 (88.6)	8.7 (4.9)	0	8.0	18	
		Week 12	CR845	359	302 (84.1)	7.3 (5.1)	0	6.0	18	
			Placebo	360	316 (87.8)	8.4 (4.9)	0	8.0	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	359	315 (87.7)	-3.7 (4.8)	-17	-3.0	10	-0.27 [-0.42, -0.11]
			Placebo	360	322 (89.4)	-2.5 (4.6)	-17	-2.0	12	
		Week 8	CR845	359	305 (85.0)	-4.6 (5.0)	-16	-5.0	11	-0.20 [-0.35, -0.04]
			Placebo	360	321 (89.2)	-3.7 (4.8)	-18	-3.0	9	
		Week 10	CR845	359	300 (83.6)	-5.4 (5.1)	-18	-5.5	9	-0.29 [-0.44, -0.13]
			Placebo	360	317 (88.1)	-4.0 (4.9)	-18	-3.0	8	
		Week 12	CR845	359	299 (83.3)	-5.7 (5.3)	-18	-6.0	9	-0.28 [-0.44, -0.12]
			Placebo	360	315 (87.5)	-4.3 (4.9)	-18	-4.0	12	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SDC_ISHE: Change from baseline in Skindex-10 disease score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	Skindex-10 disease score	Baseline	CR845	67	67 (100.0)	13.4 (3.6)	2	14.0	18	
			Placebo	65	64 (98.5)	14.6 (3.2)	7	15.0	18	
		Week 4	CR845	67	61 (91.0)	9.6 (5.2)	0	10.0	18	
			Placebo	65	57 (87.7)	11.6 (5.2)	0	12.0	18	
		Week 8	CR845	67	58 (86.6)	8.8 (5.4)	0	9.0	18	
			Placebo	65	63 (96.9)	10.6 (5.0)	0	10.0	18	
		Week 10	CR845	67	57 (85.1)	7.6 (5.2)	0	7.0	18	
			Placebo	65	59 (90.8)	10.1 (4.8)	0	9.0	18	
		Week 12	CR845	67	59 (88.1)	7.3 (4.9)	0	7.0	18	
			Placebo	65	61 (93.8)	9.7 (5.3)	0	10.0	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	67	61 (91.0)	-3.7 (4.6)	-16	-3.0	7	-0.15 [-0.52, 0.21]
			Placebo	65	56 (86.2)	-3.0 (4.8)	-16	-1.0	7	
		Week 8	CR845	67	58 (86.6)	-4.6 (5.6)	-17	-4.5	11	-0.12 [-0.47, 0.24]
			Placebo	65	62 (95.4)	-4.0 (4.3)	-15	-3.0	7	
		Week 10	CR845	67	57 (85.1)	-5.7 (5.5)	-18	-5.0	4	-0.24 [-0.61, 0.13]
			Placebo	65	58 (89.2)	-4.5 (4.3)	-14	-4.0	7	
		Week 12	CR845	67	59 (88.1)	-6.1 (5.6)	-18	-6.0	6	-0.23 [-0.59, 0.13]
			Placebo	65	60 (92.3)	-4.9 (4.6)	-16	-4.5	7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SDC_ISHF: Change from baseline in Skindex-10 disease score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	Skindex-10 disease score	Baseline	CR845	267	262 (98.1)	12.7 (4.2)	0	13.0	18	
			Placebo	262	259 (98.9)	12.8 (4.0)	0	13.0	18	
		Week 4	CR845	267	245 (91.8)	9.3 (4.9)	0	9.0	18	
			Placebo	262	236 (90.1)	10.3 (4.8)	0	10.0	18	
		Week 8	CR845	267	238 (89.1)	8.1 (5.1)	0	7.5	18	
			Placebo	262	239 (91.2)	9.1 (4.6)	0	9.0	18	
		Week 10	CR845	267	232 (86.9)	7.6 (5.0)	0	7.0	18	
			Placebo	262	235 (89.7)	8.7 (4.8)	0	9.0	18	
		Week 12	CR845	267	232 (86.9)	7.1 (5.1)	0	6.0	18	
			Placebo	262	238 (90.8)	8.4 (4.7)	0	8.0	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	267	242 (90.6)	-3.4 (4.8)	-17	-3.0	10	-0.19 [-0.37, -0.01]
			Placebo	262	233 (88.9)	-2.5 (4.8)	-17	-2.0	12	
		Week 8	CR845	267	235 (88.0)	-4.5 (5.1)	-17	-5.0	11	-0.19 [-0.37, -0.01]
			Placebo	262	237 (90.5)	-3.6 (4.7)	-18	-3.0	9	
		Week 10	CR845	267	229 (85.8)	-5.1 (5.0)	-17	-5.0	9	-0.20 [-0.39, -0.02]
			Placebo	262	233 (88.9)	-4.1 (5.1)	-18	-3.0	8	
		Week 12	CR845	267	230 (86.1)	-5.6 (5.5)	-18	-6.0	9	-0.22 [-0.40, -0.04]
			Placebo	262	236 (90.1)	-4.4 (4.8)	-18	-4.0	7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SDC_ISHF: Change from baseline in Skindex-10 disease score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	Skindex-10 disease score	Baseline	CR845	159	157 (98.7)	13.6 (3.8)	0	14.0	18	
			Placebo	163	162 (99.4)	13.3 (4.0)	2	14.0	18	
		Week 4	CR845	159	135 (84.9)	9.5 (5.1)	0	9.0	18	
			Placebo	163	145 (89.0)	10.6 (4.9)	0	10.0	18	
		Week 8	CR845	159	129 (81.1)	9.1 (5.2)	0	8.0	18	
			Placebo	163	147 (90.2)	9.5 (5.2)	0	9.0	18	
		Week 10	CR845	159	129 (81.1)	7.6 (5.1)	0	7.0	18	
			Placebo	163	143 (87.7)	9.2 (5.1)	0	9.0	18	
		Week 12	CR845	159	129 (81.1)	7.6 (5.0)	0	7.0	18	
			Placebo	163	139 (85.3)	9.0 (5.4)	0	9.0	18	
	Change from baseline in Skindex-10 disease score	Week 4	CR845	159	134 (84.3)	-4.3 (4.6)	-17	-4.0	8	-0.37 [-0.61, -0.13]
			Placebo	163	145 (89.0)	-2.7 (4.3)	-15	-2.0	10	
		Week 8	CR845	159	128 (80.5)	-4.7 (5.1)	-16	-4.5	11	-0.18 [-0.42, 0.06]
			Placebo	163	146 (89.6)	-3.8 (4.6)	-18	-3.0	6	
		Week 10	CR845	159	128 (80.5)	-6.1 (5.3)	-18	-6.0	9	-0.42 [-0.66, -0.18]
			Placebo	163	142 (87.1)	-4.0 (4.3)	-15	-4.0	5	
		Week 12	CR845	159	128 (80.5)	-6.1 (5.1)	-18	-6.0	5	-0.36 [-0.61, -0.12]
			Placebo	163	139 (85.3)	-4.3 (5.0)	-18	-4.0	12	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SMC_ISHA: Change from baseline in Skindex-10 mood/emotional distress score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
< 65 years	Skindex-10 mood/emotional distress score	Baseline	CR845	282	273 (96.8)	11.5 (4.7)	0	12.0	18	
			Placebo	290	285 (98.3)	11.4 (4.8)	0	12.0	18	
		Week 4	CR845	282	253 (89.7)	8.0 (5.1)	0	8.0	18	
			Placebo	290	259 (89.3)	9.1 (5.2)	0	9.0	18	
		Week 8	CR845	282	238 (84.4)	7.0 (5.6)	0	6.0	18	
			Placebo	290	261 (90.0)	7.9 (5.5)	0	8.0	18	
		Week 10	CR845	282	242 (85.8)	6.2 (5.4)	0	5.0	18	
			Placebo	290	258 (89.0)	7.7 (5.4)	0	7.0	18	
		Week 12	CR845	282	243 (86.2)	5.9 (5.3)	0	5.0	18	
			Placebo	290	259 (89.3)	7.1 (5.6)	0	6.0	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	282	246 (87.2)	-3.5 (4.7)	-17	-3.0	10	-0.24 [-0.42, -0.07]
			Placebo	290	254 (87.6)	-2.3 (5.2)	-17	-2.0	17	
		Week 8	CR845	282	231 (81.9)	-4.5 (5.3)	-18	-4.0	14	-0.18 [-0.36, -0.00]
			Placebo	290	257 (88.6)	-3.6 (5.1)	-18	-3.0	12	
		Week 10	CR845	282	236 (83.7)	-5.3 (5.2)	-18	-5.0	11	-0.30 [-0.48, -0.12]
			Placebo	290	254 (87.6)	-3.7 (5.5)	-18	-3.0	13	
		Week 12	CR845	282	237 (84.0)	-5.6 (5.4)	-18	-6.0	13	-0.23 [-0.41, -0.06]
			Placebo	290	255 (87.9)	-4.4 (5.6)	-18	-4.0	14	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SMC_ISHA: Change from baseline in Skindex-10 mood/emotional distress score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 65 years	Skindex-10 mood/emotional distress score	Baseline	CR845	144	143 (99.3)	11.4 (5.0)	0	12.0	18	
			Placebo	135	135 (100.0)	11.5 (5.3)	0	12.0	18	
		Week 4	CR845	144	128 (88.9)	7.9 (5.7)	0	8.0	18	
			Placebo	135	126 (93.3)	8.4 (5.9)	0	8.0	18	
		Week 8	CR845	144	125 (86.8)	6.7 (5.5)	0	5.0	18	
			Placebo	135	125 (92.6)	7.5 (5.4)	0	7.0	18	
		Week 10	CR845	144	118 (81.9)	5.8 (5.3)	0	5.0	18	
			Placebo	135	122 (90.4)	7.0 (5.4)	0	6.0	18	
		Week 12	CR845	144	121 (84.0)	5.8 (5.3)	0	4.0	18	
			Placebo	135	123 (91.1)	7.0 (5.6)	0	6.0	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	144	127 (88.2)	-3.7 (6.0)	-18	-3.0	14	-0.11 [-0.36, 0.14]
			Placebo	135	126 (93.3)	-3.1 (4.7)	-15	-2.5	10	
		Week 8	CR845	144	124 (86.1)	-4.8 (5.7)	-18	-4.0	9	-0.15 [-0.40, 0.10]
			Placebo	135	125 (92.6)	-3.9 (5.2)	-18	-4.0	15	
		Week 10	CR845	144	117 (81.3)	-5.5 (5.6)	-18	-4.0	9	-0.25 [-0.50, 0.01]
			Placebo	135	122 (90.4)	-4.2 (5.1)	-18	-4.0	11	
		Week 12	CR845	144	120 (83.3)	-5.7 (5.7)	-18	-5.0	6	-0.23 [-0.48, 0.03]
			Placebo	135	123 (91.1)	-4.4 (5.3)	-17	-4.0	8	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SMC_ISHB: Change from baseline in Skindex-10 mood/emotional distress score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Male	Skindex-10 mood/emotional distress score	Baseline	CR845	249	243 (97.6)	11.4 (4.8)	0	12.0	18	
			Placebo	258	254 (98.4)	10.9 (5.1)	0	11.0	18	
		Week 4	CR845	249	222 (89.2)	7.9 (5.0)	0	8.0	18	
			Placebo	258	228 (88.4)	8.5 (5.4)	0	8.5	18	
		Week 8	CR845	249	211 (84.7)	7.4 (5.6)	0	6.0	18	
			Placebo	258	235 (91.1)	7.5 (5.4)	0	7.0	18	
		Week 10	CR845	249	208 (83.5)	6.7 (5.4)	0	6.0	18	
			Placebo	258	229 (88.8)	7.1 (5.4)	0	6.0	18	
		Week 12	CR845	249	209 (83.9)	6.1 (5.3)	0	5.0	18	
			Placebo	258	230 (89.1)	6.7 (5.3)	0	6.0	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	249	218 (87.6)	-3.4 (4.7)	-18	-3.0	14	-0.20 [-0.39, -0.01]
			Placebo	258	224 (86.8)	-2.4 (5.2)	-17	-2.0	17	
		Week 8	CR845	249	207 (83.1)	-4.1 (5.1)	-18	-4.0	14	-0.11 [-0.30, 0.08]
			Placebo	258	232 (89.9)	-3.5 (5.0)	-18	-3.0	12	
		Week 10	CR845	249	205 (82.3)	-4.7 (4.8)	-17	-4.0	10	-0.20 [-0.39, -0.01]
			Placebo	258	226 (87.6)	-3.7 (5.4)	-18	-3.0	13	
		Week 12	CR845	249	205 (82.3)	-5.3 (5.0)	-17	-5.0	6	-0.21 [-0.40, -0.03]
			Placebo	258	227 (88.0)	-4.1 (5.6)	-18	-4.0	14	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SMC_ISHB: Change from baseline in Skindex-10 mood/emotional distress score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Female	Skindex-10 mood/emotional distress score	Baseline	CR845	177	173 (97.7)	11.6 (4.9)	0	12.0	18	
			Placebo	167	166 (99.4)	12.2 (4.6)	0	12.0	18	
		Week 4	CR845	177	159 (89.8)	8.1 (5.7)	0	8.0	18	
			Placebo	167	157 (94.0)	9.5 (5.4)	0	9.0	18	
		Week 8	CR845	177	152 (85.9)	6.2 (5.4)	0	6.0	18	
			Placebo	167	151 (90.4)	8.1 (5.6)	0	8.0	18	
		Week 10	CR845	177	152 (85.9)	5.3 (5.3)	0	4.0	18	
			Placebo	167	151 (90.4)	8.1 (5.4)	0	8.0	18	
		Week 12	CR845	177	155 (87.6)	5.5 (5.2)	0	4.0	18	
			Placebo	167	152 (91.0)	7.6 (5.9)	0	7.0	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	177	155 (87.6)	-3.7 (5.7)	-18	-3.0	12	-0.19 [-0.41, 0.03]
			Placebo	167	156 (93.4)	-2.7 (4.8)	-15	-2.0	10	
		Week 8	CR845	177	148 (83.6)	-5.4 (5.8)	-18	-5.0	11	-0.25 [-0.47, -0.02]
			Placebo	167	150 (89.8)	-4.0 (5.2)	-18	-4.0	15	
		Week 10	CR845	177	148 (83.6)	-6.3 (5.8)	-18	-6.0	11	-0.38 [-0.61, -0.15]
			Placebo	167	150 (89.8)	-4.1 (5.3)	-17	-4.0	10	
		Week 12	CR845	177	152 (85.9)	-6.2 (6.1)	-18	-6.0	13	-0.25 [-0.47, -0.02]
			Placebo	167	151 (90.4)	-4.7 (5.4)	-18	-4.0	9	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SMC_ISHC: Change from baseline in Skindex-10 mood/emotional distress score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Black/African American	Skindex-10 mood/emotional distress score	Baseline	CR845	135	133 (98.5)	11.1 (4.7)	0	12.0	18	
			Placebo	114	113 (99.1)	12.1 (4.8)	0	13.0	18	
		Week 4	CR845	135	114 (84.4)	8.2 (5.4)	0	8.0	18	
			Placebo	114	100 (87.7)	9.5 (5.1)	0	9.0	18	
		Week 8	CR845	135	112 (83.0)	6.9 (5.7)	0	6.0	18	
			Placebo	114	103 (90.4)	8.2 (5.6)	0	8.0	18	
		Week 10	CR845	135	108 (80.0)	6.1 (5.5)	0	4.5	18	
			Placebo	114	101 (88.6)	8.0 (5.7)	0	8.0	18	
		Week 12	CR845	135	110 (81.5)	5.6 (5.3)	0	4.5	18	
			Placebo	114	102 (89.5)	7.2 (5.9)	0	6.0	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	135	112 (83.0)	-3.1 (5.6)	-18	-3.0	12	-0.11 [-0.38, 0.16]
			Placebo	114	99 (86.8)	-2.5 (4.4)	-15	-2.0	10	
		Week 8	CR845	135	110 (81.5)	-4.7 (5.8)	-18	-4.0	14	-0.09 [-0.36, 0.18]
			Placebo	114	102 (89.5)	-4.2 (4.5)	-18	-4.0	8	
		Week 10	CR845	135	106 (78.5)	-5.2 (5.4)	-17	-5.0	10	-0.16 [-0.43, 0.12]
			Placebo	114	100 (87.7)	-4.4 (5.6)	-18	-4.0	10	
		Week 12	CR845	135	108 (80.0)	-5.7 (5.6)	-18	-6.0	6	-0.11 [-0.38, 0.16]
			Placebo	114	101 (88.6)	-5.1 (5.3)	-18	-5.0	14	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SMC_ISHC: Change from baseline in Skindex-10 mood/emotional distress score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
White	Skindex-10 mood/emotional distress score	Baseline	CR845	255	247 (96.9)	11.6 (4.9)	0	12.0	18	
			Placebo	262	259 (98.9)	11.0 (5.0)	0	12.0	18	
		Week 4	CR845	255	235 (92.2)	7.8 (5.3)	0	8.0	18	
			Placebo	262	241 (92.0)	8.6 (5.5)	0	9.0	18	
		Week 8	CR845	255	219 (85.9)	6.6 (5.4)	0	6.0	18	
			Placebo	262	239 (91.2)	7.5 (5.4)	0	7.0	18	
		Week 10	CR845	255	222 (87.1)	6.1 (5.3)	0	5.0	18	
			Placebo	262	236 (90.1)	7.1 (5.3)	0	6.0	18	
		Week 12	CR845	255	224 (87.8)	5.9 (5.2)	0	5.0	18	
			Placebo	262	237 (90.5)	7.1 (5.5)	0	6.0	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	255	229 (89.8)	-3.8 (5.0)	-18	-4.0	14	-0.25 [-0.43, -0.07]
			Placebo	262	238 (90.8)	-2.5 (5.4)	-17	-2.0	17	
		Week 8	CR845	255	213 (83.5)	-4.6 (5.3)	-18	-4.0	11	-0.22 [-0.40, -0.03]
			Placebo	262	236 (90.1)	-3.5 (5.3)	-18	-3.0	15	
		Week 10	CR845	255	217 (85.1)	-5.4 (5.3)	-18	-5.0	11	-0.30 [-0.49, -0.12]
			Placebo	262	233 (88.9)	-3.8 (5.3)	-18	-3.0	13	
		Week 12	CR845	255	219 (85.9)	-5.7 (5.4)	-18	-6.0	13	-0.31 [-0.49, -0.12]
			Placebo	262	234 (89.3)	-4.0 (5.5)	-18	-3.0	11	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SMC_ISHC: Change from baseline in Skindex-10 mood/emotional distress score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Other	Skindex-10 mood/emotional distress score	Baseline	CR845	35	35 (100.0)	12.4 (4.6)	5	12.0	18	
			Placebo	47	46 (97.9)	11.7 (4.8)	0	12.0	18	
		Week 4	CR845	35	31 (88.6)	9.0 (5.5)	0	9.0	18	
			Placebo	47	42 (89.4)	8.3 (5.2)	0	8.5	18	
		Week 8	CR845	35	31 (88.6)	8.3 (5.5)	0	9.0	18	
			Placebo	47	42 (89.4)	7.6 (5.4)	0	6.5	18	
		Week 10	CR845	35	29 (82.9)	6.4 (5.9)	0	5.0	18	
			Placebo	47	41 (87.2)	8.2 (5.5)	0	8.0	18	
		Week 12	CR845	35	29 (82.9)	6.7 (6.2)	0	7.0	18	
			Placebo	47	41 (87.2)	6.7 (5.6)	0	5.0	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	35	31 (88.6)	-3.4 (4.5)	-16	-3.0	4	-0.08 [-0.55, 0.39]
			Placebo	47	41 (87.2)	-3.0 (4.8)	-15	-2.0	6	
		Week 8	CR845	35	31 (88.6)	-4.5 (5.1)	-16	-3.0	5	-0.10 [-0.56, 0.36]
			Placebo	47	42 (89.4)	-4.0 (5.5)	-15	-3.0	8	
		Week 10	CR845	35	29 (82.9)	-6.0 (5.4)	-18	-5.0	3	-0.53 [-1.02, -0.05]
			Placebo	47	41 (87.2)	-3.2 (5.1)	-17	-3.0	7	
		Week 12	CR845	35	29 (82.9)	-5.8 (5.6)	-18	-4.0	2	-0.19 [-0.66, 0.29]
			Placebo	47	41 (87.2)	-4.7 (6.0)	-17	-4.0	7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SMC_ISHD: Change from baseline in Skindex-10 mood/emotional distress score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 4 to < 7	Skindex-10 mood/emotional distress score	Baseline	CR845	185	182 (98.4)	9.9 (4.9)	0	11.0	18	
			Placebo	193	190 (98.4)	9.2 (5.0)	0	10.0	18	
		Week 4	CR845	185	168 (90.8)	5.9 (4.4)	0	6.0	18	
			Placebo	193	177 (91.7)	7.0 (5.0)	0	6.0	18	
		Week 8	CR845	185	163 (88.1)	5.3 (4.7)	0	4.0	18	
			Placebo	193	174 (90.2)	6.0 (5.0)	0	5.0	18	
		Week 10	CR845	185	160 (86.5)	4.5 (4.2)	0	4.0	18	
			Placebo	193	171 (88.6)	5.7 (5.0)	0	5.0	18	
		Week 12	CR845	185	158 (85.4)	4.2 (4.1)	0	3.0	18	
			Placebo	193	173 (89.6)	5.8 (5.1)	0	5.0	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	185	166 (89.7)	-3.8 (4.8)	-18	-4.0	12	-0.32 [-0.53, -0.10]
			Placebo	193	174 (90.2)	-2.2 (5.3)	-14	-2.0	17	
		Week 8	CR845	185	161 (87.0)	-4.6 (5.3)	-15	-4.0	11	-0.27 [-0.49, -0.06]
			Placebo	193	172 (89.1)	-3.2 (5.1)	-17	-3.0	15	
		Week 10	CR845	185	158 (85.4)	-5.3 (4.9)	-18	-5.0	11	-0.35 [-0.57, -0.14]
			Placebo	193	169 (87.6)	-3.4 (5.4)	-18	-3.0	13	
		Week 12	CR845	185	156 (84.3)	-5.6 (5.2)	-18	-6.0	13	-0.43 [-0.65, -0.21]
			Placebo	193	171 (88.6)	-3.3 (5.5)	-18	-3.0	14	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SMC_ISHD: Change from baseline in Skindex-10 mood/emotional distress score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 7	Skindex-10 mood/emotional distress score	Baseline	CR845	241	234 (97.1)	12.7 (4.3)	0	13.0	18	
			Placebo	232	230 (99.1)	13.3 (4.1)	0	13.5	18	
		Week 4	CR845	241	213 (88.4)	9.6 (5.4)	0	10.0	18	
			Placebo	232	208 (89.7)	10.5 (5.2)	0	10.5	18	
		Week 8	CR845	241	200 (83.0)	8.2 (5.8)	0	8.0	18	
			Placebo	232	212 (91.4)	9.2 (5.4)	0	9.0	18	
		Week 10	CR845	241	200 (83.0)	7.4 (5.8)	0	6.5	18	
			Placebo	232	209 (90.1)	9.0 (5.3)	0	9.0	18	
		Week 12	CR845	241	206 (85.5)	7.1 (5.7)	0	6.5	18	
			Placebo	232	209 (90.1)	8.1 (5.7)	0	8.0	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	241	207 (85.9)	-3.3 (5.4)	-18	-3.0	14	-0.10 [-0.29, 0.09]
			Placebo	232	206 (88.8)	-2.8 (4.8)	-17	-2.0	10	
		Week 8	CR845	241	194 (80.5)	-4.6 (5.6)	-18	-4.0	14	-0.09 [-0.29, 0.10]
			Placebo	232	210 (90.5)	-4.1 (5.1)	-18	-4.0	9	
		Week 10	CR845	241	195 (80.9)	-5.5 (5.6)	-18	-5.0	10	-0.23 [-0.42, -0.03]
			Placebo	232	207 (89.2)	-4.3 (5.3)	-18	-4.0	10	
		Week 12	CR845	241	201 (83.4)	-5.7 (5.7)	-18	-6.0	6	-0.07 [-0.27, 0.12]
			Placebo	232	207 (89.2)	-5.3 (5.4)	-18	-5.0	7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SMC_ISHE: Change from baseline in Skindex-10 mood/emotional distress score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	Skindex-10 mood/emotional distress score	Baseline	CR845	359	349 (97.2)	11.6 (4.8)	0	12.0	18	
			Placebo	360	357 (99.2)	11.1 (5.0)	0	12.0	18	
		Week 4	CR845	359	320 (89.1)	7.9 (5.2)	0	8.0	18	
			Placebo	360	328 (91.1)	8.7 (5.4)	0	9.0	18	
		Week 8	CR845	359	305 (85.0)	6.8 (5.5)	0	6.0	18	
			Placebo	360	325 (90.3)	7.4 (5.4)	0	7.0	18	
		Week 10	CR845	359	304 (84.7)	6.2 (5.3)	0	5.0	18	
			Placebo	360	320 (88.9)	7.2 (5.4)	0	6.0	18	
		Week 12	CR845	359	305 (85.0)	5.8 (5.3)	0	5.0	18	
			Placebo	360	320 (88.9)	6.8 (5.4)	0	6.0	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	359	312 (86.9)	-3.7 (5.0)	-18	-4.0	12	-0.26 [-0.42, -0.11]
			Placebo	360	325 (90.3)	-2.4 (5.1)	-17	-2.0	17	
		Week 8	CR845	359	297 (82.7)	-4.7 (5.3)	-18	-4.0	14	-0.21 [-0.37, -0.05]
			Placebo	360	323 (89.7)	-3.6 (5.2)	-18	-3.0	15	
		Week 10	CR845	359	297 (82.7)	-5.4 (5.2)	-18	-5.0	10	-0.32 [-0.48, -0.16]
			Placebo	360	318 (88.3)	-3.7 (5.4)	-18	-3.0	13	
		Week 12	CR845	359	298 (83.0)	-5.8 (5.4)	-18	-6.0	9	-0.29 [-0.45, -0.13]
			Placebo	360	318 (88.3)	-4.2 (5.5)	-18	-4.0	14	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SMC_ISHE: Change from baseline in Skindex-10 mood/emotional distress score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	Skindex-10 mood/emotional distress score	Baseline	CR845	67	67 (100.0)	11.1 (4.9)	0	12.0	18	
			Placebo	65	63 (96.9)	13.4 (4.3)	0	13.0	18	
		Week 4	CR845	67	61 (91.0)	8.4 (5.8)	0	8.0	18	
			Placebo	65	57 (87.7)	10.1 (5.4)	0	10.0	18	
		Week 8	CR845	67	58 (86.6)	7.0 (5.5)	0	7.0	18	
			Placebo	65	61 (93.8)	9.3 (5.5)	0	10.0	18	
		Week 10	CR845	67	56 (83.6)	5.8 (5.6)	0	5.0	18	
			Placebo	65	60 (92.3)	8.9 (5.6)	0	10.0	18	
		Week 12	CR845	67	59 (88.1)	6.1 (5.3)	0	5.0	18	
			Placebo	65	62 (95.4)	8.1 (6.1)	0	8.0	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	67	61 (91.0)	-2.8 (5.9)	-17	-2.0	14	0.14 [-0.23, 0.50]
			Placebo	65	55 (84.6)	-3.5 (4.8)	-14	-2.0	5	
		Week 8	CR845	67	58 (86.6)	-4.1 (6.0)	-16	-3.5	11	0.03 [-0.33, 0.40]
			Placebo	65	59 (90.8)	-4.3 (4.6)	-17	-4.0	4	
		Week 10	CR845	67	56 (83.6)	-5.2 (6.1)	-18	-4.5	11	-0.09 [-0.46, 0.28]
			Placebo	65	58 (89.2)	-4.7 (5.0)	-18	-4.0	4	
		Week 12	CR845	67	59 (88.1)	-5.1 (5.8)	-18	-5.0	13	0.06 [-0.30, 0.42]
			Placebo	65	60 (92.3)	-5.4 (5.6)	-18	-4.0	7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SMC_ISHF: Change from baseline in Skindex-10 mood/emotional distress score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	Skindex-10 mood/emotional distress score	Baseline	CR845	267	259 (97.0)	11.3 (4.9)	0	12.0	18	
			Placebo	262	258 (98.5)	11.2 (4.9)	0	11.0	18	
		Week 4	CR845	267	246 (92.1)	7.7 (5.2)	0	7.0	18	
			Placebo	262	237 (90.5)	8.6 (5.4)	0	9.0	18	
		Week 8	CR845	267	238 (89.1)	6.5 (5.5)	0	6.0	18	
			Placebo	262	239 (91.2)	7.4 (5.2)	0	7.0	18	
		Week 10	CR845	267	229 (85.8)	6.0 (5.3)	0	5.0	18	
			Placebo	262	236 (90.1)	7.2 (5.3)	0	6.0	18	
		Week 12	CR845	267	234 (87.6)	5.7 (5.2)	0	5.0	18	
			Placebo	262	241 (92.0)	6.7 (5.4)	0	6.0	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	267	240 (89.9)	-3.6 (5.3)	-18	-3.0	14	-0.19 [-0.37, -0.01]
			Placebo	262	233 (88.9)	-2.6 (5.0)	-17	-2.0	17	
		Week 8	CR845	267	232 (86.9)	-4.7 (5.5)	-18	-4.0	11	-0.17 [-0.35, 0.01]
			Placebo	262	236 (90.1)	-3.8 (5.1)	-18	-4.0	15	
		Week 10	CR845	267	224 (83.9)	-5.2 (5.3)	-18	-4.5	11	-0.23 [-0.41, -0.04]
			Placebo	262	233 (88.9)	-4.0 (5.6)	-18	-3.0	13	
		Week 12	CR845	267	229 (85.8)	-5.6 (5.5)	-18	-6.0	13	-0.20 [-0.38, -0.02]
			Placebo	262	238 (90.8)	-4.5 (5.5)	-18	-4.0	14	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SMC_ISHF: Change from baseline in Skindex-10 mood/emotional distress score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	Skindex-10 mood/emotional distress score	Baseline	CR845	159	157 (98.7)	11.9 (4.7)	0	12.0	18	
			Placebo	163	162 (99.4)	11.8 (5.0)	0	12.0	18	
		Week 4	CR845	159	135 (84.9)	8.5 (5.5)	0	9.0	18	
			Placebo	163	148 (90.8)	9.3 (5.4)	0	9.0	18	
		Week 8	CR845	159	125 (78.6)	7.5 (5.6)	0	7.0	18	
			Placebo	163	147 (90.2)	8.3 (5.9)	0	8.0	18	
		Week 10	CR845	159	131 (82.4)	6.3 (5.4)	0	6.0	18	
			Placebo	163	144 (88.3)	8.0 (5.6)	0	8.0	18	
		Week 12	CR845	159	130 (81.8)	6.2 (5.4)	0	6.0	18	
			Placebo	163	141 (86.5)	7.6 (5.8)	0	7.0	18	
	Change from baseline in Skindex-10 mood/emotional distress score	Week 4	CR845	159	133 (83.6)	-3.4 (5.0)	-18	-3.0	10	-0.20 [-0.43, 0.04]
			Placebo	163	147 (90.2)	-2.4 (5.2)	-17	-2.0	14	
		Week 8	CR845	159	123 (77.4)	-4.4 (5.4)	-18	-4.0	14	-0.17 [-0.41, 0.07]
			Placebo	163	146 (89.6)	-3.6 (5.1)	-18	-3.0	10	
		Week 10	CR845	159	129 (81.1)	-5.6 (5.3)	-18	-6.0	10	-0.38 [-0.62, -0.14]
			Placebo	163	143 (87.7)	-3.7 (5.0)	-18	-3.0	10	
		Week 12	CR845	159	128 (80.5)	-5.8 (5.4)	-18	-6.0	6	-0.29 [-0.53, -0.05]
			Placebo	163	140 (85.9)	-4.2 (5.5)	-17	-4.0	10	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SSC_ISHA: Change from baseline in Skindex-10 social functioning score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
< 65 years	Skindex-10 social functioning score	Baseline	CR845	282	276 (97.9)	11.3 (7.5)	0	11.0	24	
			Placebo	290	286 (98.6)	11.8 (7.9)	0	12.0	24	
		Week 4	CR845	282	254 (90.1)	8.1 (7.1)	0	7.0	24	
			Placebo	290	259 (89.3)	8.8 (7.7)	0	7.0	24	
		Week 8	CR845	282	240 (85.1)	7.1 (7.2)	0	5.0	24	
			Placebo	290	263 (90.7)	8.1 (7.7)	0	6.0	24	
		Week 10	CR845	282	243 (86.2)	6.4 (6.9)	0	4.0	24	
			Placebo	290	258 (89.0)	7.9 (7.7)	0	6.0	24	
		Week 12	CR845	282	242 (85.8)	6.1 (6.9)	0	4.0	24	
			Placebo	290	258 (89.0)	7.3 (7.5)	0	4.0	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	282	250 (88.7)	-3.2 (6.4)	-24	-3.0	19	-0.03 [-0.21, 0.14]
			Placebo	290	256 (88.3)	-3.0 (7.5)	-24	-1.0	23	
		Week 8	CR845	282	236 (83.7)	-4.1 (7.0)	-23	-4.0	16	-0.07 [-0.24, 0.11]
			Placebo	290	260 (89.7)	-3.6 (7.6)	-24	-2.5	22	
		Week 10	CR845	282	239 (84.8)	-4.7 (6.9)	-24	-4.0	20	-0.13 [-0.31, 0.04]
			Placebo	290	255 (87.9)	-3.7 (8.1)	-24	-2.0	22	
		Week 12	CR845	282	239 (84.8)	-5.0 (7.3)	-23	-5.0	20	-0.08 [-0.26, 0.09]
			Placebo	290	256 (88.3)	-4.4 (7.9)	-24	-3.0	24	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SSC_ISHA: Change from baseline in Skindex-10 social functioning score by age
ITT

A: Age	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 65 years	Skindex-10 social functioning score	Baseline	CR845	144	143 (99.3)	11.2 (8.3)	0	11.0	24	
			Placebo	135	133 (98.5)	11.4 (7.9)	0	12.0	24	
		Week 4	CR845	144	127 (88.2)	7.6 (7.6)	0	5.0	24	
			Placebo	135	128 (94.8)	8.0 (7.6)	0	6.5	24	
		Week 8	CR845	144	124 (86.1)	6.4 (7.1)	0	4.0	24	
			Placebo	135	126 (93.3)	7.3 (7.2)	0	6.0	24	
		Week 10	CR845	144	120 (83.3)	6.0 (7.3)	0	3.0	24	
			Placebo	135	122 (90.4)	6.3 (6.8)	0	4.5	24	
		Week 12	CR845	144	121 (84.0)	6.0 (7.1)	0	4.0	24	
			Placebo	135	124 (91.9)	6.5 (6.9)	0	5.0	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	144	126 (87.5)	-3.7 (7.9)	-24	-2.5	19	-0.01 [-0.26, 0.23]
			Placebo	135	127 (94.1)	-3.6 (6.8)	-24	-2.0	13	
		Week 8	CR845	144	123 (85.4)	-4.9 (7.4)	-24	-3.0	24	-0.09 [-0.34, 0.16]
			Placebo	135	125 (92.6)	-4.2 (7.1)	-24	-4.0	20	
		Week 10	CR845	144	120 (83.3)	-5.1 (7.3)	-24	-4.0	13	-0.03 [-0.28, 0.23]
			Placebo	135	120 (88.9)	-4.9 (6.8)	-24	-4.0	13	
		Week 12	CR845	144	120 (83.3)	-5.3 (7.7)	-24	-5.0	15	-0.03 [-0.29, 0.22]
			Placebo	135	122 (90.4)	-5.0 (6.9)	-24	-4.0	11	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SSC_ISHB: Change from baseline in Skindex-10 social functioning score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Male	Skindex-10 social functioning score	Baseline	CR845	249	245 (98.4)	11.2 (7.6)	0	11.0	24	
			Placebo	258	254 (98.4)	11.1 (7.9)	0	10.0	24	
		Week 4	CR845	249	223 (89.6)	8.0 (7.0)	0	7.0	24	
			Placebo	258	230 (89.1)	7.9 (7.3)	0	6.0	24	
		Week 8	CR845	249	213 (85.5)	7.3 (7.0)	0	5.0	24	
			Placebo	258	237 (91.9)	7.5 (7.4)	0	5.0	24	
		Week 10	CR845	249	209 (83.9)	6.8 (7.2)	0	5.0	24	
			Placebo	258	230 (89.1)	7.1 (7.3)	0	5.0	24	
		Week 12	CR845	249	209 (83.9)	6.6 (6.9)	0	4.0	24	
			Placebo	258	231 (89.5)	6.7 (7.1)	0	4.0	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	249	221 (88.8)	-3.2 (6.3)	-24	-3.0	19	0.04 [-0.15, 0.23]
			Placebo	258	226 (87.6)	-3.5 (7.4)	-24	-2.0	23	
		Week 8	CR845	249	211 (84.7)	-3.9 (6.8)	-24	-4.0	24	-0.02 [-0.21, 0.17]
			Placebo	258	234 (90.7)	-3.8 (7.6)	-24	-2.0	22	
		Week 10	CR845	249	207 (83.1)	-4.3 (6.4)	-24	-4.0	20	-0.05 [-0.24, 0.14]
			Placebo	258	227 (88.0)	-3.9 (8.1)	-24	-3.0	22	
		Week 12	CR845	249	207 (83.1)	-4.6 (6.8)	-24	-4.0	16	-0.03 [-0.21, 0.16]
			Placebo	258	228 (88.4)	-4.4 (7.9)	-24	-3.0	24	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SSC_ISHB: Change from baseline in Skindex-10 social functioning score by sex
ITT

B: Sex	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Female	Skindex-10 social functioning score	Baseline	CR845	177	174 (98.3)	11.3 (8.2)	0	12.0	24	
			Placebo	167	165 (98.8)	12.5 (7.9)	0	13.0	24	
		Week 4	CR845	177	158 (89.3)	7.8 (7.7)	0	4.0	24	
			Placebo	167	157 (94.0)	9.6 (8.0)	0	8.0	24	
		Week 8	CR845	177	151 (85.3)	6.3 (7.2)	0	4.0	24	
			Placebo	167	152 (91.0)	8.4 (7.8)	0	7.0	24	
		Week 10	CR845	177	154 (87.0)	5.5 (6.9)	0	2.0	24	
			Placebo	167	150 (89.8)	7.9 (7.6)	0	7.0	24	
		Week 12	CR845	177	154 (87.0)	5.4 (6.9)	0	2.5	24	
			Placebo	167	151 (90.4)	7.6 (7.6)	0	5.0	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	177	155 (87.6)	-3.5 (7.8)	-24	-2.0	13	-0.11 [-0.34, 0.11]
			Placebo	167	157 (94.0)	-2.7 (7.0)	-23	-2.0	20	
		Week 8	CR845	177	148 (83.6)	-5.0 (7.6)	-24	-4.0	15	-0.16 [-0.38, 0.07]
			Placebo	167	151 (90.4)	-3.8 (7.1)	-24	-4.0	20	
		Week 10	CR845	177	152 (85.9)	-5.6 (7.7)	-24	-4.0	17	-0.17 [-0.39, 0.06]
			Placebo	167	148 (88.6)	-4.3 (6.9)	-24	-3.0	20	
		Week 12	CR845	177	152 (85.9)	-5.8 (8.2)	-24	-5.0	20	-0.12 [-0.34, 0.11]
			Placebo	167	150 (89.8)	-4.9 (7.1)	-24	-3.0	20	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SSC_ISHC: Change from baseline in Skindex-10 social functioning score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Black/African American	Skindex-10 social functioning score	Baseline	CR845	135	132 (97.8)	10.3 (7.6)	0	9.0	24	
			Placebo	114	113 (99.1)	11.8 (8.2)	0	13.0	24	
		Week 4	CR845	135	115 (85.2)	7.1 (7.4)	0	4.0	24	
			Placebo	114	101 (88.6)	7.6 (7.5)	0	5.0	24	
		Week 8	CR845	135	112 (83.0)	6.2 (7.1)	0	4.0	24	
			Placebo	114	105 (92.1)	7.7 (7.9)	0	5.0	24	
		Week 10	CR845	135	108 (80.0)	5.3 (7.1)	0	2.0	24	
			Placebo	114	102 (89.5)	7.4 (7.6)	0	5.0	24	
		Week 12	CR845	135	110 (81.5)	5.3 (6.8)	0	3.0	24	
			Placebo	114	103 (90.4)	6.6 (7.5)	0	4.0	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	135	112 (83.0)	-3.3 (6.6)	-24	-3.0	13	0.11 [-0.16, 0.38]
			Placebo	114	100 (87.7)	-4.0 (7.4)	-24	-2.0	9	
		Week 8	CR845	135	109 (80.7)	-4.4 (6.6)	-24	-3.0	12	-0.02 [-0.29, 0.25]
			Placebo	114	104 (91.2)	-4.3 (7.3)	-24	-4.0	19	
		Week 10	CR845	135	106 (78.5)	-4.7 (6.2)	-24	-4.0	9	-0.00 [-0.27, 0.27]
			Placebo	114	101 (88.6)	-4.7 (7.5)	-24	-3.0	11	
		Week 12	CR845	135	107 (79.3)	-5.0 (7.1)	-24	-5.0	15	0.05 [-0.22, 0.33]
			Placebo	114	102 (89.5)	-5.4 (7.1)	-24	-4.0	7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SSC_ISHC: Change from baseline in Skindex-10 social functioning score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
White	Skindex-10 social functioning score	Baseline	CR845	255	251 (98.4)	11.5 (8.0)	0	12.0	24	
			Placebo	262	261 (99.6)	11.5 (7.8)	0	12.0	24	
		Week 4	CR845	255	234 (91.8)	8.0 (7.2)	0	7.0	24	
			Placebo	262	242 (92.4)	8.9 (7.8)	0	8.0	24	
		Week 8	CR845	255	220 (86.3)	7.0 (7.2)	0	5.0	24	
			Placebo	262	240 (91.6)	7.7 (7.5)	0	6.0	24	
		Week 10	CR845	255	225 (88.2)	6.6 (7.0)	0	4.0	24	
			Placebo	262	235 (89.7)	7.4 (7.3)	0	5.0	24	
		Week 12	CR845	255	223 (87.5)	6.2 (6.9)	0	4.0	24	
			Placebo	262	236 (90.1)	7.2 (7.2)	0	5.0	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	255	232 (91.0)	-3.5 (7.1)	-23	-3.0	19	-0.11 [-0.29, 0.07]
			Placebo	262	241 (92.0)	-2.7 (7.2)	-22	-1.0	23	
		Week 8	CR845	255	218 (85.5)	-4.2 (7.4)	-23	-4.0	24	-0.10 [-0.28, 0.08]
			Placebo	262	239 (91.2)	-3.5 (7.4)	-24	-2.0	22	
		Week 10	CR845	255	223 (87.5)	-4.7 (7.2)	-24	-4.0	17	-0.13 [-0.31, 0.05]
			Placebo	262	234 (89.3)	-3.8 (7.8)	-24	-2.0	22	
		Week 12	CR845	255	222 (87.1)	-5.1 (7.5)	-23	-4.5	20	-0.13 [-0.32, 0.05]
			Placebo	262	235 (89.7)	-4.1 (7.8)	-24	-3.0	24	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SSC_ISHC: Change from baseline in Skindex-10 social functioning score by race
ITT

C: Race	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Other	Skindex-10 social functioning score	Baseline	CR845	35	35 (100.0)	13.1 (7.3)	0	12.0	24	
			Placebo	47	44 (93.6)	12.4 (7.8)	0	12.0	24	
		Week 4	CR845	35	31 (88.6)	10.3 (7.3)	0	10.0	24	
			Placebo	47	42 (89.4)	8.3 (6.7)	0	7.0	24	
		Week 8	CR845	35	31 (88.6)	8.1 (6.4)	0	8.0	20	
			Placebo	47	42 (89.4)	8.0 (6.9)	0	6.0	24	
		Week 10	CR845	35	29 (82.9)	6.6 (7.5)	0	4.0	21	
			Placebo	47	41 (87.2)	8.0 (8.0)	0	6.0	24	
		Week 12	CR845	35	29 (82.9)	7.7 (7.9)	0	4.0	24	
			Placebo	47	41 (87.2)	6.9 (7.5)	0	4.0	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	35	31 (88.6)	-2.7 (7.4)	-24	-2.0	19	0.18 [-0.28, 0.65]
			Placebo	47	41 (87.2)	-4.0 (7.0)	-20	-3.0	7	
		Week 8	CR845	35	31 (88.6)	-5.2 (7.7)	-24	-6.0	16	-0.10 [-0.57, 0.36]
			Placebo	47	41 (87.2)	-4.4 (7.7)	-21	-2.0	12	
		Week 10	CR845	35	29 (82.9)	-6.3 (8.4)	-24	-6.0	20	-0.29 [-0.77, 0.20]
			Placebo	47	39 (83.0)	-4.1 (7.1)	-24	-2.0	11	
		Week 12	CR845	35	29 (82.9)	-5.4 (7.8)	-24	-4.0	16	-0.05 [-0.52, 0.43]
			Placebo	47	40 (85.1)	-5.1 (7.4)	-24	-3.0	10	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SSC_ISHD: Change from baseline in Skindex-10 social functioning score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 4 to < 7	Skindex-10 social functioning score	Baseline	CR845	185	183 (98.9)	9.1 (6.9)	0	8.0	24	
			Placebo	193	192 (99.5)	9.1 (7.4)	0	8.5	24	
		Week 4	CR845	185	167 (90.3)	5.5 (5.6)	0	4.0	24	
			Placebo	193	179 (92.7)	6.4 (6.5)	0	4.0	24	
		Week 8	CR845	185	162 (87.6)	4.7 (5.3)	0	4.0	24	
			Placebo	193	176 (91.2)	5.9 (6.7)	0	4.0	24	
		Week 10	CR845	185	161 (87.0)	4.3 (5.2)	0	3.0	24	
			Placebo	193	171 (88.6)	5.5 (6.8)	0	2.0	24	
		Week 12	CR845	185	158 (85.4)	4.0 (5.2)	0	2.0	24	
			Placebo	193	174 (90.2)	5.6 (6.4)	0	3.0	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	185	166 (89.7)	-3.3 (6.0)	-24	-3.0	12	-0.11 [-0.32, 0.11]
			Placebo	193	178 (92.2)	-2.6 (7.3)	-24	-1.0	23	
		Week 8	CR845	185	161 (87.0)	-4.5 (6.3)	-24	-4.0	12	-0.22 [-0.43, -0.00]
			Placebo	193	176 (91.2)	-3.0 (7.0)	-24	-1.0	22	
		Week 10	CR845	185	160 (86.5)	-4.7 (6.4)	-24	-4.0	17	-0.20 [-0.41, 0.02]
			Placebo	193	171 (88.6)	-3.2 (7.9)	-24	-2.0	22	
		Week 12	CR845	185	157 (84.9)	-5.1 (6.5)	-24	-5.0	20	-0.25 [-0.47, -0.03]
			Placebo	193	174 (90.2)	-3.4 (7.3)	-24	-3.0	24	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SSC_ISHD: Change from baseline in Skindex-10 social functioning score by baseline WI-NRS
ITT

D: Baseline worst itching NRS score (WI-NRS)	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
>= 7	Skindex-10 social functioning score	Baseline	CR845	241	236 (97.9)	12.9 (8.1)	0	14.0	24	
			Placebo	232	227 (97.8)	13.9 (7.6)	0	15.0	24	
		Week 4	CR845	241	214 (88.8)	9.8 (7.9)	0	9.0	24	
			Placebo	232	208 (89.7)	10.4 (8.1)	0	10.0	24	
		Week 8	CR845	241	202 (83.8)	8.6 (7.9)	0	7.0	24	
			Placebo	232	213 (91.8)	9.4 (7.9)	0	8.0	24	
		Week 10	CR845	241	202 (83.8)	7.8 (7.9)	0	6.0	24	
			Placebo	232	209 (90.1)	9.0 (7.6)	0	8.0	24	
		Week 12	CR845	241	205 (85.1)	7.7 (7.7)	0	5.0	24	
			Placebo	232	208 (89.7)	8.2 (7.8)	0	6.5	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	241	210 (87.1)	-3.4 (7.6)	-24	-2.0	19	0.04 [-0.16, 0.23]
			Placebo	232	205 (88.4)	-3.7 (7.2)	-24	-2.0	18	
		Week 8	CR845	241	198 (82.2)	-4.3 (7.8)	-24	-4.0	24	0.03 [-0.17, 0.22]
			Placebo	232	209 (90.1)	-4.5 (7.7)	-24	-4.0	20	
		Week 10	CR845	241	199 (82.6)	-5.0 (7.5)	-24	-4.0	20	-0.03 [-0.22, 0.17]
			Placebo	232	204 (87.9)	-4.8 (7.4)	-24	-3.0	14	
		Week 12	CR845	241	202 (83.8)	-5.1 (8.1)	-24	-4.0	16	0.07 [-0.13, 0.26]
			Placebo	232	204 (87.9)	-5.7 (7.7)	-24	-4.0	13	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SSC_ISHE: Change from baseline in Skindex-10 social functioning score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	Skindex-10 social functioning score	Baseline	CR845	359	353 (98.3)	11.4 (7.8)	0	11.0	24	
			Placebo	360	355 (98.6)	11.2 (7.9)	0	11.0	24	
		Week 4	CR845	359	320 (89.1)	7.9 (7.2)	0	7.0	24	
			Placebo	360	327 (90.8)	8.4 (7.6)	0	6.0	24	
		Week 8	CR845	359	306 (85.2)	6.8 (7.0)	0	4.0	24	
			Placebo	360	326 (90.6)	7.6 (7.6)	0	6.0	24	
		Week 10	CR845	359	306 (85.2)	6.2 (7.0)	0	4.0	24	
			Placebo	360	321 (89.2)	7.2 (7.4)	0	5.0	24	
		Week 12	CR845	359	304 (84.7)	6.0 (7.0)	0	4.0	24	
			Placebo	360	320 (88.9)	6.9 (7.2)	0	4.0	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	359	316 (88.0)	-3.5 (6.8)	-24	-3.0	19	-0.08 [-0.24, 0.07]
			Placebo	360	324 (90.0)	-2.9 (7.1)	-24	-2.0	23	
		Week 8	CR845	359	302 (84.1)	-4.5 (7.0)	-24	-4.0	16	-0.14 [-0.30, 0.02]
			Placebo	360	323 (89.7)	-3.5 (7.3)	-24	-3.0	22	
		Week 10	CR845	359	302 (84.1)	-4.9 (6.9)	-24	-4.0	20	-0.15 [-0.31, 0.00]
			Placebo	360	317 (88.1)	-3.8 (7.7)	-24	-3.0	22	
		Week 12	CR845	359	301 (83.8)	-5.2 (7.2)	-24	-5.0	16	-0.13 [-0.29, 0.03]
			Placebo	360	317 (88.1)	-4.2 (7.5)	-24	-3.0	24	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SSC_ISHE: Change from baseline in Skindex-10 social functioning score by specific medical condition
ITT

E: Presence of specific medical conditions	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	Skindex-10 social functioning score	Baseline	CR845	67	66 (98.5)	10.7 (7.8)	0	9.0	24	
			Placebo	65	64 (98.5)	14.0 (7.6)	0	16.0	24	
		Week 4	CR845	67	61 (91.0)	8.1 (7.5)	0	6.0	24	
			Placebo	65	60 (92.3)	9.6 (7.7)	0	8.0	24	
		Week 8	CR845	67	58 (86.6)	7.5 (7.8)	0	5.5	24	
			Placebo	65	63 (96.9)	9.1 (7.4)	0	8.0	24	
		Week 10	CR845	67	57 (85.1)	6.3 (7.4)	0	3.0	24	
			Placebo	65	59 (90.8)	8.4 (7.7)	0	7.0	24	
		Week 12	CR845	67	59 (88.1)	6.4 (6.9)	0	4.0	24	
			Placebo	65	62 (95.4)	7.8 (7.6)	0	6.5	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	67	60 (89.6)	-2.8 (7.5)	-20	-1.5	19	0.24 [-0.12, 0.60]
			Placebo	65	59 (90.8)	-4.7 (8.0)	-24	-3.0	9	
		Week 8	CR845	67	57 (85.1)	-3.5 (7.8)	-21	-2.0	24	0.24 [-0.12, 0.60]
			Placebo	65	62 (95.4)	-5.4 (7.7)	-24	-4.0	10	
		Week 10	CR845	67	57 (85.1)	-4.4 (7.8)	-22	-4.0	17	0.17 [-0.20, 0.53]
			Placebo	65	58 (89.2)	-5.7 (7.6)	-24	-4.0	7	
		Week 12	CR845	67	58 (86.6)	-4.6 (8.4)	-23	-4.5	20	0.24 [-0.13, 0.60]
			Placebo	65	61 (93.8)	-6.5 (7.9)	-24	-4.0	7	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SSC_ISHF: Change from baseline in Skindex-10 social functioning score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
No	Skindex-10 social functioning score	Baseline	CR845	267	261 (97.8)	10.8 (7.9)	0	11.0	24	
			Placebo	262	260 (99.2)	11.6 (7.9)	0	12.0	24	
		Week 4	CR845	267	246 (92.1)	7.5 (7.1)	0	6.0	24	
			Placebo	262	238 (90.8)	8.2 (7.6)	0	6.0	24	
		Week 8	CR845	267	238 (89.1)	6.5 (6.9)	0	4.0	24	
			Placebo	262	241 (92.0)	7.4 (7.4)	0	6.0	24	
		Week 10	CR845	267	232 (86.9)	6.1 (7.0)	0	4.0	24	
			Placebo	262	237 (90.5)	7.0 (7.1)	0	5.0	24	
		Week 12	CR845	267	234 (87.6)	6.0 (7.0)	0	3.0	24	
			Placebo	262	241 (92.0)	6.7 (7.0)	0	5.0	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	267	242 (90.6)	-3.2 (7.3)	-24	-2.0	19	0.02 [-0.16, 0.20]
			Placebo	262	237 (90.5)	-3.4 (7.6)	-24	-2.0	23	
		Week 8	CR845	267	234 (87.6)	-4.2 (7.1)	-24	-3.0	24	-0.03 [-0.21, 0.15]
			Placebo	262	241 (92.0)	-4.0 (7.8)	-24	-3.0	22	
		Week 10	CR845	267	229 (85.8)	-4.6 (7.0)	-24	-4.0	17	-0.03 [-0.21, 0.15]
			Placebo	262	236 (90.1)	-4.3 (8.3)	-24	-3.0	22	
		Week 12	CR845	267	231 (86.5)	-4.8 (7.7)	-24	-4.0	20	-0.00 [-0.18, 0.18]
			Placebo	262	240 (91.6)	-4.8 (8.1)	-24	-3.0	24	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2SSC_ISHF: Change from baseline in Skindex-10 social functioning score by use of concomitant itch medication
ITT

F: Use of concomitant itch medication	Variable		Treatment	N	n (%)	Mean (SD)	Min	Q50	Max	Hedge's G [95% CI]
Yes	Skindex-10 social functioning score	Baseline	CR845	159	158 (99.4)	12.1 (7.6)	0	11.5	24	
			Placebo	163	159 (97.5)	11.8 (7.9)	0	12.0	24	
		Week 4	CR845	159	135 (84.9)	8.6 (7.5)	0	7.0	24	
			Placebo	163	149 (91.4)	9.2 (7.7)	0	8.0	24	
		Week 8	CR845	159	126 (79.2)	7.6 (7.5)	0	5.0	24	
			Placebo	163	148 (90.8)	8.5 (7.8)	0	6.0	24	
		Week 10	CR845	159	131 (82.4)	6.5 (7.2)	0	4.0	24	
			Placebo	163	143 (87.7)	8.1 (7.9)	0	7.0	24	
		Week 12	CR845	159	129 (81.1)	6.2 (6.8)	0	4.0	24	
			Placebo	163	141 (86.5)	7.7 (7.7)	0	4.0	24	
	Change from baseline in Skindex-10 social functioning score	Week 4	CR845	159	134 (84.3)	-3.6 (6.4)	-24	-3.0	19	-0.12 [-0.36, 0.11]
			Placebo	163	146 (89.6)	-2.8 (6.6)	-21	-1.5	15	
		Week 8	CR845	159	125 (78.6)	-4.6 (7.2)	-24	-4.0	16	-0.16 [-0.40, 0.08]
			Placebo	163	144 (88.3)	-3.5 (6.7)	-24	-2.5	19	
		Week 10	CR845	159	130 (81.8)	-5.3 (7.1)	-24	-5.0	20	-0.25 [-0.49, -0.01]
			Placebo	163	139 (85.3)	-3.6 (6.6)	-22	-3.0	17	
		Week 12	CR845	159	128 (80.5)	-5.6 (6.9)	-24	-5.0	16	-0.20 [-0.45, 0.04]
			Placebo	163	138 (84.7)	-4.2 (6.7)	-24	-3.5	19	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of evaluable values. SD = standard deviation. Q = quantile.
95% CI = 95% confidence interval for Hedges G.
Source Data: askin_i, created on: 17FEB2022

Table IT2STC_ISCA: Change from baseline in Skindex-10 total score - MMRM results by age
ITT

Change from baseline in Skindex-10 total score					Repeated measures analysis					
					Change from Baseline		Treatment Difference			
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value	
A: Age									0.466	
< 65 years	Week 4	CR845	282	245 (86.9)	-10.5 (1.0)	(-12.5, -8.6)	-3.0 (1.2)	(-5.3, -0.7)	0.010	*
		Placebo	290	247 (85.2)	-7.5 (1.0)	(-9.5, -5.5)				
>= 65 years	Week 4	CR845	144	124 (86.1)	-10.1 (1.4)	(-12.9, -7.3)	-1.1 (1.8)	(-4.6, 2.4)	0.535	
		Placebo	135	122 (90.4)	-9.0 (1.4)	(-11.8, -6.2)				
< 65 years	Week 8	CR845	282	229 (81.2)	-13.4 (1.1)	(-15.4, -11.3)	-2.3 (1.3)	(-4.7, 0.2)	0.073	
		Placebo	290	254 (87.6)	-11.1 (1.0)	(-13.2, -9.1)				
>= 65 years	Week 8	CR845	144	120 (83.3)	-13.5 (1.4)	(-16.2, -10.7)	-2.1 (1.7)	(-5.5, 1.3)	0.220	
		Placebo	135	121 (89.6)	-11.3 (1.4)	(-14.0, -8.7)				
< 65 years	Week 10	CR845	282	235 (83.3)	-15.9 (1.1)	(-18.0, -13.8)	-3.9 (1.3)	(-6.4, -1.3)	0.003	*
		Placebo	290	248 (85.5)	-12.0 (1.1)	(-14.1, -9.9)				
>= 65 years	Week 10	CR845	144	117 (81.3)	-15.5 (1.4)	(-18.3, -12.8)	-2.5 (1.7)	(-6.0, 0.9)	0.146	
		Placebo	135	119 (88.1)	-13.0 (1.4)	(-15.7, -10.3)				
< 65 years	Week 12	CR845	282	235 (83.3)	-16.9 (1.1)	(-19.0, -14.7)	-3.9 (1.3)	(-6.4, -1.3)	0.003	*
		Placebo	290	250 (86.2)	-13.0 (1.1)	(-15.1, -10.9)				
>= 65 years	Week 12	CR845	144	118 (81.9)	-15.8 (1.4)	(-18.5, -13.0)	-2.1 (1.7)	(-5.6, 1.3)	0.226	
		Placebo	135	118 (87.4)	-13.7 (1.4)	(-16.4, -11.0)				

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin_i, created on: 17FEB2022

Table IT2STC_ISCB: Change from baseline in Skindex-10 total score - MMRM results by sex
ITT

Change from baseline in Skindex-10 total score					Repeated measures analysis					
					Change from Baseline		Treatment Difference			
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value	
B: Sex									0.029	i
Male	Week 4	CR845	249	216 (86.7)	-8.9 (1.1)	(-11.0, -6.8)	-1.1 (1.2)	(-3.5, 1.3)	0.378	
		Placebo	258	216 (83.7)	-7.9 (1.1)	(-9.9, -5.8)				
Female	Week 4	CR845	177	153 (86.4)	-12.2 (1.3)	(-14.7, -9.7)	-4.4 (1.6)	(-7.6, -1.3)	0.006	*
		Placebo	167	153 (91.6)	-7.8 (1.3)	(-10.3, -5.2)				
Male	Week 8	CR845	249	205 (82.3)	-11.1 (1.1)	(-13.2, -8.9)	-0.6 (1.3)	(-3.1, 1.9)	0.650	
		Placebo	258	228 (88.4)	-10.5 (1.1)	(-12.6, -8.4)				
Female	Week 8	CR845	177	144 (81.4)	-16.4 (1.3)	(-18.9, -13.9)	-4.6 (1.7)	(-7.9, -1.4)	0.005	*
		Placebo	167	147 (88.0)	-11.7 (1.3)	(-14.3, -9.2)				
Male	Week 10	CR845	249	205 (82.3)	-12.8 (1.1)	(-15.0, -10.6)	-1.4 (1.3)	(-3.9, 1.2)	0.298	
		Placebo	258	222 (86.0)	-11.5 (1.1)	(-13.6, -9.4)				
Female	Week 10	CR845	177	147 (83.1)	-19.6 (1.3)	(-22.1, -17.0)	-6.5 (1.7)	(-9.8, -3.2)	<0.001	*
		Placebo	167	145 (86.8)	-13.1 (1.3)	(-15.7, -10.5)				
Male	Week 12	CR845	249	203 (81.5)	-14.2 (1.1)	(-16.4, -12.0)	-1.9 (1.3)	(-4.4, 0.7)	0.151	
		Placebo	258	223 (86.4)	-12.3 (1.1)	(-14.4, -10.2)				
Female	Week 12	CR845	177	150 (84.7)	-19.5 (1.3)	(-22.1, -16.9)	-5.4 (1.7)	(-8.7, -2.0)	0.002	*
		Placebo	167	145 (86.8)	-14.1 (1.4)	(-16.8, -11.4)				

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin_i, created on: 17FEB2022

Table IT2STC_ISCC: Change from baseline in Skindex-10 total score - MMRM results by race
ITT

Change from baseline in Skindex-10 total score					Repeated measures analysis					
					Change from Baseline		Treatment Difference			
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value	
C: Race									0.462	
Black/African American	Week 4	CR845	135	111 (82.2)	-9.9 (1.3)	(-12.5, -7.3)	-1.7 (1.7)	(-5.2, 1.7)	0.324	
		Placebo	114	95 (83.3)	-8.2 (1.4)	(-11.0, -5.4)				
White	Week 4	CR845	255	226 (88.6)	-10.7 (1.1)	(-12.9, -8.6)	-3.3 (1.3)	(-5.8, -0.7)	0.012	*
		Placebo	262	232 (88.5)	-7.5 (1.1)	(-9.6, -5.3)				
Other	Week 4	CR845	35	31 (88.6)	-9.0 (3.1)	(-15.2, -2.9)	0.4 (3.1)	(-5.7, 6.6)	0.891	
		Placebo	47	41 (87.2)	-9.5 (2.7)	(-14.9, -4.0)				
Black/African American	Week 8	CR845	135	108 (80.0)	-13.8 (1.4)	(-16.5, -11.0)	-2.0 (1.8)	(-5.6, 1.6)	0.276	
		Placebo	114	100 (87.7)	-11.8 (1.5)	(-14.7, -8.9)				
White	Week 8	CR845	255	209 (82.0)	-13.1 (1.1)	(-15.4, -10.9)	-2.7 (1.3)	(-5.3, -0.1)	0.043	*
		Placebo	262	234 (89.3)	-10.4 (1.1)	(-12.6, -8.3)				
Other	Week 8	CR845	35	31 (88.6)	-13.2 (3.2)	(-19.6, -6.8)	-0.3 (3.3)	(-6.9, 6.3)	0.931	
		Placebo	47	40 (85.1)	-12.9 (2.8)	(-18.6, -7.2)				
Black/African American	Week 10	CR845	135	105 (77.8)	-15.9 (1.4)	(-18.8, -13.1)	-2.5 (1.9)	(-6.2, 1.3)	0.201	
		Placebo	114	96 (84.2)	-13.5 (1.5)	(-16.5, -10.5)				
White	Week 10	CR845	255	217 (85.1)	-15.6 (1.1)	(-17.8, -13.4)	-4.0 (1.3)	(-6.6, -1.5)	0.002	*
		Placebo	262	231 (88.2)	-11.6 (1.1)	(-13.7, -9.4)				
Other	Week 10	CR845	35	29 (82.9)	-16.0 (3.4)	(-22.8, -9.2)	-3.5 (3.7)	(-10.8, 3.9)	0.352	
		Placebo	47	39 (83.0)	-12.6 (3.0)	(-18.6, -6.5)				
Black/African American	Week 12	CR845	135	104 (77.0)	-17.4 (1.5)	(-20.3, -14.5)	-3.2 (1.9)	(-7.0, 0.6)	0.099	
		Placebo	114	99 (86.8)	-14.2 (1.5)	(-17.2, -11.2)				
White	Week 12	CR845	255	219 (85.9)	-16.3 (1.1)	(-18.5, -14.1)	-4.2 (1.3)	(-6.9, -1.6)	0.001	*
		Placebo	262	228 (87.0)	-12.1 (1.1)	(-14.2, -9.9)				

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin_i, created on: 17FEB2022

Table IT2STC_ISCC: Change from baseline in Skindex-10 total score - MMRM results by race
ITT

Change from baseline in Skindex-10 total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Other	Week 12	CR845	35	29 (82.9)	-14.5 (3.5)	(-21.5, -7.4)	1.2 (3.8)	(-6.4, 8.9)	0.749
		Placebo	47	40 (85.1)	-15.7 (3.1)	(-21.9, -9.5)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin_i, created on: 17FEB2022

Table IT2STC_ISCD: Change from baseline in Skindex-10 total score - MMRM results by baseline WI-NRS
ITT

Change from baseline in Skindex-10 total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
D: Baseline worst itching NRS score (WI-NRS)									0.207
>= 4 to < 7	Week 4	CR845	185	164 (88.6)	-11.5 (1.2)	(-13.8, -9.1)	-3.8 (1.3)	(-6.4, -1.1)	0.005 *
		Placebo	193	170 (88.1)	-7.7 (1.1)	(-10.0, -5.4)			
>= 7	Week 4	CR845	241	205 (85.1)	-10.0 (1.1)	(-12.1, -7.8)	-1.5 (1.4)	(-4.3, 1.2)	0.263
		Placebo	232	199 (85.8)	-8.4 (1.1)	(-10.6, -6.2)			
>= 4 to < 7	Week 8	CR845	185	159 (85.9)	-13.8 (1.2)	(-16.2, -11.4)	-3.6 (1.4)	(-6.3, -0.9)	0.009 *
		Placebo	193	171 (88.6)	-10.2 (1.2)	(-12.5, -7.9)			
>= 7	Week 8	CR845	241	190 (78.8)	-13.4 (1.2)	(-15.7, -11.1)	-1.2 (1.5)	(-4.1, 1.6)	0.398
		Placebo	232	204 (87.9)	-12.2 (1.2)	(-14.5, -9.9)			
>= 4 to < 7	Week 10	CR845	185	158 (85.4)	-15.5 (1.2)	(-17.9, -13.1)	-4.1 (1.4)	(-6.9, -1.4)	0.003 *
		Placebo	193	169 (87.6)	-11.3 (1.2)	(-13.6, -9.0)			
>= 7	Week 10	CR845	241	194 (80.5)	-16.4 (1.2)	(-18.7, -14.1)	-3.1 (1.5)	(-6.0, -0.2)	0.039 *
		Placebo	232	198 (85.3)	-13.3 (1.2)	(-15.7, -11.0)			
>= 4 to < 7	Week 12	CR845	185	156 (84.3)	-16.1 (1.2)	(-18.5, -13.7)	-4.9 (1.4)	(-7.6, -2.2)	<0.001 *
		Placebo	193	169 (87.6)	-11.2 (1.2)	(-13.5, -9.0)			
>= 7	Week 12	CR845	241	197 (81.7)	-17.2 (1.2)	(-19.5, -14.9)	-2.2 (1.5)	(-5.2, 0.8)	0.157
		Placebo	232	199 (85.8)	-15.0 (1.2)	(-17.4, -12.7)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin_i, created on: 17FEB2022

Table IT2STC_ISCE: Change from baseline in Skindex-10 total score - MMRM results by specific medical condition
ITT

Change from baseline in Skindex-10 total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
E: Presence of specific medical conditions									0.561
No	Week 4	CR845	359	309 (86.1)	-10.3 (0.8)	(-11.8, -8.8)	-2.7 (1.0)	(-4.7, -0.6)	0.011 *
		Placebo	360	318 (88.3)	-7.6 (0.7)	(-9.1, -6.2)			
Yes	Week 4	CR845	67	60 (89.6)	-11.0 (1.9)	(-14.8, -7.2)	-1.6 (2.8)	(-7.2, 4.0)	0.571
		Placebo	65	51 (78.5)	-9.4 (2.0)	(-13.4, -5.4)			
No	Week 8	CR845	359	294 (81.9)	-13.3 (0.8)	(-14.9, -11.7)	-2.4 (1.1)	(-4.6, -0.3)	0.026 *
		Placebo	360	317 (88.1)	-10.9 (0.8)	(-12.4, -9.3)			
Yes	Week 8	CR845	67	55 (82.1)	-13.6 (1.9)	(-17.4, -9.7)	-1.3 (2.8)	(-6.8, 4.2)	0.636
		Placebo	65	58 (89.2)	-12.3 (1.9)	(-16.1, -8.4)			
No	Week 10	CR845	359	296 (82.5)	-15.5 (0.8)	(-17.1, -13.9)	-3.7 (1.1)	(-5.9, -1.5)	0.001 *
		Placebo	360	312 (86.7)	-11.8 (0.8)	(-13.4, -10.3)			
Yes	Week 10	CR845	67	56 (83.6)	-17.1 (2.0)	(-21.0, -13.2)	-2.7 (2.8)	(-8.3, 2.9)	0.344
		Placebo	65	55 (84.6)	-14.4 (2.0)	(-18.3, -10.5)			
No	Week 12	CR845	359	295 (82.2)	-16.3 (0.8)	(-17.9, -14.7)	-3.6 (1.1)	(-5.9, -1.4)	0.001 *
		Placebo	360	310 (86.1)	-12.6 (0.8)	(-14.2, -11.1)			
Yes	Week 12	CR845	67	58 (86.6)	-17.6 (2.0)	(-21.5, -13.6)	-1.9 (2.8)	(-7.5, 3.7)	0.506
		Placebo	65	58 (89.2)	-15.7 (2.0)	(-19.6, -11.7)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor previous use of anti-itch medication is also included in the model.
Source Data: askin_i, created on: 17FEB2022

Table IT2STC_ISCF: Change from baseline in Skindex-10 total score - MMRM results by use of concomitant itch medication
ITT

Change from baseline in Skindex-10 total score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
F: Use of concomitant itch medication									0.684
No	Week 4	CR845	267	236 (88.4)	-9.8 (1.1)	(-11.9, -7.7)	-2.3 (1.3)	(-4.8, 0.2)	0.067
		Placebo	262	229 (87.4)	-7.5 (1.1)	(-9.6, -5.4)			
Yes	Week 4	CR845	159	133 (83.6)	-11.4 (1.2)	(-13.8, -9.0)	-2.8 (1.6)	(-5.9, 0.3)	0.079
		Placebo	163	140 (85.9)	-8.6 (1.2)	(-11.1, -6.2)			
No	Week 8	CR845	267	229 (85.8)	-13.2 (1.1)	(-15.3, -11.0)	-2.5 (1.3)	(-5.0, -0.0)	0.048 *
		Placebo	262	234 (89.3)	-10.6 (1.1)	(-12.8, -8.5)			
Yes	Week 8	CR845	159	120 (75.5)	-13.7 (1.3)	(-16.3, -11.1)	-1.8 (1.7)	(-5.1, 1.5)	0.294
		Placebo	163	141 (86.5)	-11.9 (1.3)	(-14.4, -9.4)			
No	Week 10	CR845	267	224 (83.9)	-14.8 (1.1)	(-17.0, -12.6)	-3.0 (1.3)	(-5.6, -0.4)	0.024 *
		Placebo	262	230 (87.8)	-11.8 (1.1)	(-14.0, -9.7)			
Yes	Week 10	CR845	159	128 (80.5)	-17.4 (1.3)	(-19.9, -14.8)	-4.4 (1.6)	(-7.7, -1.2)	0.008 *
		Placebo	163	137 (84.0)	-12.9 (1.3)	(-15.4, -10.4)			
No	Week 12	CR845	267	226 (84.6)	-15.6 (1.1)	(-17.8, -13.5)	-2.6 (1.3)	(-5.2, -0.0)	0.047 *
		Placebo	262	234 (89.3)	-13.0 (1.1)	(-15.2, -10.9)			
Yes	Week 12	CR845	159	127 (79.9)	-18.0 (1.3)	(-20.6, -15.4)	-4.6 (1.7)	(-8.0, -1.3)	0.007 *
		Placebo	163	134 (82.2)	-13.3 (1.3)	(-15.9, -10.8)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor presence of medical condition is also included in the model.
Source Data: askin_i, created on: 17FEB2022

Table IT2SDC_ISCA: Change from baseline in Skindex-10 disease score - MMRM results by age
ITT

Change from baseline in Skindex-10 disease score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
A: Age									0.134
< 65 years	Week 4	CR845	282	249 (88.3)	-3.6 (0.3)	(-4.2, -3.0)	-1.6 (0.4)	(-2.3, -0.8)	<0.001 *
		Placebo	290	253 (87.2)	-2.1 (0.3)	(-2.7, -1.5)			
>= 65 years	Week 4	CR845	144	127 (88.2)	-3.5 (0.5)	(-4.4, -2.6)	-0.4 (0.6)	(-1.5, 0.8)	0.525
		Placebo	135	125 (92.6)	-3.2 (0.5)	(-4.1, -2.3)			
< 65 years	Week 8	CR845	282	238 (84.4)	-4.5 (0.3)	(-5.2, -3.9)	-1.0 (0.4)	(-1.8, -0.2)	0.012 *
		Placebo	290	260 (89.7)	-3.5 (0.3)	(-4.2, -2.9)			
>= 65 years	Week 8	CR845	144	125 (86.8)	-4.5 (0.5)	(-5.4, -3.6)	-0.6 (0.6)	(-1.7, 0.5)	0.280
		Placebo	135	123 (91.1)	-3.9 (0.4)	(-4.7, -3.0)			
< 65 years	Week 10	CR845	282	237 (84.0)	-5.4 (0.3)	(-6.1, -4.8)	-1.5 (0.4)	(-2.3, -0.7)	<0.001 *
		Placebo	290	252 (86.9)	-3.9 (0.3)	(-4.5, -3.3)			
>= 65 years	Week 10	CR845	144	120 (83.3)	-5.4 (0.5)	(-6.3, -4.4)	-1.1 (0.6)	(-2.2, 0.1)	0.070
		Placebo	135	123 (91.1)	-4.3 (0.5)	(-5.2, -3.4)			
< 65 years	Week 12	CR845	282	238 (84.4)	-5.8 (0.3)	(-6.5, -5.2)	-1.7 (0.4)	(-2.5, -0.9)	<0.001 *
		Placebo	290	254 (87.6)	-4.1 (0.3)	(-4.8, -3.4)			
>= 65 years	Week 12	CR845	144	120 (83.3)	-5.4 (0.5)	(-6.3, -4.4)	-0.7 (0.6)	(-1.9, 0.4)	0.210
		Placebo	135	121 (89.6)	-4.6 (0.5)	(-5.5, -3.7)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin_i, created on: 17FEB2022

Table IT2SDC_ISCB: Change from baseline in Skindex-10 disease score - MMRM results by sex
ITT

Change from baseline in Skindex-10 disease score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
B: Sex									0.012 i
Male	Week 4	CR845	249	219 (88.0)	-2.9 (0.3)	(-3.6, -2.2)	-0.7 (0.4)	(-1.5, 0.1)	0.087
		Placebo	258	225 (87.2)	-2.2 (0.3)	(-2.9, -1.6)			
Female	Week 4	CR845	177	157 (88.7)	-4.5 (0.4)	(-5.3, -3.7)	-1.8 (0.5)	(-2.8, -0.9)	<0.001 *
		Placebo	167	153 (91.6)	-2.7 (0.4)	(-3.5, -1.9)			
Male	Week 8	CR845	249	210 (84.3)	-3.6 (0.3)	(-4.3, -2.9)	-0.3 (0.4)	(-1.1, 0.5)	0.487
		Placebo	258	235 (91.1)	-3.3 (0.3)	(-4.0, -2.7)			
Female	Week 8	CR845	177	153 (86.4)	-5.7 (0.4)	(-6.5, -4.9)	-1.7 (0.5)	(-2.7, -0.6)	0.002 *
		Placebo	167	148 (88.6)	-4.0 (0.4)	(-4.8, -3.2)			
Male	Week 10	CR845	249	207 (83.1)	-4.2 (0.3)	(-4.9, -3.5)	-0.5 (0.4)	(-1.3, 0.3)	0.204
		Placebo	258	228 (88.4)	-3.7 (0.3)	(-4.3, -3.0)			
Female	Week 10	CR845	177	150 (84.7)	-6.9 (0.4)	(-7.7, -6.1)	-2.5 (0.5)	(-3.6, -1.4)	<0.001 *
		Placebo	167	147 (88.0)	-4.4 (0.4)	(-5.3, -3.6)			
Male	Week 12	CR845	249	205 (82.3)	-4.8 (0.4)	(-5.5, -4.0)	-0.9 (0.4)	(-1.8, -0.1)	0.027 *
		Placebo	258	228 (88.4)	-3.8 (0.3)	(-4.5, -3.1)			
Female	Week 12	CR845	177	153 (86.4)	-6.8 (0.4)	(-7.7, -6.0)	-2.0 (0.6)	(-3.1, -0.9)	<0.001 *
		Placebo	167	147 (88.0)	-4.9 (0.4)	(-5.7, -4.0)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin_i, created on: 17FEB2022

Table IT2SDC_ISCC: Change from baseline in Skindex-10 disease score - MMRM results by race
ITT

Change from baseline in Skindex-10 disease score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
C: Race									0.480
Black/African American	Week 4	CR845	135	113 (83.7)	-3.4 (0.4)	(-4.3, -2.6)	-1.1 (0.6)	(-2.2, 0.0)	0.057
		Placebo	114	97 (85.1)	-2.3 (0.5)	(-3.2, -1.4)			
White	Week 4	CR845	255	231 (90.6)	-3.7 (0.3)	(-4.4, -3.1)	-1.3 (0.4)	(-2.1, -0.5)	0.001 *
		Placebo	262	238 (90.8)	-2.4 (0.3)	(-3.1, -1.7)			
Other	Week 4	CR845	35	31 (88.6)	-3.3 (0.9)	(-5.1, -1.4)	-0.5 (1.0)	(-2.4, 1.4)	0.620
		Placebo	47	41 (87.2)	-2.8 (0.8)	(-4.5, -1.1)			
Black/African American	Week 8	CR845	135	111 (82.2)	-4.5 (0.5)	(-5.4, -3.7)	-0.7 (0.6)	(-1.9, 0.4)	0.212
		Placebo	114	103 (90.4)	-3.8 (0.5)	(-4.7, -2.9)			
White	Week 8	CR845	255	220 (86.3)	-4.5 (0.4)	(-5.2, -3.8)	-0.9 (0.4)	(-1.8, -0.1)	0.027 *
		Placebo	262	238 (90.8)	-3.6 (0.3)	(-4.2, -2.9)			
Other	Week 8	CR845	35	31 (88.6)	-4.4 (1.0)	(-6.3, -2.5)	-0.7 (1.0)	(-2.7, 1.3)	0.486
		Placebo	47	40 (85.1)	-3.7 (0.8)	(-5.4, -2.0)			
Black/African American	Week 10	CR845	135	105 (77.8)	-5.4 (0.5)	(-6.4, -4.5)	-1.2 (0.6)	(-2.5, 0.0)	0.058
		Placebo	114	98 (86.0)	-4.2 (0.5)	(-5.2, -3.2)			
White	Week 10	CR845	255	222 (87.1)	-5.4 (0.4)	(-6.1, -4.7)	-1.5 (0.4)	(-2.3, -0.7)	<0.001 *
		Placebo	262	235 (89.7)	-3.9 (0.3)	(-4.6, -3.2)			
Other	Week 10	CR845	35	29 (82.9)	-5.1 (1.0)	(-7.1, -3.1)	-0.8 (1.1)	(-3.0, 1.3)	0.438
		Placebo	47	40 (85.1)	-4.3 (0.9)	(-6.0, -2.5)			
Black/African American	Week 12	CR845	135	105 (77.8)	-6.0 (0.5)	(-7.0, -5.0)	-1.6 (0.7)	(-2.9, -0.2)	0.021 *
		Placebo	114	101 (88.6)	-4.4 (0.5)	(-5.5, -3.4)			
White	Week 12	CR845	255	223 (87.5)	-5.7 (0.4)	(-6.4, -5.0)	-1.7 (0.4)	(-2.6, -0.9)	<0.001 *
		Placebo	262	232 (88.5)	-4.0 (0.3)	(-4.6, -3.3)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin_i, created on: 17FEB2022

Table IT2SDC_ISCC: Change from baseline in Skindex-10 disease score - MMRM results by race
ITT

Change from baseline in Skindex-10 disease score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Other	Week 12	CR845	35	29 (82.9)	-4.5 (1.0)	(-6.6, -2.4)	1.0 (1.1)	(-1.2, 3.3)	0.367
		Placebo	47	41 (87.2)	-5.5 (0.9)	(-7.4, -3.7)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin_i, created on: 17FEB2022

Table IT2SDC_ISCD: Change from baseline in Skindex-10 disease score - MMRM results by baseline WI-NRS
ITT

Change from baseline in Skindex-10 disease score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
D: Baseline worst itching NRS score (WI-NRS)									0.419
>= 4 to < 7	Week 4	CR845	185	166 (89.7)	-3.8 (0.4)	(-4.6, -3.1)	-1.5 (0.4)	(-2.4, -0.6)	<0.001 *
		Placebo	193	173 (89.6)	-2.3 (0.4)	(-3.1, -1.6)			
>= 7	Week 4	CR845	241	210 (87.1)	-3.6 (0.3)	(-4.3, -2.9)	-1.0 (0.4)	(-1.8, -0.1)	0.024 *
		Placebo	232	205 (88.4)	-2.6 (0.3)	(-3.3, -2.0)			
>= 4 to < 7	Week 8	CR845	185	163 (88.1)	-4.6 (0.4)	(-5.4, -3.8)	-1.4 (0.4)	(-2.2, -0.5)	0.003 *
		Placebo	193	174 (90.2)	-3.2 (0.4)	(-4.0, -2.5)			
>= 7	Week 8	CR845	241	200 (83.0)	-4.6 (0.4)	(-5.3, -3.9)	-0.5 (0.5)	(-1.4, 0.4)	0.247
		Placebo	232	209 (90.1)	-4.1 (0.4)	(-4.8, -3.4)			
>= 4 to < 7	Week 10	CR845	185	160 (86.5)	-5.1 (0.4)	(-5.9, -4.3)	-1.4 (0.4)	(-2.3, -0.5)	0.002 *
		Placebo	193	170 (88.1)	-3.7 (0.4)	(-4.5, -3.0)			
>= 7	Week 10	CR845	241	197 (81.7)	-5.8 (0.4)	(-6.5, -5.1)	-1.4 (0.5)	(-2.3, -0.5)	0.003 *
		Placebo	232	205 (88.4)	-4.4 (0.4)	(-5.1, -3.7)			
>= 4 to < 7	Week 12	CR845	185	157 (84.9)	-5.3 (0.4)	(-6.1, -4.5)	-1.5 (0.5)	(-2.4, -0.6)	0.001 *
		Placebo	193	171 (88.6)	-3.8 (0.4)	(-4.6, -3.1)			
>= 7	Week 12	CR845	241	201 (83.4)	-6.1 (0.4)	(-6.9, -5.4)	-1.4 (0.5)	(-2.4, -0.4)	0.005 *
		Placebo	232	204 (87.9)	-4.7 (0.4)	(-5.5, -4.0)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin_i, created on: 17FEB2022

Table IT2SDC_ISCE: Change from baseline in Skindex-10 disease score - MMRM results by specific medical condition
ITT

Change from baseline in Skindex-10 disease score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
E: Presence of specific medical conditions									0.648
No	Week 4	CR845	359	315 (87.7)	-3.6 (0.2)	(-4.1, -3.1)	-1.1 (0.3)	(-1.8, -0.5)	<0.001 *
		Placebo	360	322 (89.4)	-2.5 (0.2)	(-2.9, -2.0)			
Yes	Week 4	CR845	67	61 (91.0)	-4.1 (0.6)	(-5.3, -2.9)	-1.3 (0.9)	(-3.0, 0.4)	0.146
		Placebo	65	56 (86.2)	-2.8 (0.6)	(-4.0, -1.6)			
No	Week 8	CR845	359	305 (85.0)	-4.5 (0.3)	(-5.0, -4.0)	-0.8 (0.4)	(-1.5, -0.1)	0.018 *
		Placebo	360	321 (89.2)	-3.7 (0.2)	(-4.2, -3.2)			
Yes	Week 8	CR845	67	58 (86.6)	-4.7 (0.6)	(-6.0, -3.5)	-0.9 (0.9)	(-2.7, 0.8)	0.285
		Placebo	65	62 (95.4)	-3.8 (0.6)	(-5.0, -2.6)			
No	Week 10	CR845	359	300 (83.6)	-5.3 (0.3)	(-5.9, -4.8)	-1.3 (0.4)	(-2.0, -0.6)	<0.001 *
		Placebo	360	317 (88.1)	-4.1 (0.3)	(-4.6, -3.6)			
Yes	Week 10	CR845	67	57 (85.1)	-6.0 (0.6)	(-7.2, -4.8)	-1.6 (0.9)	(-3.3, 0.1)	0.068
		Placebo	65	58 (89.2)	-4.4 (0.6)	(-5.6, -3.2)			
No	Week 12	CR845	359	299 (83.3)	-5.6 (0.3)	(-6.1, -5.1)	-1.3 (0.4)	(-2.0, -0.6)	<0.001 *
		Placebo	360	315 (87.5)	-4.3 (0.3)	(-4.8, -3.8)			
Yes	Week 12	CR845	67	59 (88.1)	-6.4 (0.6)	(-7.6, -5.1)	-1.7 (0.9)	(-3.5, 0.1)	0.060
		Placebo	65	60 (92.3)	-4.7 (0.6)	(-5.9, -3.4)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor previous use of anti-itch medication is also included in the model.
Source Data: askin_i, created on: 17FEB2022

Table IT2SDC_ISCF: Change from baseline in Skindex-10 disease score - MMRM results by use of concomitant itch medication
ITT

Change from baseline in Skindex-10 disease score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
F: Use of concomitant itch medication									0.637
No	Week 4	CR845	267	242 (90.6)	-3.2 (0.3)	(-3.9, -2.6)	-1.0 (0.4)	(-1.8, -0.3)	0.010 *
		Placebo	262	233 (88.9)	-2.2 (0.3)	(-2.9, -1.5)			
Yes	Week 4	CR845	159	134 (84.3)	-4.2 (0.4)	(-5.0, -3.4)	-1.5 (0.5)	(-2.5, -0.5)	0.004 *
		Placebo	163	145 (89.0)	-2.8 (0.4)	(-3.5, -2.0)			
No	Week 8	CR845	267	235 (88.0)	-4.4 (0.3)	(-5.1, -3.8)	-1.1 (0.4)	(-1.8, -0.3)	0.009 *
		Placebo	262	237 (90.5)	-3.4 (0.3)	(-4.1, -2.7)			
Yes	Week 8	CR845	159	128 (80.5)	-4.6 (0.4)	(-5.4, -3.7)	-0.6 (0.5)	(-1.7, 0.5)	0.286
		Placebo	163	146 (89.6)	-4.0 (0.4)	(-4.8, -3.2)			
No	Week 10	CR845	267	229 (85.8)	-5.0 (0.3)	(-5.7, -4.4)	-1.2 (0.4)	(-2.0, -0.4)	0.004 *
		Placebo	262	233 (88.9)	-3.8 (0.3)	(-4.5, -3.2)			
Yes	Week 10	CR845	159	128 (80.5)	-6.0 (0.4)	(-6.8, -5.1)	-1.7 (0.5)	(-2.8, -0.6)	0.002 *
		Placebo	163	142 (87.1)	-4.3 (0.4)	(-5.1, -3.5)			
No	Week 12	CR845	267	230 (86.1)	-5.4 (0.3)	(-6.1, -4.7)	-1.2 (0.4)	(-2.1, -0.4)	0.004 *
		Placebo	262	236 (90.1)	-4.2 (0.3)	(-4.8, -3.5)			
Yes	Week 12	CR845	159	128 (80.5)	-6.1 (0.4)	(-7.0, -5.2)	-1.7 (0.6)	(-2.9, -0.6)	0.003 *
		Placebo	163	139 (85.3)	-4.4 (0.4)	(-5.2, -3.5)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor presence of medical condition is also included in the model.
Source Data: askin_i, created on: 17FEB2022

Table IT2SMC_ISCA: Change from baseline in Skindex-10 mood/emotional distress score - MMRM results by age
ITT

Change from baseline in Skindex-10 mood/emotional distress score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
A: Age									0.479
< 65 years	Week 4	CR845	282	246 (87.2)	-3.5 (0.3)	(-4.1, -2.8)	-1.2 (0.4)	(-2.0, -0.4)	0.002 *
		Placebo	290	254 (87.6)	-2.3 (0.3)	(-2.9, -1.6)			
>= 65 years	Week 4	CR845	144	127 (88.2)	-3.0 (0.5)	(-4.0, -2.0)	-0.5 (0.6)	(-1.7, 0.7)	0.427
		Placebo	135	126 (93.3)	-2.5 (0.5)	(-3.5, -1.6)			
< 65 years	Week 8	CR845	282	231 (81.9)	-4.5 (0.4)	(-5.2, -3.8)	-0.9 (0.4)	(-1.8, -0.1)	0.028 *
		Placebo	290	257 (88.6)	-3.6 (0.3)	(-4.3, -2.9)			
>= 65 years	Week 8	CR845	144	124 (86.1)	-4.3 (0.5)	(-5.2, -3.3)	-0.8 (0.6)	(-2.0, 0.4)	0.167
		Placebo	135	125 (92.6)	-3.5 (0.5)	(-4.4, -2.5)			
< 65 years	Week 10	CR845	282	236 (83.7)	-5.3 (0.4)	(-6.0, -4.6)	-1.5 (0.4)	(-2.4, -0.7)	<0.001 *
		Placebo	290	254 (87.6)	-3.8 (0.3)	(-4.5, -3.1)			
>= 65 years	Week 10	CR845	144	117 (81.3)	-5.0 (0.5)	(-5.9, -4.1)	-1.1 (0.6)	(-2.3, 0.1)	0.068
		Placebo	135	122 (90.4)	-3.9 (0.5)	(-4.8, -3.0)			
< 65 years	Week 12	CR845	282	237 (84.0)	-5.7 (0.4)	(-6.4, -5.0)	-1.4 (0.4)	(-2.2, -0.5)	0.002 *
		Placebo	290	255 (87.9)	-4.3 (0.4)	(-5.0, -3.6)			
>= 65 years	Week 12	CR845	144	120 (83.3)	-5.2 (0.5)	(-6.2, -4.3)	-1.2 (0.6)	(-2.4, 0.0)	0.055
		Placebo	135	123 (91.1)	-4.0 (0.5)	(-5.0, -3.1)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin_i, created on: 17FEB2022

Table IT2SMC_ISCB: Change from baseline in Skindex-10 mood/emotional distress score - MMRM results by sex
ITT

Change from baseline in Skindex-10 mood/emotional distress score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
B: Sex									0.109
Male	Week 4	CR845	249	218 (87.6)	-2.9 (0.4)	(-3.6, -2.2)	-0.8 (0.4)	(-1.7, -0.0)	0.050 *
		Placebo	258	224 (86.8)	-2.1 (0.4)	(-2.8, -1.4)			
Female	Week 4	CR845	177	155 (87.6)	-3.7 (0.4)	(-4.6, -2.9)	-1.2 (0.6)	(-2.3, -0.2)	0.025 *
		Placebo	167	156 (93.4)	-2.5 (0.4)	(-3.3, -1.6)			
Male	Week 8	CR845	249	207 (83.1)	-3.6 (0.4)	(-4.4, -2.9)	-0.4 (0.4)	(-1.3, 0.5)	0.362
		Placebo	258	232 (89.9)	-3.2 (0.4)	(-3.9, -2.5)			
Female	Week 8	CR845	177	148 (83.6)	-5.4 (0.4)	(-6.3, -4.6)	-1.7 (0.6)	(-2.8, -0.5)	0.004 *
		Placebo	167	150 (89.8)	-3.8 (0.4)	(-4.6, -2.9)			
Male	Week 10	CR845	249	205 (82.3)	-4.2 (0.4)	(-5.0, -3.5)	-0.7 (0.4)	(-1.6, 0.2)	0.112
		Placebo	258	226 (87.6)	-3.5 (0.4)	(-4.2, -2.8)			
Female	Week 10	CR845	177	148 (83.6)	-6.4 (0.4)	(-7.3, -5.6)	-2.4 (0.6)	(-3.5, -1.3)	<0.001 *
		Placebo	167	150 (89.8)	-4.0 (0.4)	(-4.9, -3.1)			
Male	Week 12	CR845	249	205 (82.3)	-4.8 (0.4)	(-5.6, -4.1)	-0.9 (0.4)	(-1.8, -0.1)	0.037 *
		Placebo	258	227 (88.0)	-3.9 (0.4)	(-4.6, -3.2)			
Female	Week 12	CR845	177	152 (85.9)	-6.3 (0.5)	(-7.2, -5.4)	-1.9 (0.6)	(-3.0, -0.7)	0.002 *
		Placebo	167	151 (90.4)	-4.5 (0.5)	(-5.4, -3.5)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin_i, created on: 17FEB2022

Table IT2SMC_ISCC: Change from baseline in Skindex-10 mood/emotional distress score - MMRM results by race
ITT

Change from baseline in Skindex-10 mood/emotional distress score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
C: Race									0.740
Black/African American	Week 4	CR845	135	112 (83.0)	-3.1 (0.5)	(-4.0, -2.1)	-1.0 (0.6)	(-2.2, 0.3)	0.118
		Placebo	114	99 (86.8)	-2.1 (0.5)	(-3.1, -1.1)			
White	Week 4	CR845	255	229 (89.8)	-3.4 (0.4)	(-4.1, -2.7)	-1.1 (0.4)	(-2.0, -0.2)	0.011 *
		Placebo	262	238 (90.8)	-2.3 (0.4)	(-3.0, -1.6)			
Other	Week 4	CR845	35	31 (88.6)	-3.1 (1.0)	(-5.1, -1.1)	-0.4 (1.0)	(-2.4, 1.6)	0.681
		Placebo	47	41 (87.2)	-2.7 (0.9)	(-4.5, -0.9)			
Black/African American	Week 8	CR845	135	110 (81.5)	-4.6 (0.5)	(-5.6, -3.6)	-0.9 (0.7)	(-2.2, 0.5)	0.198
		Placebo	114	102 (89.5)	-3.8 (0.5)	(-4.8, -2.7)			
White	Week 8	CR845	255	213 (83.5)	-4.4 (0.4)	(-5.1, -3.7)	-1.1 (0.4)	(-1.9, -0.2)	0.017 *
		Placebo	262	236 (90.1)	-3.3 (0.4)	(-4.0, -2.6)			
Other	Week 8	CR845	35	31 (88.6)	-3.8 (1.1)	(-6.0, -1.6)	-0.0 (1.2)	(-2.3, 2.3)	0.986
		Placebo	47	42 (89.4)	-3.8 (1.0)	(-5.7, -1.9)			
Black/African American	Week 10	CR845	135	106 (78.5)	-5.2 (0.5)	(-6.2, -4.2)	-1.1 (0.7)	(-2.4, 0.3)	0.119
		Placebo	114	100 (87.7)	-4.1 (0.5)	(-5.2, -3.1)			
White	Week 10	CR845	255	217 (85.1)	-5.2 (0.4)	(-5.9, -4.5)	-1.5 (0.4)	(-2.3, -0.6)	<0.001 *
		Placebo	262	233 (88.9)	-3.7 (0.4)	(-4.4, -3.0)			
Other	Week 10	CR845	35	29 (82.9)	-5.2 (1.1)	(-7.5, -3.0)	-2.0 (1.2)	(-4.4, 0.3)	0.093
		Placebo	47	41 (87.2)	-3.2 (1.0)	(-5.2, -1.3)			
Black/African American	Week 12	CR845	135	108 (80.0)	-5.9 (0.5)	(-6.9, -4.9)	-1.3 (0.7)	(-2.6, 0.1)	0.063
		Placebo	114	101 (88.6)	-4.6 (0.5)	(-5.7, -3.6)			
White	Week 12	CR845	255	219 (85.9)	-5.4 (0.4)	(-6.1, -4.7)	-1.5 (0.4)	(-2.4, -0.6)	<0.001 *
		Placebo	262	234 (89.3)	-3.9 (0.4)	(-4.6, -3.2)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin_i, created on: 17FEB2022

Table IT2SMC_ISCC: Change from baseline in Skindex-10 mood/emotional distress score - MMRM results by race
ITT

Change from baseline in Skindex-10 mood/emotional distress score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Other	Week 12	CR845	35	29 (82.9)	-5.1 (1.2)	(-7.5, -2.7)	-0.6 (1.3)	(-3.3, 2.0)	0.623
		Placebo	47	41 (87.2)	-4.4 (1.0)	(-6.5, -2.4)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin_i, created on: 17FEB2022

Table IT2SMC_ISCD: Change from baseline in Skindex-10 mood/emotional distress score - MMRM results by baseline WI-NRS
ITT

Change from baseline in Skindex-10 mood/emotional distress score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
D: Baseline worst itching NRS score (WI-NRS)									0.393
>= 4 to < 7	Week 4	CR845	185	166 (89.7)	-3.8 (0.4)	(-4.6, -3.0)	-1.3 (0.5)	(-2.2, -0.4)	0.004 *
		Placebo	193	174 (90.2)	-2.5 (0.4)	(-3.2, -1.7)			
>= 7	Week 4	CR845	241	207 (85.9)	-3.1 (0.4)	(-3.8, -2.4)	-0.7 (0.5)	(-1.7, 0.2)	0.114
		Placebo	232	206 (88.8)	-2.3 (0.4)	(-3.1, -1.6)			
>= 4 to < 7	Week 8	CR845	185	161 (87.0)	-4.5 (0.4)	(-5.3, -3.7)	-1.0 (0.5)	(-2.0, -0.1)	0.033 *
		Placebo	193	172 (89.1)	-3.5 (0.4)	(-4.3, -2.7)			
>= 7	Week 8	CR845	241	194 (80.5)	-4.5 (0.4)	(-5.3, -3.7)	-0.8 (0.5)	(-1.8, 0.2)	0.098
		Placebo	232	210 (90.5)	-3.7 (0.4)	(-4.4, -2.9)			
>= 4 to < 7	Week 10	CR845	185	158 (85.4)	-5.3 (0.4)	(-6.1, -4.5)	-1.5 (0.5)	(-2.4, -0.5)	0.002 *
		Placebo	193	169 (87.6)	-3.8 (0.4)	(-4.6, -3.0)			
>= 7	Week 10	CR845	241	195 (80.9)	-5.3 (0.4)	(-6.1, -4.5)	-1.4 (0.5)	(-2.3, -0.4)	0.007 *
		Placebo	232	207 (89.2)	-3.9 (0.4)	(-4.7, -3.2)			
>= 4 to < 7	Week 12	CR845	185	156 (84.3)	-5.5 (0.4)	(-6.3, -4.7)	-1.8 (0.5)	(-2.7, -0.9)	<0.001 *
		Placebo	193	171 (88.6)	-3.7 (0.4)	(-4.5, -2.9)			
>= 7	Week 12	CR845	241	201 (83.4)	-5.7 (0.4)	(-6.5, -4.9)	-0.9 (0.5)	(-1.9, 0.1)	0.073
		Placebo	232	207 (89.2)	-4.8 (0.4)	(-5.5, -4.0)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin_i, created on: 17FEB2022

Table IT2SMC_ISCE: Change from baseline in Skindex-10 mood/emotional distress score - MMRM results by specific medical condition
ITT

Change from baseline in Skindex-10 mood/emotional distress score					Repeated measures analysis					
					Change from Baseline		Treatment Difference			
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value	
E: Presence of specific medical conditions									0.689	
No	Week 4	CR845	359	312 (86.9)	-3.4 (0.3)	(-3.9, -2.9)	-1.1 (0.4)	(-1.8, -0.4)	0.003	*
		Placebo	360	325 (90.3)	-2.3 (0.3)	(-2.8, -1.8)				
Yes	Week 4	CR845	67	61 (91.0)	-3.3 (0.7)	(-4.6, -2.0)	-0.6 (0.9)	(-2.4, 1.3)	0.551	
		Placebo	65	55 (84.6)	-2.7 (0.7)	(-4.0, -1.4)				
No	Week 8	CR845	359	297 (82.7)	-4.5 (0.3)	(-5.0, -3.9)	-0.9 (0.4)	(-1.6, -0.2)	0.017	*
		Placebo	360	323 (89.7)	-3.5 (0.3)	(-4.1, -3.0)				
Yes	Week 8	CR845	67	58 (86.6)	-4.6 (0.6)	(-5.8, -3.3)	-0.9 (0.9)	(-2.7, 0.9)	0.331	
		Placebo	65	59 (90.8)	-3.7 (0.6)	(-5.0, -2.5)				
No	Week 10	CR845	359	297 (82.7)	-5.2 (0.3)	(-5.7, -4.7)	-1.4 (0.4)	(-2.1, -0.7)	<0.001	*
		Placebo	360	318 (88.3)	-3.8 (0.3)	(-4.3, -3.3)				
Yes	Week 10	CR845	67	56 (83.6)	-5.6 (0.7)	(-6.9, -4.3)	-1.5 (1.0)	(-3.3, 0.4)	0.130	
		Placebo	65	58 (89.2)	-4.2 (0.7)	(-5.5, -2.8)				
No	Week 12	CR845	359	298 (83.0)	-5.6 (0.3)	(-6.1, -5.0)	-1.4 (0.4)	(-2.2, -0.7)	<0.001	*
		Placebo	360	318 (88.3)	-4.2 (0.3)	(-4.7, -3.6)				
Yes	Week 12	CR845	67	59 (88.1)	-5.6 (0.7)	(-6.9, -4.3)	-0.8 (1.0)	(-2.7, 1.1)	0.426	
		Placebo	65	60 (92.3)	-4.8 (0.7)	(-6.2, -3.5)				

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor previous use of anti-itch medication is also included in the model.
Source Data: askin_i, created on: 17FEB2022

Table IT2SMC_ISCF: Change from baseline in Skindex-10 mood/emotional distress score - MMRM results by use of concomitant itch medication
ITT

Change from baseline in Skindex-10 mood/emotional distress score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
F: Use of concomitant itch medication									0.807
No	Week 4	CR845	267	240 (89.9)	-3.2 (0.4)	(-3.9, -2.5)	-1.0 (0.4)	(-1.8, -0.2)	0.017 *
		Placebo	262	233 (88.9)	-2.2 (0.4)	(-2.9, -1.5)			
Yes	Week 4	CR845	159	133 (83.6)	-3.5 (0.4)	(-4.3, -2.6)	-0.9 (0.6)	(-2.0, 0.2)	0.092
		Placebo	163	147 (90.2)	-2.5 (0.4)	(-3.4, -1.7)			
No	Week 8	CR845	267	232 (86.9)	-4.4 (0.4)	(-5.1, -3.7)	-1.0 (0.4)	(-1.9, -0.2)	0.021 *
		Placebo	262	236 (90.1)	-3.4 (0.4)	(-4.1, -2.7)			
Yes	Week 8	CR845	159	123 (77.4)	-4.4 (0.5)	(-5.4, -3.5)	-0.8 (0.6)	(-1.9, 0.4)	0.197
		Placebo	163	146 (89.6)	-3.7 (0.4)	(-4.6, -2.8)			
No	Week 10	CR845	267	224 (83.9)	-4.9 (0.4)	(-5.6, -4.2)	-1.2 (0.4)	(-2.1, -0.4)	0.005 *
		Placebo	262	233 (88.9)	-3.7 (0.4)	(-4.4, -3.0)			
Yes	Week 10	CR845	159	129 (81.1)	-5.7 (0.4)	(-6.6, -4.8)	-1.7 (0.6)	(-2.8, -0.6)	0.003 *
		Placebo	163	143 (87.7)	-4.0 (0.4)	(-4.9, -3.2)			
No	Week 12	CR845	267	229 (85.8)	-5.3 (0.4)	(-6.0, -4.5)	-1.1 (0.4)	(-2.0, -0.2)	0.014 *
		Placebo	262	238 (90.8)	-4.2 (0.4)	(-4.9, -3.5)			
Yes	Week 12	CR845	159	128 (80.5)	-5.9 (0.5)	(-6.8, -5.0)	-1.7 (0.6)	(-2.9, -0.5)	0.005 *
		Placebo	163	140 (85.9)	-4.2 (0.5)	(-5.1, -3.4)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor presence of medical condition is also included in the model.
Source Data: askin_i, created on: 17FEB2022

Table IT2SSC_ISCA: Change from baseline in Skindex-10 social functioning score - MMRM results by age
ITT

Change from baseline in Skindex-10 social functioning score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
A: Age									0.610
< 65 years	Week 4	CR845	282	250 (88.7)	-3.2 (0.4)	(-4.1, -2.4)	-0.5 (0.5)	(-1.5, 0.5)	0.343
		Placebo	290	256 (88.3)	-2.7 (0.5)	(-3.6, -1.8)			
>= 65 years	Week 4	CR845	144	126 (87.5)	-3.6 (0.6)	(-4.8, -2.4)	-0.2 (0.8)	(-1.8, 1.3)	0.775
		Placebo	135	127 (94.1)	-3.4 (0.6)	(-4.5, -2.2)			
< 65 years	Week 8	CR845	282	236 (83.7)	-4.2 (0.5)	(-5.1, -3.3)	-0.6 (0.6)	(-1.7, 0.5)	0.267
		Placebo	290	260 (89.7)	-3.6 (0.5)	(-4.5, -2.7)			
>= 65 years	Week 8	CR845	144	123 (85.4)	-4.7 (0.6)	(-5.9, -3.5)	-0.7 (0.7)	(-2.2, 0.7)	0.325
		Placebo	135	125 (92.6)	-4.0 (0.6)	(-5.1, -2.8)			
< 65 years	Week 10	CR845	282	239 (84.8)	-4.9 (0.5)	(-5.9, -4.0)	-1.2 (0.6)	(-2.3, -0.1)	0.030 *
		Placebo	290	255 (87.9)	-3.7 (0.5)	(-4.6, -2.8)			
>= 65 years	Week 10	CR845	144	120 (83.3)	-5.0 (0.6)	(-6.1, -3.8)	-0.2 (0.7)	(-1.6, 1.2)	0.797
		Placebo	135	120 (88.9)	-4.8 (0.6)	(-5.9, -3.7)			
< 65 years	Week 12	CR845	282	239 (84.8)	-5.2 (0.5)	(-6.1, -4.2)	-0.9 (0.6)	(-2.0, 0.2)	0.101
		Placebo	290	256 (88.3)	-4.2 (0.5)	(-5.2, -3.3)			
>= 65 years	Week 12	CR845	144	120 (83.3)	-5.1 (0.6)	(-6.3, -4.0)	-0.3 (0.7)	(-1.8, 1.1)	0.658
		Placebo	135	122 (90.4)	-4.8 (0.6)	(-5.9, -3.7)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin_i, created on: 17FEB2022

Table IT2SSC_ISCB: Change from baseline in Skindex-10 social functioning score - MMRM results by sex
ITT

Change from baseline in Skindex-10 social functioning score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
B: Sex									0.060
Male	Week 4	CR845	249	221 (88.8)	-3.0 (0.5)	(-3.9, -2.0)	0.2 (0.5)	(-0.8, 1.3)	0.649
		Placebo	258	226 (87.6)	-3.2 (0.5)	(-4.1, -2.3)			
Female	Week 4	CR845	177	155 (87.6)	-3.8 (0.6)	(-4.9, -2.7)	-1.4 (0.7)	(-2.8, 0.0)	0.051
		Placebo	167	157 (94.0)	-2.4 (0.6)	(-3.5, -1.3)			
Male	Week 8	CR845	249	211 (84.7)	-3.7 (0.5)	(-4.7, -2.8)	-0.1 (0.6)	(-1.2, 1.0)	0.831
		Placebo	258	234 (90.7)	-3.6 (0.5)	(-4.5, -2.7)			
Female	Week 8	CR845	177	148 (83.6)	-5.1 (0.6)	(-6.2, -4.0)	-1.4 (0.7)	(-2.8, -0.0)	0.044 *
		Placebo	167	151 (90.4)	-3.7 (0.6)	(-4.8, -2.5)			
Male	Week 10	CR845	249	207 (83.1)	-4.2 (0.5)	(-5.2, -3.2)	-0.4 (0.6)	(-1.5, 0.8)	0.545
		Placebo	258	227 (88.0)	-3.9 (0.5)	(-4.8, -2.9)			
Female	Week 10	CR845	177	152 (85.9)	-5.9 (0.5)	(-7.0, -4.9)	-1.7 (0.7)	(-3.0, -0.3)	0.016 *
		Placebo	167	148 (88.6)	-4.2 (0.6)	(-5.3, -3.2)			
Male	Week 12	CR845	249	207 (83.1)	-4.4 (0.5)	(-5.4, -3.5)	-0.2 (0.6)	(-1.3, 0.9)	0.735
		Placebo	258	228 (88.4)	-4.2 (0.5)	(-5.2, -3.3)			
Female	Week 12	CR845	177	152 (85.9)	-6.1 (0.6)	(-7.2, -5.0)	-1.5 (0.7)	(-2.9, -0.1)	0.036 *
		Placebo	167	150 (89.8)	-4.6 (0.6)	(-5.7, -3.5)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin_i, created on: 17FEB2022

Table IT2SSC_ISCC: Change from baseline in Skindex-10 social functioning score - MMRM results by race
ITT

Change from baseline in Skindex-10 social functioning score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
C: Race									0.633
Black/African American	Week 4	CR845	135	112 (83.0)	-3.3 (0.6)	(-4.5, -2.1)	0.1 (0.8)	(-1.5, 1.7)	0.897
		Placebo	114	100 (87.7)	-3.4 (0.6)	(-4.7, -2.1)			
White	Week 4	CR845	255	232 (91.0)	-3.4 (0.5)	(-4.4, -2.5)	-0.9 (0.6)	(-2.0, 0.2)	0.117
		Placebo	262	241 (92.0)	-2.5 (0.5)	(-3.5, -1.6)			
Other	Week 4	CR845	35	31 (88.6)	-2.6 (1.4)	(-5.3, 0.2)	1.3 (1.4)	(-1.5, 4.1)	0.354
		Placebo	47	41 (87.2)	-3.9 (1.2)	(-6.3, -1.4)			
Black/African American	Week 8	CR845	135	109 (80.7)	-4.5 (0.6)	(-5.7, -3.3)	-0.8 (0.8)	(-2.3, 0.8)	0.329
		Placebo	114	104 (91.2)	-3.7 (0.6)	(-5.0, -2.5)			
White	Week 8	CR845	255	218 (85.5)	-4.1 (0.5)	(-5.1, -3.2)	-0.7 (0.6)	(-1.8, 0.5)	0.237
		Placebo	262	239 (91.2)	-3.4 (0.5)	(-4.4, -2.5)			
Other	Week 8	CR845	35	31 (88.6)	-4.9 (1.4)	(-7.7, -2.1)	-0.2 (1.4)	(-3.1, 2.7)	0.900
		Placebo	47	41 (87.2)	-4.7 (1.3)	(-7.2, -2.2)			
Black/African American	Week 10	CR845	135	106 (78.5)	-5.2 (0.6)	(-6.4, -4.0)	-0.9 (0.8)	(-2.5, 0.6)	0.237
		Placebo	114	101 (88.6)	-4.2 (0.6)	(-5.5, -3.0)			
White	Week 10	CR845	255	223 (87.5)	-4.7 (0.5)	(-5.7, -3.8)	-0.9 (0.6)	(-2.0, 0.2)	0.114
		Placebo	262	234 (89.3)	-3.8 (0.5)	(-4.8, -2.9)			
Other	Week 10	CR845	35	29 (82.9)	-5.7 (1.5)	(-8.7, -2.6)	-1.0 (1.6)	(-4.2, 2.3)	0.560
		Placebo	47	39 (83.0)	-4.7 (1.3)	(-7.4, -2.0)			
Black/African American	Week 12	CR845	135	107 (79.3)	-5.3 (0.6)	(-6.5, -4.1)	-0.6 (0.8)	(-2.1, 1.0)	0.489
		Placebo	114	102 (89.5)	-4.8 (0.6)	(-6.0, -3.5)			
White	Week 12	CR845	255	222 (87.1)	-5.1 (0.5)	(-6.0, -4.1)	-1.0 (0.6)	(-2.2, 0.1)	0.073
		Placebo	262	235 (89.7)	-4.0 (0.5)	(-5.0, -3.1)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin_i, created on: 17FEB2022

Table IT2SSC_ISCC: Change from baseline in Skindex-10 social functioning score - MMRM results by race
ITT

Change from baseline in Skindex-10 social functioning score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
Other	Week 12	CR845	35	29 (82.9)	-4.9 (1.5)	(-7.9, -1.9)	0.5 (1.6)	(-2.7, 3.7)	0.743
		Placebo	47	40 (85.1)	-5.4 (1.3)	(-8.0, -2.8)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin_i, created on: 17FEB2022

Table IT2SSC_ISCD: Change from baseline in Skindex-10 social functioning score - MMRM results by baseline WI-NRS
ITT

Change from baseline in Skindex-10 social functioning score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
D: Baseline worst itching NRS score (WI-NRS)									0.281
>= 4 to < 7	Week 4	CR845	185	166 (89.7)	-3.8 (0.5)	(-4.8, -2.8)	-0.9 (0.6)	(-2.0, 0.2)	0.123
		Placebo	193	178 (92.2)	-2.9 (0.5)	(-3.9, -2.0)			
>= 7	Week 4	CR845	241	210 (87.1)	-3.2 (0.5)	(-4.2, -2.3)	-0.2 (0.6)	(-1.4, 1.1)	0.808
		Placebo	232	205 (88.4)	-3.1 (0.5)	(-4.1, -2.1)			
>= 4 to < 7	Week 8	CR845	185	161 (87.0)	-4.7 (0.5)	(-5.7, -3.8)	-1.2 (0.6)	(-2.4, -0.1)	0.030 *
		Placebo	193	176 (91.2)	-3.5 (0.5)	(-4.5, -2.6)			
>= 7	Week 8	CR845	241	198 (82.2)	-4.3 (0.5)	(-5.3, -3.2)	-0.3 (0.7)	(-1.5, 1.0)	0.691
		Placebo	232	209 (90.1)	-4.0 (0.5)	(-5.0, -3.0)			
>= 4 to < 7	Week 10	CR845	185	160 (86.5)	-5.0 (0.5)	(-6.1, -4.0)	-1.2 (0.6)	(-2.4, -0.0)	0.045 *
		Placebo	193	171 (88.6)	-3.8 (0.5)	(-4.8, -2.9)			
>= 7	Week 10	CR845	241	199 (82.6)	-5.2 (0.5)	(-6.2, -4.2)	-0.7 (0.6)	(-2.0, 0.5)	0.260
		Placebo	232	204 (87.9)	-4.4 (0.5)	(-5.4, -3.4)			
>= 4 to < 7	Week 12	CR845	185	157 (84.9)	-5.4 (0.5)	(-6.4, -4.3)	-1.5 (0.6)	(-2.6, -0.4)	0.009 *
		Placebo	193	174 (90.2)	-3.8 (0.5)	(-4.8, -2.9)			
>= 7	Week 12	CR845	241	202 (83.8)	-5.3 (0.5)	(-6.3, -4.2)	-0.2 (0.7)	(-1.5, 1.1)	0.796
		Placebo	232	204 (87.9)	-5.1 (0.5)	(-6.1, -4.1)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factors previous use of anti-itch medication and presence of medical condition are also included in the model.
Source Data: askin_i, created on: 17FEB2022

Table IT2SSC_ISCE: Change from baseline in Skindex-10 social functioning score - MMRM results by specific medical condition
ITT

Change from baseline in Skindex-10 social functioning score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
E: Presence of specific medical conditions									0.444
No	Week 4	CR845	359	316 (88.0)	-3.3 (0.3)	(-3.9, -2.6)	-0.5 (0.5)	(-1.4, 0.4)	0.280
		Placebo	360	324 (90.0)	-2.7 (0.3)	(-3.4, -2.1)			
Yes	Week 4	CR845	67	60 (89.6)	-3.7 (0.9)	(-5.4, -2.0)	-0.2 (1.2)	(-2.6, 2.3)	0.895
		Placebo	65	59 (90.8)	-3.6 (0.9)	(-5.3, -1.9)			
No	Week 8	CR845	359	302 (84.1)	-4.3 (0.3)	(-5.0, -3.6)	-0.8 (0.5)	(-1.8, 0.1)	0.084
		Placebo	360	323 (89.7)	-3.5 (0.3)	(-4.2, -2.8)			
Yes	Week 8	CR845	67	57 (85.1)	-4.3 (0.9)	(-6.0, -2.6)	0.0 (1.2)	(-2.3, 2.4)	0.976
		Placebo	65	62 (95.4)	-4.3 (0.8)	(-6.0, -2.7)			
No	Week 10	CR845	359	302 (84.1)	-4.9 (0.4)	(-5.5, -4.2)	-1.0 (0.5)	(-2.0, -0.1)	0.032 *
		Placebo	360	317 (88.1)	-3.8 (0.3)	(-4.5, -3.2)			
Yes	Week 10	CR845	67	57 (85.1)	-5.4 (0.8)	(-7.1, -3.8)	-0.4 (1.2)	(-2.7, 2.0)	0.761
		Placebo	65	58 (89.2)	-5.1 (0.8)	(-6.7, -3.4)			
No	Week 12	CR845	359	301 (83.8)	-5.1 (0.4)	(-5.8, -4.4)	-0.9 (0.5)	(-1.8, 0.1)	0.064
		Placebo	360	317 (88.1)	-4.2 (0.3)	(-4.8, -3.5)			
Yes	Week 12	CR845	67	58 (86.6)	-5.5 (0.9)	(-7.2, -3.8)	-0.1 (1.2)	(-2.5, 2.3)	0.922
		Placebo	65	61 (93.8)	-5.4 (0.8)	(-7.1, -3.7)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor previous use of anti-itch medication is also included in the model.
Source Data: askin_i, created on: 17FEB2022

Table IT2SSC_ISCF: Change from baseline in Skindex-10 social functioning score - MMRM results by use of concomitant itch medication
ITT

Change from baseline in Skindex-10 social functioning score					Repeated measures analysis				
					Change from Baseline		Treatment Difference		
Subgroup	Time	Treatment	N	n (%)	LS-Mean (SE)	95% CI	LS-Mean (SE)	95% CI	p-value
F: Use of concomitant itch medication									0.474
No	Week 4	CR845	267	242 (90.6)	-3.2 (0.5)	(-4.2, -2.3)	-0.3 (0.6)	(-1.4, 0.8)	0.575
		Placebo	262	237 (90.5)	-2.9 (0.5)	(-3.9, -2.0)			
Yes	Week 4	CR845	159	134 (84.3)	-3.6 (0.5)	(-4.6, -2.5)	-0.7 (0.7)	(-2.0, 0.7)	0.334
		Placebo	163	146 (89.6)	-2.9 (0.5)	(-3.9, -1.9)			
No	Week 8	CR845	267	234 (87.6)	-4.2 (0.5)	(-5.1, -3.3)	-0.6 (0.6)	(-1.7, 0.5)	0.289
		Placebo	262	241 (92.0)	-3.6 (0.5)	(-4.5, -2.7)			
Yes	Week 8	CR845	159	125 (78.6)	-4.6 (0.6)	(-5.7, -3.5)	-0.8 (0.7)	(-2.2, 0.6)	0.255
		Placebo	163	144 (88.3)	-3.8 (0.5)	(-4.9, -2.7)			
No	Week 10	CR845	267	229 (85.8)	-4.6 (0.5)	(-5.6, -3.7)	-0.7 (0.6)	(-1.8, 0.4)	0.232
		Placebo	262	236 (90.1)	-4.0 (0.5)	(-4.9, -3.0)			
Yes	Week 10	CR845	159	130 (81.8)	-5.5 (0.6)	(-6.6, -4.5)	-1.3 (0.7)	(-2.8, 0.1)	0.060
		Placebo	163	139 (85.3)	-4.2 (0.5)	(-5.3, -3.1)			
No	Week 12	CR845	267	231 (86.5)	-4.8 (0.5)	(-5.8, -3.9)	-0.4 (0.6)	(-1.5, 0.7)	0.502
		Placebo	262	240 (91.6)	-4.4 (0.5)	(-5.4, -3.5)			
Yes	Week 12	CR845	159	128 (80.5)	-5.8 (0.6)	(-6.9, -4.7)	-1.4 (0.7)	(-2.8, -0.0)	0.048 *
		Placebo	163	138 (84.7)	-4.4 (0.5)	(-5.4, -3.3)			

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of non-missing values. MMRM = mixed repeated measures model.
LS-Mean = Least square mean. SE = Standard error. 95% CI = 95% confidence interval. * = significant treatment effect.
i = significant treatment and subgroup interaction.
A MMRM was applied with fixed factors for treatment, time, interaction treatment-by-time and baseline as covariate per subgroup.
Interaction test was performed on the model adding factors subgroup and subgroup*treatment.
Stratification factor presence of medical condition is also included in the model.
Source Data: askin_i, created on: 17FEB2022

Table IT2STCD15_ISPA: Decrease of Skindex-10 total score of at least 15 points by age
ITT

Decrease of Skindex-10 total score of at least 15 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	A: Age										0.328	
	< 65 years	282	235 (83.3)	130 (46.1) [40.2, 52.1]	290	250 (86.2)	100 (34.5) [29.0, 40.3]	1.337 [1.092, 1.637]	1.625 [1.160, 2.276]	11.6 [3.3, 20.0]	0.005	*
	>= 65 years	144	118 (81.9)	61 (42.4) [34.2, 50.9]	135	118 (87.4)	51 (37.8) [29.6, 46.5]	1.121 [0.840, 1.496]	1.210 [0.749, 1.956]	4.6 [-7.6, 16.8]	0.436	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin_i, created on: 17FEB2022

Table IT2STCD15_ISPB: Decrease of Skindex-10 total score of at least 15 points by sex
ITT

Decrease of Skindex-10 total score of at least 15 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	B: Sex										0.333	
	Male	249	203 (81.5)	103 (41.4) [35.2, 47.8]	258	223 (86.4)	91 (35.3) [29.4, 41.4]	1.173 [0.939, 1.464]	1.295 [0.904, 1.854]	6.1 [-2.8, 14.9]	0.159	
	Female	177	150 (84.7)	88 (49.7) [42.1, 57.3]	167	145 (86.8)	60 (35.9) [28.7, 43.7]	1.384 [1.077, 1.779]	1.763 [1.145, 2.716]	13.8 [2.9, 24.7]	0.010	*

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin_i, created on: 17FEB2022

Table IT2STCD15_ISPC: Decrease of Skindex-10 total score of at least 15 points by race
ITT

Decrease of Skindex-10 total score of at least 15 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	C: Race										0.517	
	Black/African American	135	104 (77.0)	61 (45.2) [36.6, 54.0]	114	99 (86.8)	43 (37.7) [28.8, 47.3]	1.198 [0.887, 1.617]	1.361 [0.819, 2.263]	7.5 [-5.6, 20.5]	0.235	
	White	255	219 (85.9)	116 (45.5) [39.3, 51.8]	262	228 (87.0)	88 (33.6) [27.9, 39.7]	1.354 [1.090, 1.682]	1.650 [1.156, 2.355]	11.9 [3.1, 20.7]	0.006	*
	Other	35	29 (82.9)	14 (40.0) [23.9, 57.9]	47	40 (85.1)	19 (40.4) [26.4, 55.7]	0.989 [0.580, 1.688]	0.982 [0.402, 2.399]	-0.4 [-24.4, 23.5]	0.969	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin_i, created on: 17FEB2022

Table IT2STCD15_ISPD: Decrease of Skindex-10 total score of at least 15 points by baseline WI-NRS
ITT

		CR845			Placebo							
Decrease of Skindex-10 total score of at least 15 points		N	nval	n (%) [95 % CI]	N	nval	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.006	i
	>= 4 to < 7	185	156 (84.3)	83 (44.9) [37.6, 52.3]	193	169 (87.6)	51 (26.4) [20.4, 33.2]	1.698 [1.277, 2.257]	2.266 [1.471, 3.489]	18.4 [8.4, 28.5]	<0.001	*
	>= 7	241	197 (81.7)	108 (44.8) [38.4, 51.3]	232	199 (85.8)	100 (43.1) [36.6, 49.7]	1.040 [0.848, 1.275]	1.072 [0.745, 1.541]	1.7 [-7.7, 11.1]	0.708	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin_i, created on: 17FEB2022

Table IT2STCD15_ISPE: Decrease of Skindex-10 total score of at least 15 points by specific medical condition
ITT

Decrease of Skindex-10 total score of at least 15 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	E: Presence of specific medical conditions										0.184	
	No	359	295 (82.2)	160 (44.6) [39.4, 49.9]	360	310 (86.1)	121 (33.6) [28.7, 38.7]	1.326 [1.102, 1.596]	1.588 [1.174, 2.148]	11.0 [3.6, 18.3]	0.003	*
	Yes	67	58 (86.6)	31 (46.3) [34.0, 58.9]	65	58 (89.2)	30 (46.2) [33.7, 59.0]	1.002 [0.694, 1.449]	1.005 [0.507, 1.992]	0.1 [-18.4, 18.6]	0.989	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin_i, created on: 17FEB2022

Table IT2STCD15_ISPF: Decrease of Skindex-10 total score of at least 15 points by use of concomitant itch medication
ITT

Decrease of Skindex-10 total score of at least 15 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	F: Use of concomitant itch medication										0.256	
	No	267	226 (84.6)	117 (43.8) [37.8, 50.0]	262	234 (89.3)	98 (37.4) [31.5, 43.6]	1.172 [0.952, 1.441]	1.305 [0.922, 1.849]	6.4 [-2.3, 15.1]	0.133	
	Yes	159	127 (79.9)	74 (46.5) [38.6, 54.6]	163	134 (82.2)	53 (32.5) [25.4, 40.3]	1.431 [1.085, 1.888]	1.807 [1.150, 2.840]	14.0 [2.8, 25.2]	0.010	*

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin_i, created on: 17FEB2022

Table IT2SDCD3_ISPA: Decrease of Skindex-10 disease score of at least 3 points by age
ITT

Decrease of Skindex-10 disease score of at least 3 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	A: Age										0.022	i
	< 65 years	282	238 (84.4)	170 (60.3) [54.3, 66.0]	290	254 (87.6)	151 (52.1) [46.2, 57.9]	1.158 [1.001, 1.339]	1.397 [1.003, 1.947]	8.2 [-0.2, 16.7]	0.048	*
	>= 65 years	144	120 (83.3)	80 (55.6) [47.1, 63.8]	135	121 (89.6)	86 (63.7) [55.0, 71.8]	0.872 [0.718, 1.059]	0.712 [0.440, 1.152]	-8.1 [-20.3, 4.0]	0.167	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin_i, created on: 17FEB2022

Table IT2SDCD3_ISPB: Decrease of Skindex-10 disease score of at least 3 points by sex
ITT

Decrease of Skindex-10 disease score of at least 3 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	B: Sex										0.026	i
	Male	249	205 (82.3)	132 (53.0) [46.6, 59.3]	258	228 (88.4)	146 (56.6) [50.3, 62.7]	0.937 [0.800, 1.098]	0.865 [0.610, 1.228]	-3.6 [-12.6, 5.5]	0.419	
	Female	177	153 (86.4)	118 (66.7) [59.2, 73.6]	167	147 (88.0)	91 (54.5) [46.6, 62.2]	1.223 [1.029, 1.455]	1.670 [1.080, 2.584]	12.2 [1.3, 23.0]	0.021	*

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin_i, created on: 17FEB2022

Table IT2SDCD3_ISPC: Decrease of Skindex-10 disease score of at least 3 points by race
ITT

		CR845			Placebo							
Decrease of Skindex-10 disease score of at least 3 points		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	C: Race										0.041	i
	Black/African American	135	105 (77.8)	72 (53.3) [44.6, 62.0]	114	101 (88.6)	65 (57.0) [47.4, 66.3]	0.935 [0.747, 1.171]	0.862 [0.522, 1.423]	-3.7 [-16.9, 9.5]	0.561	
	White	255	223 (87.5)	160 (62.7) [56.5, 68.7]	262	232 (88.5)	139 (53.1) [46.8, 59.2]	1.183 [1.020, 1.371]	1.490 [1.049, 2.117]	9.7 [0.8, 18.5]	0.026	*
	Other	35	29 (82.9)	18 (51.4) [34.0, 68.6]	47	41 (87.2)	32 (68.1) [52.9, 80.9]	0.755 [0.518, 1.101]	0.496 [0.201, 1.225]	-16.7 [-40.4, 7.1]	0.129	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin_i, created on: 17FEB2022

Table IT2SDCD3_ISPD: Decrease of Skindex-10 disease score of at least 3 points by baseline WI-NRS
ITT

Decrease of Skindex-10 disease score of at least 3 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.158
	>= 4 to < 7	185	157 (84.9)	112 (60.5) [53.1, 67.6]	193	171 (88.6)	101 (52.3) [45.0, 59.6]	1.157 [0.968, 1.382]	1.398 [0.929, 2.102]	8.2 [-2.3, 18.7]	0.108
	>= 7	241	201 (83.4)	138 (57.3) [50.8, 63.6]	232	204 (87.9)	136 (58.6) [52.0, 65.0]	0.977 [0.838, 1.139]	0.946 [0.656, 1.363]	-1.4 [-10.7, 8.0]	0.765

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin_i, created on: 17FEB2022

Table IT2SDCD3_ISPE: Decrease of Skindex-10 disease score of at least 3 points by specific medical condition
ITT

Decrease of Skindex-10 disease score of at least 3 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	E: Presence of specific medical conditions										0.495
	No	359	299 (83.3)	207 (57.7) [52.4, 62.8]	360	315 (87.5)	194 (53.9) [48.6, 59.1]	1.070 [0.939, 1.219]	1.165 [0.868, 1.564]	3.8 [-3.8, 11.3]	0.309
	Yes	67	59 (88.1)	43 (64.2) [51.5, 75.5]	65	60 (92.3)	43 (66.2) [53.4, 77.4]	0.970 [0.756, 1.245]	0.917 [0.448, 1.877]	-2.0 [-19.7, 15.8]	0.813

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin_i, created on: 17FEB2022

Table IT2SDCD3_ISPF: Decrease of Skindex-10 disease score of at least 3 points by use of concomitant itch medication
ITT

		CR845			Placebo						
Decrease of Skindex-10 disease score of at least 3 points		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	F: Use of concomitant itch medication										0.926
	No	267	230 (86.1)	158 (59.2) [53.0, 65.1]	262	236 (90.1)	148 (56.5) [50.2, 62.6]	1.048 [0.906, 1.212]	1.117 [0.791, 1.577]	2.7 [-6.1, 11.5]	0.532
	Yes	159	128 (80.5)	92 (57.9) [49.8, 65.6]	163	139 (85.3)	89 (54.6) [46.6, 62.4]	1.060 [0.874, 1.285]	1.142 [0.735, 1.774]	3.3 [-8.2, 14.7]	0.556

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin_i, created on: 17FEB2022

Table IT2SMCD3_ISPA: Decrease of Skindex-10 mood/emotional distress score of at least 3 points by age
ITT

Decrease of Skindex-10 mood/emotional distress score of at least 3 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	A: Age										0.358
	< 65 years	282	237 (84.0)	173 (61.3) [55.4, 67.1]	290	255 (87.9)	160 (55.2) [49.2, 61.0]	1.112 [0.968, 1.278]	1.290 [0.924, 1.799]	6.2 [-2.2, 14.6]	0.135
	>= 65 years	144	120 (83.3)	79 (54.9) [46.4, 63.2]	135	123 (91.1)	75 (55.6) [46.8, 64.1]	0.988 [0.799, 1.220]	0.972 [0.606, 1.559]	-0.7 [-13.1, 11.7]	0.907

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin_i, created on: 17FEB2022

Table IT2SMCD3_ISPB: Decrease of Skindex-10 mood/emotional distress score of at least 3 points by sex
ITT

Decrease of Skindex-10 mood/emotional distress score of at least 3 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	B: Sex										0.906
	Male	249	205 (82.3)	142 (57.0) [50.6, 63.3]	258	227 (88.0)	137 (53.1) [46.8, 59.3]	1.074 [0.918, 1.257]	1.172 [0.826, 1.664]	3.9 [-5.1, 13.0]	0.375
	Female	177	152 (85.9)	110 (62.1) [54.6, 69.3]	167	151 (90.4)	98 (58.7) [50.8, 66.2]	1.059 [0.892, 1.257]	1.156 [0.750, 1.782]	3.5 [-7.5, 14.4]	0.512

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin_i, created on: 17FEB2022

Table IT2SMCD3_ISPC: Decrease of Skindex-10 mood/emotional distress score of at least 3 points by race
ITT

Decrease of Skindex-10 mood/emotional distress score of at least 3 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	C: Race										0.093	
	Black/African American	135	108 (80.0)	77 (57.0) [48.2, 65.5]	114	101 (88.6)	73 (64.0) [54.5, 72.8]	0.891 [0.729, 1.089]	0.746 [0.447, 1.245]	-7.0 [-19.9, 5.9]	0.262	
	White	255	219 (85.9)	157 (61.6) [55.3, 67.6]	262	234 (89.3)	137 (52.3) [46.1, 58.5]	1.177 [1.012, 1.369]	1.462 [1.030, 2.074]	9.3 [0.4, 18.2]	0.033	*
	Other	35	29 (82.9)	18 (51.4) [34.0, 68.6]	47	41 (87.2)	23 (48.9) [34.1, 63.9]	1.051 [0.680, 1.623]	1.105 [0.460, 2.652]	2.5 [-21.9, 26.9]	0.824	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin_i, created on: 17FEB2022

Table IT2SMCD3_ISPD: Decrease of Skindex-10 mood/emotional distress score of at least 3 points by baseline WI-NRS
ITT

Decrease of Skindex-10 mood/emotional distress score of at least 3 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.010	i
	>= 4 to < 7	185	156 (84.3)	114 (61.6) [54.2, 68.7]	193	171 (88.6)	93 (48.2) [41.0, 55.5]	1.279 [1.063, 1.539]	1.726 [1.147, 2.600]	13.4 [3.0, 23.9]	0.009	*
	>= 7	241	201 (83.4)	138 (57.3) [50.8, 63.6]	232	207 (89.2)	142 (61.2) [54.6, 67.5]	0.936 [0.806, 1.087]	0.849 [0.588, 1.226]	-3.9 [-13.2, 5.3]	0.383	

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin_i, created on: 17FEB2022

Table IT2SMCD3_ISPE: Decrease of Skindex-10 mood/emotional distress score of at least 3 points by specific medical condition
ITT

Decrease of Skindex-10 mood/emotional distress score of at least 3 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	E: Presence of specific medical conditions										0.840
	No	359	298 (83.0)	209 (58.2) [52.9, 63.4]	360	318 (88.3)	195 (54.2) [48.9, 59.4]	1.075 [0.944, 1.223]	1.179 [0.878, 1.583]	4.1 [-3.5, 11.6]	0.274
	Yes	67	59 (88.1)	43 (64.2) [51.5, 75.5]	65	60 (92.3)	40 (61.5) [48.6, 73.3]	1.043 [0.802, 1.356]	1.120 [0.552, 2.270]	2.6 [-15.4, 20.6]	0.754

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin_i, created on: 17FEB2022

Table IT2SMCD3_ISPF: Decrease of Skindex-10 mood/emotional distress score of at least 3 points by use of concomitant itch medication
ITT

Decrease of Skindex-10 mood/emotional distress score of at least 3 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	F: Use of concomitant itch medication										0.507
	No	267	229 (85.8)	165 (61.8) [55.7, 67.7]	262	238 (90.8)	147 (56.1) [49.9, 62.2]	1.101 [0.955, 1.270]	1.266 [0.894, 1.791]	5.7 [-3.1, 14.4]	0.184
	Yes	159	128 (80.5)	87 (54.7) [46.6, 62.6]	163	140 (85.9)	88 (54.0) [46.0, 61.8]	1.014 [0.830, 1.238]	1.030 [0.664, 1.597]	0.7 [-10.8, 12.2]	0.896

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin_i, created on: 17FEB2022

Table IT2SSCD4_ISPA: Decrease of Skindex-10 social functioning score of at least 4 points by age
ITT

Decrease of Skindex-10 social functioning score of at least 4 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	A: Age										0.377
	< 65 years	282	239 (84.8)	136 (48.2) [42.3, 54.2]	290	256 (88.3)	122 (42.1) [36.3, 48.0]	1.146 [0.956, 1.374]	1.283 [0.922, 1.784]	6.2 [-2.3, 14.6]	0.139
	>= 65 years	144	120 (83.3)	67 (46.5) [38.2, 55.0]	135	122 (90.4)	63 (46.7) [38.0, 55.4]	0.997 [0.775, 1.282]	0.994 [0.621, 1.592]	-0.1 [-12.6, 12.3]	0.981

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin_i, created on: 17FEB2022

Table IT2SSCD4_ISPB: Decrease of Skindex-10 social functioning score of at least 4 points by sex
ITT

Decrease of Skindex-10 social functioning score of at least 4 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	B: Sex										0.771
	Male	249	207 (83.1)	115 (46.2) [39.9, 52.6]	258	228 (88.4)	111 (43.0) [36.9, 49.3]	1.073 [0.884, 1.304]	1.137 [0.801, 1.614]	3.2 [-5.9, 12.2]	0.474
	Female	177	152 (85.9)	88 (49.7) [42.1, 57.3]	167	150 (89.8)	74 (44.3) [36.6, 52.2]	1.122 [0.895, 1.406]	1.243 [0.813, 1.899]	5.4 [-5.7, 16.5]	0.316

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin_i, created on: 17FEB2022

Table IT2SSCD4_ISPC: Decrease of Skindex-10 social functioning score of at least 4 points by race
ITT

Decrease of Skindex-10 social functioning score of at least 4 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	C: Race										0.518
	Black/African American	135	107 (79.3)	63 (46.7) [38.0, 55.4]	114	102 (89.5)	55 (48.2) [38.8, 57.8]	0.967 [0.744, 1.257]	0.939 [0.570, 1.546]	-1.6 [-14.8, 11.7]	0.804
	White	255	222 (87.1)	125 (49.0) [42.7, 55.3]	262	235 (89.7)	110 (42.0) [35.9, 48.2]	1.168 [0.966, 1.411]	1.329 [0.939, 1.880]	7.0 [-1.9, 16.0]	0.109
	Other	35	29 (82.9)	15 (42.9) [26.3, 60.6]	47	40 (85.1)	19 (40.4) [26.4, 55.7]	1.060 [0.632, 1.777]	1.105 [0.455, 2.685]	2.4 [-21.6, 26.5]	0.826

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin_i, created on: 17FEB2022

Table IT2SSCD4_ISPD: Decrease of Skindex-10 social functioning score of at least 4 points by baseline WI-NRS
ITT

		CR845			Placebo						
Decrease of Skindex-10 social functioning score of at least 4 points		N	nval (%)	n (%) [95 % CI]	N	nval (%)	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	D: Baseline worst itching NRS score (WI-NRS)										0.096
	>= 4 to < 7	185	157 (84.9)	92 (49.7) [42.3, 57.2]	193	174 (90.2)	76 (39.4) [32.4, 46.7]	1.263 [1.006, 1.585]	1.523 [1.013, 2.290]	10.4 [-0.1, 20.9]	0.043 *
	>= 7	241	202 (83.8)	111 (46.1) [39.6, 52.6]	232	204 (87.9)	109 (47.0) [40.4, 53.6]	0.980 [0.808, 1.189]	0.964 [0.671, 1.383]	-0.9 [-10.3, 8.5]	0.840

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin_i, created on: 17FEB2022

Table IT2SSCD4_ISPE: Decrease of Skindex-10 social functioning score of at least 4 points by specific medical condition
ITT

Decrease of Skindex-10 social functioning score of at least 4 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	E: Presence of specific medical conditions										0.709
	No	359	301 (83.8)	169 (47.1) [41.8, 52.4]	360	317 (88.1)	153 (42.5) [37.3, 47.8]	1.108 [0.941, 1.303]	1.203 [0.897, 1.615]	4.6 [-3.0, 12.1]	0.218
	Yes	67	58 (86.6)	34 (50.7) [38.2, 63.2]	65	61 (93.8)	32 (49.2) [36.6, 61.9]	1.031 [0.733, 1.450]	1.063 [0.537, 2.103]	1.5 [-17.1, 20.1]	0.862

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin_i, created on: 17FEB2022

Table IT2SSCD4_ISPF: Decrease of Skindex-10 social functioning score of at least 4 points by use of concomitant itch medication
ITT

Decrease of Skindex-10 social functioning score of at least 4 points		CR845 N	CR845 nval (%)	CR845 n (%) [95 % CI]	Placebo N	Placebo nval (%)	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
Week 12	F: Use of concomitant itch medication										0.467
	No	267	231 (86.5)	124 (46.4) [40.3, 52.6]	262	240 (91.6)	116 (44.3) [38.2, 50.5]	1.049 [0.870, 1.265]	1.091 [0.775, 1.537]	2.2 [-6.7, 11.0]	0.617
	Yes	159	128 (80.5)	79 (49.7) [41.7, 57.7]	163	138 (84.7)	69 (42.3) [34.6, 50.3]	1.174 [0.925, 1.489]	1.345 [0.867, 2.088]	7.4 [-4.1, 18.8]	0.186

Note: ITT = Intent-to-treat Set.
N = total number of patients in analysis set. n = number of patients with response. nval = number of patients with non-missing values.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: askin_i, created on: 17FEB2022

Table IT2A_SSIA: Incidence of TEAEs by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
A: Age								0.242
< 65 years	281	187 (66.5) [60.7, 72.0]	289	167 (57.8) [51.9, 63.5]	1.152 [1.012, 1.310]	1.453 [1.034, 2.043]	8.8 [0.5, 17.0]	0.031 *
>= 65 years	143	103 (72.0) [63.9, 79.2]	135	95 (70.4) [61.9, 77.9]	1.024 [0.881, 1.189]	1.084 [0.645, 1.823]	1.7 [-9.7, 13.0]	0.761

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSIB: Incidence of TEAEs by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
B: Sex								0.995
Male	247	159 (64.4) [58.1, 70.3]	257	150 (58.4) [52.1, 64.5]	1.103 [0.960, 1.267]	1.289 [0.900, 1.847]	6.0 [-2.9, 14.9]	0.167
Female	177	131 (74.0) [66.9, 80.3]	167	112 (67.1) [59.4, 74.1]	1.104 [0.962, 1.266]	1.398 [0.878, 2.228]	6.9 [-3.3, 17.1]	0.158

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSIC: Incidence of TEAEs by race
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
C: Race								0.766
Black/African American	135	102 (75.6) [67.4, 82.5]	113	74 (65.5) [56.0, 74.2]	1.154 [0.979, 1.360]	1.629 [0.938, 2.829]	10.1 [-2.1, 22.3]	0.083
White	253	159 (62.8) [56.6, 68.8]	262	154 (58.8) [52.6, 64.8]	1.069 [0.931, 1.228]	1.186 [0.832, 1.691]	4.1 [-4.7, 12.9]	0.345
Other	35	28 (80.0) [63.1, 91.6]	47	33 (70.2) [55.1, 82.7]	1.139 [0.888, 1.462]	1.697 [0.601, 4.790]	9.8 [-11.3, 30.9]	0.318

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSID: Incidence of TEAEs by baseline WI-NRS
SAF-S

	CR845		Placebo						
		n (%)		n (%)	RR	OR	RD		
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value	
D: Baseline worst itching NRS score (WI-NRS)								0.042	i
>= 4 to < 7	184	129 (70.1) [62.9, 76.6]	192	108 (56.3) [48.9, 63.4]	1.246 [1.066, 1.457]	1.824 [1.192, 2.791]	13.9 [3.7, 24.0]	0.005	*
>= 7	240	161 (67.1) [60.7, 73.0]	232	154 (66.4) [59.9, 72.4]	1.011 [0.890, 1.148]	1.032 [0.704, 1.514]	0.7 [-8.2, 9.6]	0.871	

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSIE: Incidence of TEAEs by specific medical condition
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
E: Presence of specific medical conditions								0.034 i
No	358	242 (67.6) [62.5, 72.4]	359	210 (58.5) [53.2, 63.6]	1.156 [1.032, 1.294]	1.480 [1.091, 2.008]	9.1 [1.8, 16.4]	0.012 *
Yes	66	48 (72.7) [60.4, 83.0]	65	52 (80.0) [68.2, 88.9]	0.909 [0.751, 1.101]	0.667 [0.295, 1.505]	-7.3 [-23.3, 8.7]	0.329

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSIF: Incidence of TEAEs by use of concomitant itch medication
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
F: Use of concomitant itch medication								0.066
No	265	174 (65.7) [59.6, 71.4]	261	143 (54.8) [48.5, 60.9]	1.198 [1.041, 1.379]	1.578 [1.110, 2.243]	10.9 [2.2, 19.6]	0.011 *
Yes	159	116 (73.0) [65.3, 79.7]	163	119 (73.0) [65.5, 79.7]	0.999 [0.875, 1.141]	0.997 [0.610, 1.631]	-0.1 [-10.4, 10.3]	0.992

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AS_SSIA: Incidence of serious TEAEs by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Serious TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
A: Age								0.144
< 65 years	281	63 (22.4) [17.7, 27.8]	289	64 (22.1) [17.5, 27.4]	1.012 [0.745, 1.376]	1.016 [0.685, 1.507]	0.3 [-6.9, 7.5]	0.937
>= 65 years	143	44 (30.8) [23.3, 39.0]	135	28 (20.7) [14.2, 28.6]	1.484 [0.983, 2.238]	1.698 [0.983, 2.935]	10.0 [-0.9, 20.9]	0.057

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AS_SSIB: Incidence of serious TEAEs by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Serious TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
B: Sex								0.888
Male	247	60 (24.3) [19.1, 30.1]	257	53 (20.6) [15.8, 26.1]	1.178 [0.851, 1.631]	1.235 [0.812, 1.878]	3.7 [-4.0, 11.4]	0.324
Female	177	47 (26.6) [20.2, 33.7]	167	39 (23.4) [17.2, 30.5]	1.137 [0.787, 1.643]	1.187 [0.727, 1.936]	3.2 [-6.5, 12.9]	0.494

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AS_SSIC: Incidence of serious TEAEs by race
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Serious TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
C: Race								0.138
Black/African American	135	43 (31.9) [24.1, 40.4]	113	27 (23.9) [16.4, 32.8]	1.333 [0.884, 2.011]	1.489 [0.847, 2.617]	8.0 [-4.0, 19.9]	0.166
White	253	55 (21.7) [16.8, 27.3]	262	60 (22.9) [18.0, 28.5]	0.949 [0.688, 1.311]	0.935 [0.617, 1.416]	-1.2 [-8.7, 6.4]	0.752
Other	35	9 (25.7) [12.5, 43.3]	47	5 (10.6) [3.5, 23.1]	2.417 [0.888, 6.582]	2.908 [0.878, 9.631]	15.1 [-4.4, 34.5]	0.074

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AS_SSID: Incidence of serious TEAEs by baseline WI-NRS
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Serious TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)								0.957
>= 4 to < 7	184	38 (20.7) [15.0, 27.2]	192	34 (17.7) [12.6, 23.9]	1.166 [0.769, 1.768]	1.210 [0.723, 2.023]	2.9 [-5.5, 11.4]	0.469
>= 7	240	69 (28.8) [23.1, 34.9]	232	58 (25.0) [19.6, 31.1]	1.150 [0.853, 1.551]	1.211 [0.805, 1.820]	3.8 [-4.7, 12.2]	0.359

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AS_SSIE: Incidence of serious TEAEs by specific medical condition
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Serious TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
E: Presence of specific medical conditions								0.883
No	358	85 (23.7) [19.4, 28.5]	359	74 (20.6) [16.5, 25.2]	1.152 [0.875, 1.517]	1.199 [0.842, 1.707]	3.1 [-3.2, 9.5]	0.313
Yes	66	22 (33.3) [22.2, 46.0]	65	18 (27.7) [17.3, 40.2]	1.204 [0.715, 2.025]	1.306 [0.619, 2.754]	5.6 [-11.6, 22.9]	0.485

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AS_SSIF: Incidence of serious TEAEs by use of concomitant itch medication
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Serious TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
F: Use of concomitant itch medication								0.070
No	265	71 (26.8) [21.6, 32.6]	261	50 (19.2) [14.6, 24.5]	1.399 [1.017, 1.924]	1.544 [1.024, 2.330]	7.6 [0.1, 15.2]	0.038 *
Yes	159	36 (22.6) [16.4, 29.9]	163	42 (25.8) [19.2, 33.2]	0.879 [0.596, 1.295]	0.843 [0.506, 1.406]	-3.1 [-13.1, 6.8]	0.513

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AC_SSIA: Incidence of severe TEAEs by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Severe TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
A: Age								0.406
< 65 years	281	36 (12.8) [9.1, 17.3]	289	33 (11.4) [8.0, 15.7]	1.122 [0.721, 1.747]	1.140 [0.689, 1.886]	1.4 [-4.3, 7.1]	0.611
>= 65 years	143	23 (16.1) [10.5, 23.1]	135	14 (10.4) [5.8, 16.8]	1.551 [0.833, 2.887]	1.657 [0.814, 3.372]	5.7 [-2.9, 14.4]	0.162

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AC_SSIB: Incidence of severe TEAEs by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Severe TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
B: Sex								0.381
Male	247	29 (11.7) [8.0, 16.4]	257	28 (10.9) [7.4, 15.4]	1.078 [0.661, 1.757]	1.088 [0.627, 1.888]	0.8 [-5.1, 6.8]	0.765
Female	177	30 (16.9) [11.7, 23.3]	167	19 (11.4) [7.0, 17.2]	1.490 [0.873, 2.542]	1.590 [0.857, 2.950]	5.6 [-2.3, 13.5]	0.140

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AC_SSIC: Incidence of severe TEAEs by race
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Severe TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
C: Race								0.293
Black/African American	135	23 (17.0) [11.1, 24.5]	113	14 (12.4) [6.9, 19.9]	1.375 [0.743, 2.545]	1.452 [0.709, 2.975]	4.6 [-4.9, 14.2]	0.307
White	253	32 (12.6) [8.8, 17.4]	262	32 (12.2) [8.5, 16.8]	1.036 [0.655, 1.638]	1.041 [0.616, 1.757]	0.4 [-5.7, 6.5]	0.881
Other	35	4 (11.4) [3.2, 26.7]	47	1 (2.1) [0.1, 11.3]	5.371 [0.627, 45.983]	5.935 [0.633, 55.650]	9.3 [-4.5, 23.1]	0.158 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AC_SSID: Incidence of severe TEAEs by baseline WI-NRS
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Severe TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)								0.675
>= 4 to < 7	184	17 (9.2) [5.5, 14.4]	192	16 (8.3) [4.8, 13.2]	1.109 [0.578, 2.128]	1.120 [0.548, 2.288]	0.9 [-5.4, 7.2]	0.757
>= 7	240	42 (17.5) [12.9, 22.9]	232	31 (13.4) [9.3, 18.4]	1.310 [0.854, 2.008]	1.375 [0.831, 2.276]	4.1 [-2.8, 11.1]	0.214

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AC_SSIE: Incidence of severe TEAEs by specific medical condition
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Severe TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
E: Presence of specific medical conditions								0.459
No	358	47 (13.1) [9.8, 17.1]	359	40 (11.1) [8.1, 14.9]	1.178 [0.793, 1.750]	1.205 [0.769, 1.889]	2.0 [-3.1, 7.0]	0.416
Yes	66	12 (18.2) [9.8, 29.6]	65	7 (10.8) [4.4, 20.9]	1.688 [0.709, 4.018]	1.841 [0.675, 5.021]	7.4 [-6.1, 20.9]	0.230

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AC_SSIF: Incidence of severe TEAEs by use of concomitant itch medication
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Severe TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
F: Use of concomitant itch medication								0.262
No	265	33 (12.5) [8.7, 17.0]	261	21 (8.0) [5.0, 12.0]	1.548 [0.920, 2.603]	1.626 [0.914, 2.892]	4.4 [-1.1, 10.0]	0.096
Yes	159	26 (16.4) [11.0, 23.0]	163	26 (16.0) [10.7, 22.5]	1.025 [0.623, 1.686]	1.030 [0.569, 1.865]	0.4 [-8.3, 9.1]	0.922

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AN_SSIA: Incidence of non-severe TEAEs by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Non-severe TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
A: Age								0.155
< 65 years	281	185 (65.8) [60.0, 71.4]	289	160 (55.4) [49.4, 61.2]	1.189 [1.041, 1.359]	1.554 [1.108, 2.180]	10.5 [2.1, 18.8]	0.011 *
>= 65 years	143	101 (70.6) [62.4, 77.9]	135	93 (68.9) [60.4, 76.6]	1.025 [0.878, 1.197]	1.086 [0.651, 1.812]	1.7 [-9.8, 13.3]	0.753

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AN_SSIB: Incidence of non-severe TEAEs by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Non-severe TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
B: Sex								0.997
Male	247	157 (63.6) [57.2, 69.6]	257	145 (56.4) [50.1, 62.6]	1.127 [0.976, 1.300]	1.347 [0.942, 1.927]	7.1 [-1.8, 16.1]	0.102
Female	177	129 (72.9) [65.7, 79.3]	167	108 (64.7) [56.9, 71.9]	1.127 [0.976, 1.301]	1.468 [0.928, 2.323]	8.2 [-2.1, 18.6]	0.101

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AN_SSIC: Incidence of non-severe TEAEs by race
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Non-severe TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
C: Race								0.956
Black/African American	135	99 (73.3) [65.0, 80.6]	113	72 (63.7) [54.1, 72.6]	1.151 [0.969, 1.367]	1.566 [0.912, 2.690]	9.6 [-2.8, 22.0]	0.104
White	253	158 (62.5) [56.2, 68.4]	262	147 (56.1) [49.9, 62.2]	1.113 [0.964, 1.285]	1.301 [0.915, 1.851]	6.3 [-2.5, 15.2]	0.143
Other	35	28 (80.0) [63.1, 91.6]	47	33 (70.2) [55.1, 82.7]	1.139 [0.888, 1.462]	1.697 [0.601, 4.790]	9.8 [-11.3, 30.9]	0.318

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AN_SSID: Incidence of non-severe TEAEs by baseline WI-NRS
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Non-severe TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)								0.051
>= 4 to < 7	184	129 (70.1) [62.9, 76.6]	192	106 (55.2) [47.9, 62.4]	1.270 [1.084, 1.488]	1.903 [1.244, 2.910]	14.9 [4.7, 25.1]	0.003 *
>= 7	240	157 (65.4) [59.0, 71.4]	232	147 (63.4) [56.8, 69.6]	1.032 [0.903, 1.181]	1.094 [0.750, 1.594]	2.1 [-7.0, 11.1]	0.642

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AN_SSIE: Incidence of non-severe TEAEs by specific medical condition
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Non-severe TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
E: Presence of specific medical conditions								0.064
No	358	238 (66.5) [61.3, 71.4]	359	203 (56.5) [51.2, 61.7]	1.176 [1.046, 1.321]	1.524 [1.126, 2.063]	9.9 [2.6, 17.3]	0.006 *
Yes	66	48 (72.7) [60.4, 83.0]	65	50 (76.9) [64.8, 86.5]	0.945 [0.775, 1.153]	0.800 [0.363, 1.765]	-4.2 [-20.6, 12.2]	0.582

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AN_SSIF: Incidence of non-severe TEAEs by use of concomitant itch medication
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
Non-severe TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
F: Use of concomitant itch medication								0.088
No	265	171 (64.5) [58.4, 70.3]	261	138 (52.9) [46.6, 59.1]	1.220 [1.055, 1.411]	1.621 [1.143, 2.301]	11.7 [2.9, 20.4]	0.007 *
Yes	159	115 (72.3) [64.7, 79.1]	163	115 (70.6) [62.9, 77.4]	1.025 [0.893, 1.177]	1.091 [0.672, 1.770]	1.8 [-8.7, 12.3]	0.725

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AT_SSIA: Incidence of TEAEs leading to study drug discontinuation by age
SAF-S

TEAEs leading to study drug discontinuation	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
A: Age								0.540
< 65 years	281	15 (5.3) [3.0, 8.7]	289	11 (3.8) [1.9, 6.7]	1.402 [0.656, 3.000]	1.425 [0.643, 3.159]	1.5 [-2.3, 5.3]	0.381
>= 65 years	143	13 (9.1) [4.9, 15.0]	135	6 (4.4) [1.6, 9.4]	2.045 [0.800, 5.227]	2.150 [0.793, 5.830]	4.6 [-1.9, 11.2]	0.126

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AT_SSIB: Incidence of TEAEs leading to study drug discontinuation by sex
SAF-S

TEAEs leading to study drug discontinuation	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
B: Sex								0.239
Male	247	16 (6.5) [3.7, 10.3]	257	13 (5.1) [2.7, 8.5]	1.281 [0.629, 2.607]	1.300 [0.612, 2.762]	1.4 [-3.1, 5.9]	0.494
Female	177	12 (6.8) [3.6, 11.5]	167	4 (2.4) [0.7, 6.0]	2.831 [0.931, 8.603]	2.964 [0.936, 9.379]	4.4 [-0.6, 9.3]	0.054

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AT_SSIC: Incidence of TEAEs leading to study drug discontinuation by race
SAF-S

TEAEs leading to study drug discontinuation	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
C: Race								0.305	
Black/African American	135	13 (9.6) [5.2, 15.9]	113	4 (3.5) [1.0, 8.8]	2.720 [0.912, 8.111]	2.904 [0.919, 9.171]	6.1 [-0.8, 12.9]	0.059	
White	253	11 (4.3) [2.2, 7.6]	262	11 (4.2) [2.1, 7.4]	1.036 [0.457, 2.346]	1.037 [0.441, 2.437]	0.1 [-3.7, 4.0]	0.933	
Other	35	4 (11.4) [3.2, 26.7]	47	2 (4.3) [0.5, 14.5]	2.686 [0.521, 13.845]	2.903 [0.501, 16.840]	7.2 [-7.3, 21.7]	0.394	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AT_SSID: Incidence of TEAEs leading to study drug discontinuation by baseline WI-NRS
SAF-S

TEAEs leading to study drug discontinuation	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)								0.422
>= 4 to < 7	184	11 (6.0) [3.0, 10.4]	192	5 (2.6) [0.9, 6.0]	2.296 [0.813, 6.479]	2.378 [0.810, 6.983]	3.4 [-1.3, 8.0]	0.106
>= 7	240	17 (7.1) [4.2, 11.1]	232	12 (5.2) [2.7, 8.9]	1.369 [0.669, 2.804]	1.398 [0.652, 2.995]	1.9 [-2.8, 6.7]	0.388

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AT_SSIE: Incidence of TEAEs leading to study drug discontinuation by specific medical condition
SAF-S

TEAEs leading to study drug discontinuation	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
E: Presence of specific medical conditions								0.592	
No	358	25 (7.0) [4.6, 10.1]	359	16 (4.5) [2.6, 7.1]	1.567 [0.851, 2.884]	1.609 [0.844, 3.069]	2.5 [-1.1, 6.2]	0.145	
Yes	66	3 (4.5) [0.9, 12.7]	65	1 (1.5) [0.0, 8.3]	2.955 [0.315, 27.673]	3.048 [0.309, 30.087]	3.0 [-4.4, 10.4]	0.619	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AT_SSIF: Incidence of TEAEs leading to study drug discontinuation by use of concomitant itch medication
SAF-S

TEAEs leading to study drug discontinuation	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
F: Use of concomitant itch medication								0.396
No	265	17 (6.4) [3.8, 10.1]	261	8 (3.1) [1.3, 5.9]	2.093 [0.919, 4.765]	2.168 [0.919, 5.115]	3.3 [-0.6, 7.3]	0.071
Yes	159	11 (6.9) [3.5, 12.0]	163	9 (5.5) [2.6, 10.2]	1.253 [0.534, 2.942]	1.272 [0.512, 3.157]	1.4 [-4.5, 7.3]	0.604

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell.
NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSSA: TEAEs - significant SOC and PT by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Gastrointestinal disorders								
A: Age								0.259
< 65 years	281	66 (23.5) [18.7, 28.9]	289	53 (18.3) [14.0, 23.3]	1.281 [0.928, 1.767]	1.367 [0.911, 2.051]	5.1 [-1.9, 12.2]	0.131
>= 65 years	143	38 (26.6) [19.5, 34.6]	135	20 (14.8) [9.3, 21.9]	1.794 [1.101, 2.921]	2.081 [1.139, 3.802]	11.8 [1.6, 21.9]	0.016 *

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSSA: TEAEs - significant SOC and PT by age
SAF-S

	CR845		Placebo						
		n (%)		n (%)	RR	OR	RD		
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value	
PT: Diarrhoea									
A: Age								0.045	i
< 65 years	281	23 (8.2) [5.3, 12.0]	289	18 (6.2) [3.7, 9.7]	1.314 [0.725, 2.381]	1.342 [0.708, 2.545]	2.0 [-2.6, 6.6]	0.366	
>= 65 years	143	14 (9.8) [5.5, 15.9]	135	2 (1.5) [0.2, 5.2]	6.608 [1.530, 28.535]	7.217 [1.608, 32.385]	8.3 [2.3, 14.3]	0.003	*

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSSA: TEAEs - significant SOC and PT by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Injury, poisoning and procedural complications								
A: Age								0.396
< 65 years	281	37 (13.2) [9.4, 17.7]	289	49 (17.0) [12.8, 21.8]	0.777 [0.524, 1.152]	0.743 [0.468, 1.180]	-3.8 [-10.0, 2.4]	0.207
>= 65 years	143	27 (18.9) [12.8, 26.3]	135	25 (18.5) [12.4, 26.1]	1.020 [0.624, 1.665]	1.024 [0.560, 1.872]	0.4 [-9.5, 10.3]	0.938

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSSA: TEAEs - significant SOC and PT by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Nervous system disorders								
A: Age								0.259
< 65 years	281	44 (15.7) [11.6, 20.4]	289	27 (9.3) [6.2, 13.3]	1.676 [1.069, 2.629]	1.802 [1.081, 3.001]	6.3 [0.6, 12.1]	0.023 *
>= 65 years	143	36 (25.2) [18.3, 33.1]	135	29 (21.5) [14.9, 29.4]	1.172 [0.763, 1.799]	1.230 [0.704, 2.149]	3.7 [-7.0, 14.3]	0.468

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSSA: TEAEs - significant SOC and PT by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
PT: Dizziness								
A: Age								0.418
< 65 years	281	14 (5.0) [2.8, 8.2]	289	6 (2.1) [0.8, 4.5]	2.400 [0.935, 6.157]	2.473 [0.937, 6.530]	2.9 [-0.5, 6.3]	0.060
>= 65 years	143	12 (8.4) [4.4, 14.2]	135	8 (5.9) [2.6, 11.3]	1.416 [0.597, 3.357]	1.454 [0.575, 3.676]	2.5 [-4.3, 9.2]	0.427

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSSA: TEAEs - significant SOC and PT by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Skin and subcutaneous tissue disorders								
A: Age								0.641
< 65 years	281	10 (3.6)	289	12 (4.2)	0.857	0.852	-0.6	0.713
		[1.7, 6.4]		[2.2, 7.1]	[0.376, 1.952]	[0.362, 2.004]	[-4.1, 2.9]	
>= 65 years	143	6 (4.2)	135	9 (6.7)	0.629	0.613	-2.5	0.363
		[1.6, 8.9]		[3.1, 12.3]	[0.230, 1.721]	[0.212, 1.771]	[-8.5, 3.6]	

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSSB: TEAEs - significant SOC and PT by sex
SAF-S

	CR845		Placebo						
		n (%)		n (%)	RR	OR	RD		
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value	
SOC: Gastrointestinal disorders									
B: Sex								0.202	
Male	247	62 (25.1) [19.8, 31.0]	257	39 (15.2) [11.0, 20.2]	1.654 [1.153, 2.372]	1.873 [1.199, 2.926]	9.9 [2.6, 17.3]	0.005	*
Female	177	42 (23.7) [17.7, 30.7]	167	34 (20.4) [14.5, 27.3]	1.166 [0.782, 1.738]	1.217 [0.730, 2.030]	3.4 [-6.0, 12.7]	0.452	

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSSB: TEAEs - significant SOC and PT by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
PT: Diarrhoea								
B: Sex								0.650
Male	247	18 (7.3) [4.4, 11.3]	257	9 (3.5) [1.6, 6.5]	2.081 [0.953, 4.543]	2.166 [0.954, 4.918]	3.8 [-0.6, 8.1]	0.059
Female	177	19 (10.7) [6.6, 16.3]	167	11 (6.6) [3.3, 11.5]	1.630 [0.800, 3.321]	1.705 [0.786, 3.701]	4.1 [-2.3, 10.6]	0.174

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSSB: TEAEs - significant SOC and PT by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Injury, poisoning and procedural complications								
B: Sex								0.846
Male	247	34 (13.8) [9.7, 18.7]	257	40 (15.6) [11.4, 20.6]	0.884 [0.580, 1.349]	0.866 [0.528, 1.420]	-1.8 [-8.4, 4.8]	0.569
Female	177	30 (16.9) [11.7, 23.3]	167	34 (20.4) [14.5, 27.3]	0.833 [0.535, 1.297]	0.798 [0.463, 1.376]	-3.4 [-12.2, 5.4]	0.417

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSSB: TEAEs - significant SOC and PT by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Nervous system disorders								
B: Sex								0.973
Male	247	44 (17.8) [13.3, 23.2]	257	32 (12.5) [8.7, 17.1]	1.431 [0.940, 2.179]	1.524 [0.931, 2.496]	5.4 [-1.3, 12.0]	0.093
Female	177	36 (20.3) [14.7, 27.0]	167	24 (14.4) [9.4, 20.6]	1.415 [0.883, 2.267]	1.521 [0.863, 2.681]	6.0 [-2.6, 14.5]	0.145

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSSB: TEAEs - significant SOC and PT by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
PT: Dizziness								
B: Sex								0.671
Male	247	16 (6.5) [3.7, 10.3]	257	8 (3.1) [1.4, 6.0]	2.081 [0.907, 4.775]	2.156 [0.906, 5.132]	3.4 [-0.8, 7.5]	0.076
Female	177	10 (5.6) [2.7, 10.1]	167	6 (3.6) [1.3, 7.7]	1.573 [0.584, 4.231]	1.607 [0.571, 4.523]	2.1 [-2.9, 7.1]	0.366

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSSB: TEAEs - significant SOC and PT by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Skin and subcutaneous tissue disorders								
B: Sex								0.501
Male	247	7 (2.8) [1.1, 5.8]	257	12 (4.7) [2.4, 8.0]	0.607 [0.243, 1.516]	0.595 [0.231, 1.538]	-1.8 [-5.5, 1.9]	0.280
Female	177	9 (5.1) [2.4, 9.4]	167	9 (5.4) [2.5, 10.0]	0.944 [0.384, 2.319]	0.940 [0.364, 2.430]	-0.3 [-5.6, 5.0]	0.899

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSSC: TEAEs - significant SOC and PT by race
SAF-S

	CR845		Placebo						
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
SOC: Gastrointestinal disorders									
C: Race								0.602	
Black/African American	135	39 (28.9) [21.4, 37.3]	113	20 (17.7) [11.2, 26.0]	1.632 [1.012, 2.632]	1.889 [1.027, 3.476]	11.2 [-0.0, 22.4]	0.040	*
White	253	54 (21.3) [16.5, 26.9]	262	45 (17.2) [12.8, 22.3]	1.243 [0.871, 1.774]	1.309 [0.843, 2.032]	4.2 [-3.0, 11.4]	0.231	
Other	35	10 (28.6) [14.6, 46.3]	47	8 (17.0) [7.6, 30.8]	1.679 [0.739, 3.812]	1.950 [0.678, 5.610]	11.6 [-9.4, 32.5]	0.214	

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSSC: TEAEs - significant SOC and PT by race
SAF-S

	CR845		Placebo						
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
PT: Diarrhoea									
C: Race								0.398	
Black/African American	135	14 (10.4) [5.8, 16.8]	113	7 (6.2) [2.5, 12.3]	1.674 [0.700, 4.005]	1.752 [0.682, 4.503]	4.2 [-3.4, 11.8]	0.240	
White	253	23 (9.1) [5.9, 13.3]	262	11 (4.2) [2.1, 7.4]	2.165 [1.078, 4.349]	2.282 [1.088, 4.785]	4.9 [0.2, 9.6]	0.026	*
Other	35	0 (0.0) [0.0, 10.0]	47	2 (4.3) [0.5, 14.5]	0.267 + [0.013, 5.385]	0.256 + [0.012, 5.511]	-4.3 [-12.5, 4.0]	0.505	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSSC: TEAEs - significant SOC and PT by race
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Injury, poisoning and procedural complications								
C: Race								0.636
Black/African American	135	16 (11.9) [6.9, 18.5]	113	14 (12.4) [6.9, 19.9]	0.957 [0.488, 1.874]	0.951 [0.442, 2.044]	-0.5 [-9.5, 8.4]	0.897
White	253	44 (17.4) [12.9, 22.6]	262	50 (19.1) [14.5, 24.4]	0.911 [0.632, 1.315]	0.893 [0.570, 1.397]	-1.7 [-8.7, 5.4]	0.619
Other	35	4 (11.4) [3.2, 26.7]	47	10 (21.3) [10.7, 35.7]	0.537 [0.184, 1.572]	0.477 [0.136, 1.673]	-9.8 [-28.1, 8.4]	0.244

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSSC: TEAEs - significant SOC and PT by race
SAF-S

	CR845		Placebo						
		n (%)		n (%)	RR	OR	RD		
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value	
SOC: Nervous system disorders									
C: Race								0.112	
Black/African American	135	33 (24.4) [17.5, 32.6]	113	17 (15.0) [9.0, 23.0]	1.625 [0.957, 2.758]	1.827 [0.956, 3.493]	9.4 [-1.2, 20.0]	0.067	
White	253	36 (14.2) [10.2, 19.2]	262	35 (13.4) [9.5, 18.1]	1.065 [0.692, 1.641]	1.076 [0.652, 1.776]	0.9 [-5.5, 7.2]	0.775	
Other	35	10 (28.6) [14.6, 46.3]	47	4 (8.5) [2.4, 20.4]	3.357 [1.147, 9.824]	4.300 [1.220, 15.159]	20.1 [0.6, 39.5]	0.018	*

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSSC: TEAEs - significant SOC and PT by race
SAF-S

	CR845		Placebo						
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
PT: Dizziness									
C: Race								0.232	
Black/African American	135	14 (10.4) [5.8, 16.8]	113	3 (2.7) [0.6, 7.6]	3.906 [1.151, 13.253]	4.242 [1.187, 15.158]	7.7 [1.0, 14.5]	0.017	*
White	253	9 (3.6) [1.6, 6.6]	262	8 (3.1) [1.3, 5.9]	1.165 [0.457, 2.972]	1.171 [0.445, 3.085]	0.5 [-3.0, 4.0]	0.749	
Other	35	2 (5.7) [0.7, 19.2]	47	3 (6.4) [1.3, 17.5]	0.895 [0.158, 5.074]	0.889 [0.140, 5.626]	-0.7 [-13.6, 12.2]	1.000	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSSC: TEAEs - significant SOC and PT by race
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Skin and subcutaneous tissue disorders								
C: Race								0.974
Black/African American	135	4 (3.0) [0.8, 7.4]	113	4 (3.5) [1.0, 8.8]	0.837 [0.214, 3.272]	0.832 [0.203, 3.405]	-0.6 [-5.8, 4.7]	1.000 #
White	253	10 (4.0) [1.9, 7.1]	262	14 (5.3) [3.0, 8.8]	0.740 [0.335, 1.635]	0.729 [0.318, 1.673]	-1.4 [-5.4, 2.6]	0.455
Other	35	2 (5.7) [0.7, 19.2]	47	3 (6.4) [1.3, 17.5]	0.895 [0.158, 5.074]	0.889 [0.140, 5.626]	-0.7 [-13.6, 12.2]	1.000 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSSD: TEAEs - significant SOC and PT by baseline WI-NRS
SAF-S

	CR845		Placebo						
		n (%)		n (%)	RR	OR	RD		
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value	
SOC: Gastrointestinal disorders									
D: Baseline worst itching NRS score (WI-NRS)								0.346	
>= 4 to < 7	184	46 (25.0) [18.9, 31.9]	192	29 (15.1) [10.4, 21.0]	1.655 [1.089, 2.515]	1.874 [1.117, 3.142]	9.9 [1.3, 18.5]	0.017	*
>= 7	240	58 (24.2) [18.9, 30.1]	232	44 (19.0) [14.1, 24.6]	1.274 [0.900, 1.804]	1.362 [0.875, 2.118]	5.2 [-2.6, 13.0]	0.170	

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSSD: TEAEs - significant SOC and PT by baseline WI-NRS
SAF-S

	CR845		Placebo						
		n (%)		n (%)	RR	OR	RD		
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value	
PT: Diarrhoea									
D: Baseline worst itching NRS score (WI-NRS)								0.541	
>= 4 to < 7	184	13 (7.1) [3.8, 11.8]	192	9 (4.7) [2.2, 8.7]	1.507 [0.660, 3.441]	1.546 [0.644, 3.709]	2.4 [-2.9, 7.7]	0.327	
>= 7	240	24 (10.0) [6.5, 14.5]	232	11 (4.7) [2.4, 8.3]	2.109 [1.057, 4.207]	2.232 [1.067, 4.669]	5.3 [0.2, 10.4]	0.029	*

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSSD: TEAEs - significant SOC and PT by baseline WI-NRS
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Injury, poisoning and procedural complications								
D: Baseline worst itching NRS score (WI-NRS)								0.780
>= 4 to < 7	184	27 (14.7) [9.9, 20.6]	192	31 (16.1) [11.2, 22.1]	0.909 [0.565, 1.461]	0.893 [0.510, 1.565]	-1.5 [-9.3, 6.4]	0.693
>= 7	240	37 (15.4) [11.1, 20.6]	232	43 (18.5) [13.8, 24.1]	0.832 [0.557, 1.242]	0.801 [0.495, 1.297]	-3.1 [-10.3, 4.1]	0.367

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSSD: TEAEs - significant SOC and PT by baseline WI-NRS
SAF-S

	CR845		Placebo						
		n (%)		n (%)	RR	OR	RD		
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value	
SOC: Nervous system disorders									
D: Baseline worst itching NRS score (WI-NRS)								0.425	
>= 4 to < 7	184	35 (19.0) [13.6, 25.4]	192	22 (11.5) [7.3, 16.8]	1.660 [1.014, 2.719]	1.815 [1.020, 3.232]	7.6 [-0.2, 15.3]	0.041	*
>= 7	240	45 (18.8) [14.0, 24.3]	232	34 (14.7) [10.4, 19.9]	1.279 [0.851, 1.922]	1.344 [0.826, 2.188]	4.1 [-3.0, 11.2]	0.234	

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSSD: TEAEs - significant SOC and PT by baseline WI-NRS
SAF-S

	CR845		Placebo						
		n (%)		n (%)	RR	OR	RD		
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value	
PT: Dizziness									
D: Baseline worst itching NRS score (WI-NRS)								0.229	
>= 4 to < 7	184	12 (6.5) [3.4, 11.1]	192	4 (2.1) [0.6, 5.2]	3.130 [1.028, 9.531]	3.279 [1.038, 10.359]	4.4 [-0.2, 9.1]	0.033	*
>= 7	240	14 (5.8) [3.2, 9.6]	232	10 (4.3) [2.1, 7.8]	1.353 [0.613, 2.985]	1.375 [0.598, 3.161]	1.5 [-2.9, 5.9]	0.452	

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSSD: TEAEs - significant SOC and PT by baseline WI-NRS
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Skin and subcutaneous tissue disorders								
D: Baseline worst itching NRS score (WI-NRS)								0.249
>= 4 to < 7	184	8 (4.3) [1.9, 8.4]	192	7 (3.6) [1.5, 7.4]	1.193 [0.441, 3.222]	1.201 [0.427, 3.382]	0.7 [-3.8, 5.2]	0.728
>= 7	240	8 (3.3) [1.4, 6.5]	232	14 (6.0) [3.3, 9.9]	0.552 [0.236, 1.292]	0.537 [0.221, 1.305]	-2.7 [-6.9, 1.5]	0.164

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSSE: TEAEs - significant SOC and PT by specific medical condition
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Gastrointestinal disorders								
E: Presence of specific medical conditions								0.208
No	358	89 (24.9) [20.5, 29.7]	359	58 (16.2) [12.5, 20.4]	1.539 [1.144, 2.070]	1.717 [1.187, 2.484]	8.7 [2.5, 14.9]	0.004 *
Yes	66	15 (22.7) [13.3, 34.7]	65	15 (23.1) [13.5, 35.2]	0.985 [0.525, 1.846]	0.980 [0.434, 2.215]	-0.3 [-16.3, 15.6]	0.962

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSSE: TEAEs - significant SOC and PT by specific medical condition
SAF-S

	CR845		Placebo						
TEAEs	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
PT: Diarrhoea									
E: Presence of specific medical conditions								0.939	
No	358	33 (9.2) [6.4, 12.7]	359	18 (5.0) [3.0, 7.8]	1.838 [1.055, 3.204]	1.924 [1.062, 3.484]	4.2 [0.2, 8.2]	0.029	*
Yes	66	4 (6.1) [1.7, 14.8]	65	2 (3.1) [0.4, 10.7]	1.970 [0.374, 10.385]	2.032 [0.359, 11.500]	3.0 [-5.7, 11.6]	0.680	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSSE: TEAEs - significant SOC and PT by specific medical condition
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Injury, poisoning and procedural complications								
E: Presence of specific medical conditions								0.497
No	358	49 (13.7) [10.3, 17.7]	359	60 (16.7) [13.0, 21.0]	0.819 [0.578, 1.160]	0.790 [0.525, 1.190]	-3.0 [-8.6, 2.5]	0.260
Yes	66	15 (22.7) [13.3, 34.7]	65	14 (21.5) [12.3, 33.5]	1.055 [0.555, 2.007]	1.071 [0.469, 2.446]	1.2 [-14.6, 16.9]	0.870

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSSE: TEAEs - significant SOC and PT by specific medical condition
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Nervous system disorders								
E: Presence of specific medical conditions								0.221
No	358	62 (17.3) [13.5, 21.6]	359	39 (10.9) [7.8, 14.6]	1.594 [1.098, 2.315]	1.719 [1.117, 2.644]	6.5 [1.1, 11.8]	0.013 *
Yes	66	18 (27.3) [17.0, 39.6]	65	17 (26.2) [16.0, 38.5]	1.043 [0.591, 1.839]	1.059 [0.488, 2.297]	1.1 [-15.6, 17.8]	0.885

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSSE: TEAEs - significant SOC and PT by specific medical condition
SAF-S

	CR845		Placebo						
		n (%)		n (%)	RR	OR	RD		
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value	
PT: Dizziness									
E: Presence of specific medical conditions								0.069	
No	358	23 (6.4) [4.1, 9.5]	359	9 (2.5) [1.2, 4.7]	2.563 [1.203, 5.461]	2.670 [1.218, 5.854]	3.9 [0.6, 7.2]	0.011	*
Yes	66	3 (4.5) [0.9, 12.7]	65	5 (7.7) [2.5, 17.0]	0.591 [0.147, 2.372]	0.571 [0.131, 2.496]	-3.1 [-12.9, 6.6]	0.492	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSSE: TEAEs - significant SOC and PT by specific medical condition
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Skin and subcutaneous tissue disorders								
E: Presence of specific medical conditions								0.687
No	358	13 (3.6) [1.9, 6.1]	359	16 (4.5) [2.6, 7.1]	0.815 [0.398, 1.669]	0.808 [0.383, 1.705]	-0.8 [-4.0, 2.3]	0.575
Yes	66	3 (4.5) [0.9, 12.7]	65	5 (7.7) [2.5, 17.0]	0.591 [0.147, 2.372]	0.571 [0.131, 2.496]	-3.1 [-12.9, 6.6]	0.492 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSSF: TEAEs - significant SOC and PT by use of concomitant itch medication
SAF-S

	CR845		Placebo						
		n (%)		n (%)	RR	OR	RD		
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value	
SOC: Gastrointestinal disorders									
F: Use of concomitant itch medication								0.260	
No	265	56 (21.1) [16.4, 26.5]	261	33 (12.6) [8.9, 17.3]	1.671 [1.126, 2.480]	1.851 [1.158, 2.960]	8.5 [1.8, 15.2]	0.009	*
Yes	159	48 (30.2) [23.2, 38.0]	163	40 (24.5) [18.1, 31.9]	1.230 [0.860, 1.760]	1.330 [0.813, 2.175]	5.6 [-4.7, 16.0]	0.256	

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSSF: TEAEs - significant SOC and PT by use of concomitant itch medication
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
PT: Diarrhoea								
F: Use of concomitant itch medication								0.954
No	265	21 (7.9) [5.0, 11.9]	261	11 (4.2) [2.1, 7.4]	1.880 [0.925, 3.821]	1.956 [0.923, 4.143]	3.7 [-0.7, 8.2]	0.075
Yes	159	16 (10.1) [5.9, 15.8]	163	9 (5.5) [2.6, 10.2]	1.823 [0.830, 4.003]	1.915 [0.820, 4.469]	4.5 [-1.9, 11.0]	0.128

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSSF: TEAEs - significant SOC and PT by use of concomitant itch medication
SAF-S

	CR845		Placebo						
		n (%)		n (%)	RR	OR	RD		
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value	
SOC: Injury, poisoning and procedural complications									
F: Use of concomitant itch medication								0.034	i
No	265	44 (16.6) [12.3, 21.6]	261	38 (14.6) [10.5, 19.4]	1.140 [0.765, 1.700]	1.168 [0.729, 1.874]	2.0 [-4.5, 8.6]	0.519	
Yes	159	20 (12.6) [7.9, 18.8]	163	36 (22.1) [16.0, 29.2]	0.570 [0.345, 0.940]	0.508 [0.279, 0.922]	-9.5 [-18.3, -0.7]	0.025	*

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSSF: TEAEs - significant SOC and PT by use of concomitant itch medication
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Nervous system disorders								
F: Use of concomitant itch medication								0.743
No	265	43 (16.2) [12.0, 21.2]	261	31 (11.9) [8.2, 16.4]	1.366 [0.890, 2.098]	1.437 [0.874, 2.363]	4.3 [-2.0, 10.7]	0.152
Yes	159	37 (23.3) [16.9, 30.6]	163	25 (15.3) [10.2, 21.8]	1.517 [0.960, 2.399]	1.674 [0.954, 2.939]	7.9 [-1.3, 17.1]	0.072

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSSF: TEAEs - significant SOC and PT by use of concomitant itch medication
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
PT: Dizziness								
F: Use of concomitant itch medication								0.951
No	265	13 (4.9) [2.6, 8.2]	261	7 (2.7) [1.1, 5.4]	1.829 [0.742, 4.512]	1.872 [0.735, 4.769]	2.2 [-1.4, 5.9]	0.183
Yes	159	13 (8.2) [4.4, 13.6]	163	7 (4.3) [1.7, 8.6]	1.904 [0.780, 4.648]	1.984 [0.770, 5.111]	3.9 [-2.0, 9.8]	0.150

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae_i, created on: 17FEB2022

Table IT2A_SSSF: TEAEs - significant SOC and PT by use of concomitant itch medication
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
TEAEs	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
SOC: Skin and subcutaneous tissue disorders								
F: Use of concomitant itch medication								0.142
No	265	4 (1.5) [0.4, 3.8]	261	10 (3.8) [1.9, 6.9]	0.394 [0.125, 1.240]	0.385 [0.119, 1.242]	-2.3 [-5.5, 0.8]	0.098
Yes	159	12 (7.5) [4.0, 12.8]	163	11 (6.7) [3.4, 11.8]	1.118 [0.508, 2.460]	1.128 [0.483, 2.636]	0.8 [-5.5, 7.0]	0.781

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method). NE = not evaluable.
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
TEAE = treatment emergent adverse event. SOC = system organ class. PT = preferred term. RR = relative risk. OR = odds ratio.
RD = risk difference. + = adding of 0.5 to each cell.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEG_SSIA: Incidence of AESI gait disturbance by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI gait disturbance	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
A: Age		n<10 for all subgroups						NE
< 65 years	281	6 (2.1) [0.8, 4.6]	289	3 (1.0) [0.2, 3.0]				
>= 65 years	143	4 (2.8) [0.8, 7.0]	135	1 (0.7) [0.0, 4.1]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEG_SSIB: Incidence of AESI gait disturbance by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI gait disturbance	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
B: Sex		n<10 for all subgroups						NE
Male	247	6 (2.4) [0.9, 5.2]	257	2 (0.8) [0.1, 2.8]				
Female	177	4 (2.3) [0.6, 5.7]	167	2 (1.2) [0.1, 4.3]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEG_SSIC: Incidence of AESI gait disturbance by race
SAF-S

	CR845		Placebo					
AESI gait disturbance	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
C: Race		n<10 for all subgroups						NE
Black/African American	135	4 (3.0) [0.8, 7.4]	113	0 (0.0) [0.0, 3.2]				
White	253	5 (2.0) [0.6, 4.6]	262	4 (1.5) [0.4, 3.9]				
Other	35	1 (2.9) [0.1, 14.9]	47	0 (0.0) [0.0, 7.5]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEG_SSID: Incidence of AESI gait disturbance by baseline WI-NRS
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI gait disturbance	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)		n<10 for all subgroups						NE
>= 4 to < 7	184	5 (2.7) [0.9, 6.2]	192	3 (1.6) [0.3, 4.5]				
>= 7	240	5 (2.1) [0.7, 4.8]	232	1 (0.4) [0.0, 2.4]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEG_SSIE: Incidence of AESI gait disturbance by specific medical condition
SAF-S

	CR845		Placebo					
AESI gait disturbance	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
E: Presence of specific medical conditions								0.861
No	358	7 (2.0) [0.8, 4.0]	359	3 (0.8) [0.2, 2.4]	2.340 [0.610, 8.977]	2.367 [0.607, 9.225]	1.1 [-0.9, 3.1]	0.223 #
Yes	66	3 (4.5) [0.9, 12.7]	65	1 (1.5) [0.0, 8.3]	2.955 [0.315, 27.673]	3.048 [0.309, 30.087]	3.0 [-4.4, 10.4]	0.619 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEG_SSIF: Incidence of AESI gait disturbance by use of concomitant itch medication
SAF-S

	CR845		Placebo					
AESI gait disturbance	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
F: Use of concomitant itch medication		n<10 for all subgroups						NE
No	265	5 (1.9) [0.6, 4.3]	261	2 (0.8) [0.1, 2.7]				
Yes	159	5 (3.1) [1.0, 7.2]	163	2 (1.2) [0.1, 4.4]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEGN_SSIA: Incidence of AESI gait disturbance - non-severe by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI gait disturbance - non-severe	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
A: Age		n<10 for all subgroups						NE
< 65 years	281	6 (2.1) [0.8, 4.6]	289	3 (1.0) [0.2, 3.0]				
>= 65 years	143	4 (2.8) [0.8, 7.0]	135	1 (0.7) [0.0, 4.1]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEGN_SSIB: Incidence of AESI gait disturbance - non-severe by sex
SAF-S

	CR845		Placebo					
AESI gait disturbance - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
B: Sex		n<10 for all subgroups						NE
Male	247	6 (2.4) [0.9, 5.2]	257	2 (0.8) [0.1, 2.8]				
Female	177	4 (2.3) [0.6, 5.7]	167	2 (1.2) [0.1, 4.3]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEGN_SSIC: Incidence of AESI gait disturbance - non-severe by race
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI gait disturbance - non-severe	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
C: Race		n<10 for all subgroups						NE
Black/African American	135	4 (3.0) [0.8, 7.4]	113	0 (0.0) [0.0, 3.2]				
White	253	5 (2.0) [0.6, 4.6]	262	4 (1.5) [0.4, 3.9]				
Other	35	1 (2.9) [0.1, 14.9]	47	0 (0.0) [0.0, 7.5]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEGN_SSID: Incidence of AESI gait disturbance - non-severe by baseline WI-NRS
SAF-S

	CR845		Placebo					
AESI gait disturbance - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)		n<10 for all subgroups						NE
>= 4 to < 7	184	5 (2.7) [0.9, 6.2]	192	3 (1.6) [0.3, 4.5]				
>= 7	240	5 (2.1) [0.7, 4.8]	232	1 (0.4) [0.0, 2.4]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEGN_SSIE: Incidence of AESI gait disturbance - non-severe by specific medical condition
SAF-S

	CR845		Placebo					
AESI gait disturbance - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
E: Presence of specific medical conditions								0.861
No	358	7 (2.0) [0.8, 4.0]	359	3 (0.8) [0.2, 2.4]	2.340 [0.610, 8.977]	2.367 [0.607, 9.225]	1.1 [-0.9, 3.1]	0.223 #
Yes	66	3 (4.5) [0.9, 12.7]	65	1 (1.5) [0.0, 8.3]	2.955 [0.315, 27.673]	3.048 [0.309, 30.087]	3.0 [-4.4, 10.4]	0.619 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEGN_SSIF: Incidence of AESI gait disturbance - non-severe by use of concomitant itch medication
SAF-S

	CR845		Placebo					
AESI gait disturbance - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
F: Use of concomitant itch medication		n<10 for all subgroups						NE
No	265	5 (1.9) [0.6, 4.3]	261	2 (0.8) [0.1, 2.7]				
Yes	159	5 (3.1) [1.0, 7.2]	163	2 (1.2) [0.1, 4.4]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEF_SSIA: Incidence of AESI falls/injuries by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI falls/injuries	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
A: Age								0.865
< 65 years	281	17 (6.0) [3.6, 9.5]	289	13 (4.5) [2.4, 7.6]	1.345 [0.666, 2.717]	1.367 [0.651, 2.870]	1.6 [-2.5, 5.6]	0.407
>= 65 years	143	13 (9.1) [4.9, 15.0]	135	10 (7.4) [3.6, 13.2]	1.227 [0.557, 2.705]	1.250 [0.529, 2.955]	1.7 [-5.5, 8.9]	0.611

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEF_SSIB: Incidence of AESI falls/injuries by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI falls/injuries	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
B: Sex								0.699
Male	247	16 (6.5) [3.7, 10.3]	257	14 (5.4) [3.0, 9.0]	1.189 [0.593, 2.384]	1.202 [0.574, 2.519]	1.0 [-3.5, 5.6]	0.625
Female	177	14 (7.9) [4.4, 12.9]	167	9 (5.4) [2.5, 10.0]	1.468 [0.653, 3.300]	1.508 [0.635, 3.583]	2.5 [-3.3, 8.3]	0.350

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEF_SSIC: Incidence of AESI falls/injuries by race
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI falls/injuries	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
C: Race								0.776
Black/African American	135	9 (6.7) [3.1, 12.3]	113	4 (3.5) [1.0, 8.8]	1.883 [0.596, 5.954]	1.946 [0.583, 6.497]	3.1 [-3.1, 9.4]	0.272
White	253	18 (7.1) [4.3, 11.0]	262	16 (6.1) [3.5, 9.7]	1.165 [0.608, 2.234]	1.178 [0.587, 2.364]	1.0 [-3.7, 5.7]	0.646
Other	35	3 (8.6) [1.8, 23.1]	47	3 (6.4) [1.3, 17.5]	1.343 [0.288, 6.260]	1.375 [0.260, 7.259]	2.2 [-11.9, 16.3]	1.000 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEF_SSID: Incidence of AESI falls/injuries by baseline WI-NRS
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI falls/injuries	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)								0.483
>= 4 to < 7	184	11 (6.0) [3.0, 10.4]	192	11 (5.7) [2.9, 10.0]	1.043 [0.464, 2.348]	1.046 [0.442, 2.476]	0.2 [-5.0, 5.5]	0.918
>= 7	240	19 (7.9) [4.8, 12.1]	232	12 (5.2) [2.7, 8.9]	1.531 [0.760, 3.082]	1.576 [0.747, 3.325]	2.7 [-2.1, 7.6]	0.229

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEF_SSIE: Incidence of AESI falls/injuries by specific medical condition
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI falls/injuries	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
E: Presence of specific medical conditions								0.349
No	358	20 (5.6) [3.4, 8.5]	359	18 (5.0) [3.0, 7.8]	1.114 [0.600, 2.071]	1.121 [0.583, 2.157]	0.6 [-3.0, 4.1]	0.732
Yes	66	10 (15.2) [7.5, 26.1]	65	5 (7.7) [2.5, 17.0]	1.970 [0.712, 5.448]	2.143 [0.690, 6.658]	7.5 [-4.9, 19.8]	0.182

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEF_SSIF: Incidence of AESI falls/injuries by use of concomitant itch medication
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI falls/injuries	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
F: Use of concomitant itch medication								0.656
No	265	19 (7.2) [4.4, 11.0]	261	13 (5.0) [2.7, 8.4]	1.439 [0.726, 2.854]	1.473 [0.712, 3.049]	2.2 [-2.3, 6.6]	0.294
Yes	159	11 (6.9) [3.5, 12.0]	163	10 (6.1) [3.0, 11.0]	1.128 [0.493, 2.581]	1.137 [0.469, 2.757]	0.8 [-5.2, 6.8]	0.776

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEFN_SSIA: Incidence of AESI falls/injuries - non-severe by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI falls/injuries - non-severe	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
A: Age								0.722
< 65 years	281	16 (5.7) [3.3, 9.1]	289	11 (3.8) [1.9, 6.7]	1.496 [0.707, 3.167]	1.526 [0.695, 3.348]	1.9 [-2.0, 5.7]	0.289
>= 65 years	143	13 (9.1) [4.9, 15.0]	135	10 (7.4) [3.6, 13.2]	1.227 [0.557, 2.705]	1.250 [0.529, 2.955]	1.7 [-5.5, 8.9]	0.611

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEFN_SSIB: Incidence of AESI falls/injuries - non-severe by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI falls/injuries - non-severe	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
B: Sex								0.502
Male	247	16 (6.5) [3.7, 10.3]	257	14 (5.4) [3.0, 9.0]	1.189 [0.593, 2.384]	1.202 [0.574, 2.519]	1.0 [-3.5, 5.6]	0.625
Female	177	13 (7.3) [4.0, 12.2]	167	7 (4.2) [1.7, 8.4]	1.752 [0.717, 4.285]	1.812 [0.705, 4.658]	3.2 [-2.3, 8.6]	0.212

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEFN_SSIC: Incidence of AESI falls/injuries - non-severe by race
SAF-S

	CR845		Placebo					
AESI falls/injuries - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
C: Race								0.557
Black/African American	135	9 (6.7) [3.1, 12.3]	113	3 (2.7) [0.6, 7.6]	2.511 [0.696, 9.054]	2.619 [0.692, 9.917]	4.0 [-1.9, 10.0]	0.143
White	253	18 (7.1) [4.3, 11.0]	262	15 (5.7) [3.2, 9.3]	1.243 [0.640, 2.412]	1.261 [0.621, 2.561]	1.4 [-3.2, 6.0]	0.520
Other	35	2 (5.7) [0.7, 19.2]	47	3 (6.4) [1.3, 17.5]	0.895 [0.158, 5.074]	0.889 [0.140, 5.626]	-0.7 [-13.6, 12.2]	1.000 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEFN_SSID: Incidence of AESI falls/injuries - non-severe by baseline WI-NRS
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI falls/injuries - non-severe	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)								0.365
>= 4 to < 7	184	11 (6.0) [3.0, 10.4]	192	11 (5.7) [2.9, 10.0]	1.043 [0.464, 2.348]	1.046 [0.442, 2.476]	0.2 [-5.0, 5.5]	0.918
>= 7	240	18 (7.5) [4.5, 11.6]	232	10 (4.3) [2.1, 7.8]	1.740 [0.821, 3.690]	1.800 [0.813, 3.986]	3.2 [-1.5, 7.8]	0.143

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEFN_SSIE: Incidence of AESI falls/injuries - non-severe by specific medical condition
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI falls/injuries - non-severe	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
E: Presence of specific medical conditions								0.339
No	358	20 (5.6) [3.4, 8.5]	359	17 (4.7) [2.8, 7.5]	1.180 [0.628, 2.215]	1.190 [0.613, 2.312]	0.9 [-2.7, 4.4]	0.607
Yes	66	9 (13.6) [6.4, 24.3]	65	4 (6.2) [1.7, 15.0]	2.216 [0.718, 6.838]	2.408 [0.702, 8.254]	7.5 [-4.2, 19.1]	0.154

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEFN_SSIF: Incidence of AESI falls/injuries - non-severe by use of concomitant itch medication
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI falls/injuries - non-severe	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
F: Use of concomitant itch medication								0.583
No	265	19 (7.2) [4.4, 11.0]	261	12 (4.6) [2.4, 7.9]	1.559 [0.773, 3.147]	1.603 [0.762, 3.372]	2.6 [-1.8, 7.0]	0.211
Yes	159	10 (6.3) [3.1, 11.3]	163	9 (5.5) [2.6, 10.2]	1.139 [0.475, 2.729]	1.148 [0.454, 2.906]	0.8 [-5.0, 6.5]	0.770

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEV_SSIA: Incidence of AESI dizziness by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI dizziness	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
A: Age								0.263
< 65 years	281	15 (5.3) [3.0, 8.7]	289	6 (2.1) [0.8, 4.5]	2.571 [1.012, 6.532]	2.660 [1.017, 6.956]	3.3 [-0.2, 6.7]	0.039 *
>= 65 years	143	12 (8.4) [4.4, 14.2]	135	9 (6.7) [3.1, 12.3]	1.259 [0.548, 2.891]	1.282 [0.522, 3.149]	1.7 [-5.2, 8.6]	0.587

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEV_SSIB: Incidence of AESI dizziness by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI dizziness	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
B: Sex								0.917
Male	247	16 (6.5) [3.7, 10.3]	257	9 (3.5) [1.6, 6.5]	1.850 [0.833, 4.107]	1.909 [0.827, 4.404]	3.0 [-1.2, 7.2]	0.124
Female	177	11 (6.2) [3.1, 10.8]	167	6 (3.6) [1.3, 7.7]	1.730 [0.654, 4.572]	1.778 [0.642, 4.922]	2.6 [-2.5, 7.7]	0.263

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEV_SSIC: Incidence of AESI dizziness by race
SAF-S

	CR845		Placebo						
AESI dizziness	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
C: Race								0.221	
Black/African American	135	14 (10.4) [5.8, 16.8]	113	3 (2.7) [0.6, 7.6]	3.906 [1.151, 13.253]	4.242 [1.187, 15.158]	7.7 [1.0, 14.5]	0.017	*
White	253	10 (4.0) [1.9, 7.1]	262	9 (3.4) [1.6, 6.4]	1.151 [0.475, 2.785]	1.157 [0.462, 2.896]	0.5 [-3.1, 4.2]	0.756	
Other	35	2 (5.7) [0.7, 19.2]	47	3 (6.4) [1.3, 17.5]	0.895 [0.158, 5.074]	0.889 [0.140, 5.626]	-0.7 [-13.6, 12.2]	1.000	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEV_SSID: Incidence of AESI dizziness by baseline WI-NRS
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI dizziness	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)								0.288
>= 4 to < 7	184	13 (7.1) [3.8, 11.8]	192	5 (2.6) [0.9, 6.0]	2.713 [0.987, 7.459]	2.843 [0.993, 8.142]	4.5 [-0.4, 9.3]	0.043 *
>= 7	240	14 (5.8) [3.2, 9.6]	232	10 (4.3) [2.1, 7.8]	1.353 [0.613, 2.985]	1.375 [0.598, 3.161]	1.5 [-2.9, 5.9]	0.452

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEV_SSIE: Incidence of AESI dizziness by specific medical condition
SAF-S

	CR845		Placebo						
		n (%)		n (%)	RR	OR	RD		
AESI dizziness	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value	
E: Presence of specific medical conditions								0.079	
No	358	24 (6.7) [4.3, 9.8]	359	10 (2.8) [1.3, 5.1]	2.407 [1.168, 4.959]	2.508 [1.181, 5.324]	3.9 [0.5, 7.3]	0.014	*
Yes	66	3 (4.5) [0.9, 12.7]	65	5 (7.7) [2.5, 17.0]	0.591 [0.147, 2.372]	0.571 [0.131, 2.496]	-3.1 [-12.9, 6.6]	0.492	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEV_SSIF: Incidence of AESI dizziness by use of concomitant itch medication
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI dizziness	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
F: Use of concomitant itch medication								0.874
No	265	14 (5.3) [2.9, 8.7]	261	8 (3.1) [1.3, 5.9]	1.724 [0.735, 4.039]	1.764 [0.727, 4.278]	2.2 [-1.6, 6.0]	0.204
Yes	159	13 (8.2) [4.4, 13.6]	163	7 (4.3) [1.7, 8.6]	1.904 [0.780, 4.648]	1.984 [0.770, 5.111]	3.9 [-2.0, 9.8]	0.150

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEVN_SSIA: Incidence of AESI dizziness - non-severe by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI dizziness - non-severe	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
A: Age								0.376
< 65 years	281	13 (4.6) [2.5, 7.8]	289	6 (2.1) [0.8, 4.5]	2.228 [0.859, 5.781]	2.288 [0.857, 6.106]	2.6 [-0.8, 5.9]	0.090
>= 65 years	143	12 (8.4) [4.4, 14.2]	135	9 (6.7) [3.1, 12.3]	1.259 [0.548, 2.891]	1.282 [0.522, 3.149]	1.7 [-5.2, 8.6]	0.587

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEVN_SSIB: Incidence of AESI dizziness - non-severe by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI dizziness - non-severe	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
B: Sex								0.881
Male	247	15 (6.1) [3.4, 9.8]	257	9 (3.5) [1.6, 6.5]	1.734 [0.773, 3.889]	1.782 [0.765, 4.150]	2.6 [-1.6, 6.7]	0.176
Female	177	10 (5.6) [2.7, 10.1]	167	6 (3.6) [1.3, 7.7]	1.573 [0.584, 4.231]	1.607 [0.571, 4.523]	2.1 [-2.9, 7.1]	0.366

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEVN_SSIC: Incidence of AESI dizziness - non-severe by race
SAF-S

	CR845		Placebo						
AESI dizziness - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
C: Race								0.228	
Black/African American	135	13 (9.6) [5.2, 15.9]	113	3 (2.7) [0.6, 7.6]	3.627 [1.060, 12.413]	3.907 [1.085, 14.074]	7.0 [0.4, 13.6]	0.026	*
White	253	9 (3.6) [1.6, 6.6]	262	9 (3.4) [1.6, 6.4]	1.036 [0.418, 2.567]	1.037 [0.405, 2.656]	0.1 [-3.4, 3.7]	0.940	
Other	35	2 (5.7) [0.7, 19.2]	47	3 (6.4) [1.3, 17.5]	0.895 [0.158, 5.074]	0.889 [0.140, 5.626]	-0.7 [-13.6, 12.2]	1.000	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEVN_SSID: Incidence of AESI dizziness - non-severe by baseline WI-NRS
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI dizziness - non-severe	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)								0.299
>= 4 to < 7	184	12 (6.5) [3.4, 11.1]	192	5 (2.6) [0.9, 6.0]	2.504 [0.900, 6.969]	2.609 [0.901, 7.559]	3.9 [-0.8, 8.7]	0.068
>= 7	240	13 (5.4) [2.9, 9.1]	232	10 (4.3) [2.1, 7.8]	1.257 [0.562, 2.809]	1.271 [0.546, 2.959]	1.1 [-3.2, 5.4]	0.577

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEVN_SSIE: Incidence of AESI dizziness - non-severe by specific medical condition
SAF-S

	CR845		Placebo						
AESI dizziness - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
E: Presence of specific medical conditions								0.100	
No	358	22 (6.1) [3.9, 9.2]	359	10 (2.8) [1.3, 5.1]	2.206 [1.060, 4.592]	2.285 [1.066, 4.898]	3.4 [0.1, 6.7]	0.029	*
Yes	66	3 (4.5) [0.9, 12.7]	65	5 (7.7) [2.5, 17.0]	0.591 [0.147, 2.372]	0.571 [0.131, 2.496]	-3.1 [-12.9, 6.6]	0.492	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEVN_SSIF: Incidence of AESI dizziness - non-severe by use of concomitant itch medication
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI dizziness - non-severe	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
F: Use of concomitant itch medication								0.691
No	265	12 (4.5) [2.4, 7.8]	261	8 (3.1) [1.3, 5.9]	1.477 [0.614, 3.555]	1.500 [0.603, 3.732]	1.5 [-2.2, 5.1]	0.381
Yes	159	13 (8.2) [4.4, 13.6]	163	7 (4.3) [1.7, 8.6]	1.904 [0.780, 4.648]	1.984 [0.770, 5.111]	3.9 [-2.0, 9.8]	0.150

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEO_SSIA: Incidence of AESI somnolence by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI somnolence	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
A: Age								0.322
< 65 years	281	8 (2.8) [1.2, 5.5]	289	6 (2.1) [0.8, 4.5]	1.371 [0.482, 3.902]	1.382 [0.473, 4.036]	0.8 [-2.1, 3.7]	0.553
>= 65 years	143	10 (7.0) [3.4, 12.5]	135	3 (2.2) [0.5, 6.4]	3.147 [0.885, 11.190]	3.308 [0.890, 12.292]	4.8 [-0.8, 10.4]	0.060

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEO_SSIB: Incidence of AESI somnolence by sex
SAF-S

	CR845		Placebo					
AESI somnolence	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
B: Sex								0.689
Male	247	11 (4.5) [2.2, 7.8]	257	5 (1.9) [0.6, 4.5]	2.289 [0.807, 6.493]	2.349 [0.804, 6.862]	2.5 [-1.0, 6.0]	0.109
Female	177	7 (4.0) [1.6, 8.0]	167	4 (2.4) [0.7, 6.0]	1.651 [0.492, 5.538]	1.678 [0.482, 5.840]	1.6 [-2.7, 5.8]	0.412

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEO_SSIC: Incidence of AESI somnolence by race
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI somnolence	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
C: Race								0.399
Black/African American	135	5 (3.7) [1.2, 8.4]	113	4 (3.5) [1.0, 8.8]	1.046 [0.288, 3.804]	1.048 [0.275, 3.999]	0.2 [-5.3, 5.6]	1.000 #
White	253	9 (3.6) [1.6, 6.6]	262	4 (1.5) [0.4, 3.9]	2.330 [0.727, 7.470]	2.379 [0.723, 7.826]	2.0 [-1.1, 5.1]	0.142
Other	35	4 (11.4) [3.2, 26.7]	47	1 (2.1) [0.1, 11.3]	5.371 [0.627, 45.983]	5.935 [0.633, 55.650]	9.3 [-4.5, 23.1]	0.158 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEO_SSID: Incidence of AESI somnolence by baseline WI-NRS
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI somnolence	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)								0.230
>= 4 to < 7	184	8 (4.3) [1.9, 8.4]	192	2 (1.0) [0.1, 3.7]	4.174 [0.898, 19.396]	4.318 [0.905, 20.611]	3.3 [-0.5, 7.1]	0.057 #
>= 7	240	10 (4.2) [2.0, 7.5]	232	7 (3.0) [1.2, 6.1]	1.381 [0.535, 3.567]	1.398 [0.523, 3.736]	1.1 [-2.6, 4.9]	0.503

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEO_SSIE: Incidence of AESI somnolence by specific medical condition
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI somnolence	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
E: Presence of specific medical conditions								0.514
No	358	14 (3.9) [2.2, 6.5]	359	6 (1.7) [0.6, 3.6]	2.340 [0.909, 6.021]	2.394 [0.910, 6.303]	2.2 [-0.4, 4.9]	0.069
Yes	66	4 (6.1) [1.7, 14.8]	65	3 (4.6) [1.0, 12.9]	1.313 [0.306, 5.639]	1.333 [0.286, 6.206]	1.4 [-7.8, 10.7]	1.000 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEO_SSIF: Incidence of AESI somnolence by use of concomitant itch medication
SAF-S

	CR845		Placebo					
AESI somnolence	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
F: Use of concomitant itch medication								0.100
No	265	8 (3.0) [1.3, 5.9]	261	7 (2.7) [1.1, 5.4]	1.126 [0.414, 3.059]	1.130 [0.404, 3.161]	0.3 [-2.9, 3.6]	0.817
Yes	159	10 (6.3) [3.1, 11.3]	163	2 (1.2) [0.1, 4.4]	5.126 [1.141, 23.027]	5.403 [1.165, 25.062]	5.1 [0.3, 9.8]	0.017 *

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEON_SSIA: Incidence of AESI somnolence - non-severe by age
SAF-S

	CR845		Placebo					
AESI somnolence - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
A: Age								0.322
< 65 years	281	8 (2.8) [1.2, 5.5]	289	6 (2.1) [0.8, 4.5]	1.371 [0.482, 3.902]	1.382 [0.473, 4.036]	0.8 [-2.1, 3.7]	0.553
>= 65 years	143	10 (7.0) [3.4, 12.5]	135	3 (2.2) [0.5, 6.4]	3.147 [0.885, 11.190]	3.308 [0.890, 12.292]	4.8 [-0.8, 10.4]	0.060

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEON_SSIB: Incidence of AESI somnolence - non-severe by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI somnolence - non-severe	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
B: Sex								0.689
Male	247	11 (4.5) [2.2, 7.8]	257	5 (1.9) [0.6, 4.5]	2.289 [0.807, 6.493]	2.349 [0.804, 6.862]	2.5 [-1.0, 6.0]	0.109
Female	177	7 (4.0) [1.6, 8.0]	167	4 (2.4) [0.7, 6.0]	1.651 [0.492, 5.538]	1.678 [0.482, 5.840]	1.6 [-2.7, 5.8]	0.412

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEON_SSIC: Incidence of AESI somnolence - non-severe by race
SAF-S

	CR845		Placebo					
AESI somnolence - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
C: Race								0.399
Black/African American	135	5 (3.7) [1.2, 8.4]	113	4 (3.5) [1.0, 8.8]	1.046 [0.288, 3.804]	1.048 [0.275, 3.999]	0.2 [-5.3, 5.6]	1.000 #
White	253	9 (3.6) [1.6, 6.6]	262	4 (1.5) [0.4, 3.9]	2.330 [0.727, 7.470]	2.379 [0.723, 7.826]	2.0 [-1.1, 5.1]	0.142
Other	35	4 (11.4) [3.2, 26.7]	47	1 (2.1) [0.1, 11.3]	5.371 [0.627, 45.983]	5.935 [0.633, 55.650]	9.3 [-4.5, 23.1]	0.158 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEON_SSID: Incidence of AESI somnolence - non-severe by baseline WI-NRS
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI somnolence - non-severe	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)								0.230
>= 4 to < 7	184	8 (4.3) [1.9, 8.4]	192	2 (1.0) [0.1, 3.7]	4.174 [0.898, 19.396]	4.318 [0.905, 20.611]	3.3 [-0.5, 7.1]	0.057 #
>= 7	240	10 (4.2) [2.0, 7.5]	232	7 (3.0) [1.2, 6.1]	1.381 [0.535, 3.567]	1.398 [0.523, 3.736]	1.1 [-2.6, 4.9]	0.503

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEON_SSIE: Incidence of AESI somnolence - non-severe by specific medical condition
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI somnolence - non-severe	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
E: Presence of specific medical conditions								0.514
No	358	14 (3.9) [2.2, 6.5]	359	6 (1.7) [0.6, 3.6]	2.340 [0.909, 6.021]	2.394 [0.910, 6.303]	2.2 [-0.4, 4.9]	0.069
Yes	66	4 (6.1) [1.7, 14.8]	65	3 (4.6) [1.0, 12.9]	1.313 [0.306, 5.639]	1.333 [0.286, 6.206]	1.4 [-7.8, 10.7]	1.000 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEON_SSIF: Incidence of AESI somnolence - non-severe by use of concomitant itch medication
SAF-S

	CR845		Placebo					
AESI somnolence - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
F: Use of concomitant itch medication								0.100
No	265	8 (3.0) [1.3, 5.9]	261	7 (2.7) [1.1, 5.4]	1.126 [0.414, 3.059]	1.130 [0.404, 3.161]	0.3 [-2.9, 3.6]	0.817
Yes	159	10 (6.3) [3.1, 11.3]	163	2 (1.2) [0.1, 4.4]	5.126 [1.141, 23.027]	5.403 [1.165, 25.062]	5.1 [0.3, 9.8]	0.017 *

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEM_SSIA: Incidence of AESI mental status change by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI mental status change	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
A: Age								0.622
< 65 years	281	8 (2.8) [1.2, 5.5]	289	7 (2.4) [1.0, 4.9]	1.175 [0.432, 3.198]	1.181 [0.422, 3.300]	0.4 [-2.6, 3.4]	0.752
>= 65 years	143	9 (6.3) [2.9, 11.6]	135	5 (3.7) [1.2, 8.4]	1.699 [0.584, 4.942]	1.746 [0.570, 5.350]	2.6 [-3.2, 8.4]	0.325

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEM_SSIB: Incidence of AESI mental status change by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI mental status change	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
B: Sex								0.414
Male	247	12 (4.9) [2.5, 8.3]	257	7 (2.7) [1.1, 5.5]	1.784 [0.714, 4.456]	1.824 [0.706, 4.711]	2.1 [-1.6, 5.9]	0.209
Female	177	5 (2.8) [0.9, 6.5]	167	5 (3.0) [1.0, 6.8]	0.944 [0.278, 3.200]	0.942 [0.268, 3.314]	-0.2 [-4.3, 4.0]	1.000 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEM_SSIC: Incidence of AESI mental status change by race
SAF-S

	CR845		Placebo					
AESI mental status change	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
C: Race								0.702
Black/African American	135	8 (5.9) [2.6, 11.3]	113	4 (3.5) [1.0, 8.8]	1.674 [0.518, 5.415]	1.717 [0.503, 5.856]	2.4 [-3.7, 8.4]	0.384
White	253	7 (2.8) [1.1, 5.6]	262	7 (2.7) [1.1, 5.4]	1.036 [0.368, 2.910]	1.037 [0.358, 2.999]	0.1 [-3.1, 3.3]	0.947
Other	35	2 (5.7) [0.7, 19.2]	47	1 (2.1) [0.1, 11.3]	2.686 [0.254, 28.451]	2.788 [0.243, 32.041]	3.6 [-7.6, 14.8]	0.573 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEM_SSID: Incidence of AESI mental status change by baseline WI-NRS
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI mental status change	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)								0.340
>= 4 to < 7	184	8 (4.3) [1.9, 8.4]	192	8 (4.2) [1.8, 8.0]	1.043 [0.400, 2.722]	1.045 [0.384, 2.846]	0.2 [-4.4, 4.8]	0.931
>= 7	240	9 (3.8) [1.7, 7.0]	232	4 (1.7) [0.5, 4.4]	2.175 [0.679, 6.965]	2.221 [0.674, 7.314]	2.0 [-1.3, 5.4]	0.179

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEM_SSIE: Incidence of AESI mental status change by specific medical condition
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI mental status change	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
E: Presence of specific medical conditions								0.193
No	358	12 (3.4) [1.7, 5.8]	359	11 (3.1) [1.5, 5.4]	1.094 [0.489, 2.447]	1.097 [0.478, 2.520]	0.3 [-2.6, 3.1]	0.827
Yes	66	5 (7.6) [2.5, 16.8]	65	1 (1.5) [0.0, 8.3]	4.924 [0.591, 41.006]	5.246 [0.596, 46.198]	6.0 [-2.5, 14.6]	0.208 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEM_SSIF: Incidence of AESI mental status change by use of concomitant itch medication
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI mental status change	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
F: Use of concomitant itch medication								0.338
No	265	10 (3.8) [1.8, 6.8]	261	9 (3.4) [1.6, 6.4]	1.094 [0.452, 2.649]	1.098 [0.439, 2.748]	0.3 [-3.2, 3.9]	0.842
Yes	159	7 (4.4) [1.8, 8.9]	163	3 (1.8) [0.4, 5.3]	2.392 [0.630, 9.087]	2.456 [0.624, 9.672]	2.6 [-1.9, 7.0]	0.214 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEMN_SSIA: Incidence of AESI mental status change - non-severe by age
SAF-S

AESI mental status change - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
A: Age								0.447
< 65 years	281	6 (2.1) [0.8, 4.6]	289	7 (2.4) [1.0, 4.9]	0.882 [0.300, 2.591]	0.879 [0.292, 2.648]	-0.3 [-3.1, 2.5]	0.819
>= 65 years	143	7 (4.9) [2.0, 9.8]	135	4 (3.0) [0.8, 7.4]	1.652 [0.495, 5.517]	1.686 [0.482, 5.893]	1.9 [-3.3, 7.2]	0.410

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEMN_SSIB: Incidence of AESI mental status change - non-severe by sex
SAF-S

AESI mental status change - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
B: Sex								0.409	
Male	247	10 (4.0) [2.0, 7.3]	257	7 (2.7) [1.1, 5.5]	1.486 [0.575, 3.843]	1.507 [0.564, 4.024]	1.3 [-2.2, 4.9]	0.411	
Female	177	3 (1.7) [0.4, 4.9]	167	4 (2.4) [0.7, 6.0]	0.708 [0.161, 3.115]	0.703 [0.155, 3.187]	-0.7 [-4.3, 2.9]	0.717	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEMN_SSIC: Incidence of AESI mental status change - non-severe by race
SAF-S

AESI mental status change - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
C: Race								0.701	
Black/African American	135	4 (3.0) [0.8, 7.4]	113	4 (3.5) [1.0, 8.8]	0.837 [0.214, 3.272]	0.832 [0.203, 3.405]	-0.6 [-5.8, 4.7]	1.000	#
White	253	7 (2.8) [1.1, 5.6]	262	6 (2.3) [0.8, 4.9]	1.208 [0.412, 3.546]	1.214 [0.402, 3.663]	0.5 [-2.6, 3.6]	0.731	
Other	35	2 (5.7) [0.7, 19.2]	47	1 (2.1) [0.1, 11.3]	2.686 [0.254, 28.451]	2.788 [0.243, 32.041]	3.6 [-7.6, 14.8]	0.573	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEMN_SSID: Incidence of AESI mental status change - non-severe by baseline WI-NRS
SAF-S

AESI mental status change - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
D: Baseline worst itching NRS score (WI-NRS)								0.221	
>= 4 to < 7	184	6 (3.3) [1.2, 7.0]	192	8 (4.2) [1.8, 8.0]	0.783 [0.277, 2.212]	0.775 [0.264, 2.279]	-0.9 [-5.3, 3.4]	0.643	
>= 7	240	7 (2.9) [1.2, 5.9]	232	3 (1.3) [0.3, 3.7]	2.256 [0.590, 8.618]	2.293 [0.586, 8.978]	1.6 [-1.4, 4.6]	0.339	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEMN_SSIE: Incidence of AESI mental status change - non-severe by specific medical condition
SAF-S

AESI mental status change - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
E: Presence of specific medical conditions								0.217	
No	358	9 (2.5) [1.2, 4.7]	359	10 (2.8) [1.3, 5.1]	0.903 [0.371, 2.195]	0.900 [0.361, 2.242]	-0.3 [-2.9, 2.4]	0.821	
Yes	66	4 (6.1) [1.7, 14.8]	65	1 (1.5) [0.0, 8.3]	3.939 [0.452, 34.309]	4.129 [0.449, 37.978]	4.5 [-3.5, 12.5]	0.365	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEMN_SSIF: Incidence of AESI mental status change - non-severe by use of concomitant itch medication
SAF-S

AESI mental status change - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
F: Use of concomitant itch medication								0.528	
No	265	8 (3.0) [1.3, 5.9]	261	8 (3.1) [1.3, 5.9]	0.985 [0.375, 2.585]	0.984 [0.364, 2.663]	-0.0 [-3.4, 3.3]	0.975	
Yes	159	5 (3.1) [1.0, 7.2]	163	3 (1.8) [0.4, 5.3]	1.709 [0.415, 7.030]	1.732 [0.407, 7.370]	1.3 [-2.7, 5.3]	0.498	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEE_SSIA: Incidence of AESI mood change by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI mood change	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
A: Age		n<10 for all subgroups						NE
< 65 years	281	6 (2.1) [0.8, 4.6]	289	2 (0.7) [0.1, 2.5]				
>= 65 years	143	2 (1.4) [0.2, 5.0]	135	3 (2.2) [0.5, 6.4]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEE_SSIB: Incidence of AESI mood change by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI mood change	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
B: Sex		n<10 for all subgroups						NE
Male	247	4 (1.6) [0.4, 4.1]	257	1 (0.4) [0.0, 2.1]				
Female	177	4 (2.3) [0.6, 5.7]	167	4 (2.4) [0.7, 6.0]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEE_SSIC: Incidence of AESI mood change by race
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI mood change	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
C: Race		n<10 for all subgroups						NE
Black/African American	135	2 (1.5) [0.2, 5.2]	113	0 (0.0) [0.0, 3.2]				
White	253	5 (2.0) [0.6, 4.6]	262	4 (1.5) [0.4, 3.9]				
Other	35	1 (2.9) [0.1, 14.9]	47	1 (2.1) [0.1, 11.3]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEE_SSID: Incidence of AESI mood change by baseline WI-NRS
SAF-S

	CR845		Placebo					
AESI mood change	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)		n<10 for all subgroups						NE
>= 4 to < 7	184	3 (1.6) [0.3, 4.7]	192	3 (1.6) [0.3, 4.5]				
>= 7	240	5 (2.1) [0.7, 4.8]	232	2 (0.9) [0.1, 3.1]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEE_SSIE: Incidence of AESI mood change by specific medical condition
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI mood change	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
E: Presence of specific medical conditions		n<10 for all subgroups						NE
No	358	6 (1.7) [0.6, 3.6]	359	3 (0.8) [0.2, 2.4]				
Yes	66	2 (3.0) [0.4, 10.5]	65	2 (3.1) [0.4, 10.7]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEE_SSIF: Incidence of AESI mood change by use of concomitant itch medication
SAF-S

	CR845		Placebo					
AESI mood change	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
F: Use of concomitant itch medication		n<10 for all subgroups						NE
No	265	4 (1.5) [0.4, 3.8]	261	4 (1.5) [0.4, 3.9]				
Yes	159	4 (2.5) [0.7, 6.3]	163	1 (0.6) [0.0, 3.4]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEEN_SSIA: Incidence of AESI mood change - non-severe by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI mood change - non-severe	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
A: Age		n<10 for all subgroups						NE
< 65 years	281	6 (2.1) [0.8, 4.6]	289	2 (0.7) [0.1, 2.5]				
>= 65 years	143	2 (1.4) [0.2, 5.0]	135	3 (2.2) [0.5, 6.4]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEEN_SSIB: Incidence of AESI mood change - non-severe by sex
SAF-S

	CR845		Placebo					
AESI mood change - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
B: Sex		n<10 for all subgroups						NE
Male	247	4 (1.6) [0.4, 4.1]	257	1 (0.4) [0.0, 2.1]				
Female	177	4 (2.3) [0.6, 5.7]	167	4 (2.4) [0.7, 6.0]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEEN_SSIC: Incidence of AESI mood change - non-severe by race
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI mood change - non-severe	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
C: Race		n<10 for all subgroups						NE
Black/African American	135	2 (1.5) [0.2, 5.2]	113	0 (0.0) [0.0, 3.2]				
White	253	5 (2.0) [0.6, 4.6]	262	4 (1.5) [0.4, 3.9]				
Other	35	1 (2.9) [0.1, 14.9]	47	1 (2.1) [0.1, 11.3]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEEN_SSID: Incidence of AESI mood change - non-severe by baseline WI-NRS
SAF-S

	CR845		Placebo					
AESI mood change - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)		n<10 for all subgroups						NE
>= 4 to < 7	184	3 (1.6) [0.3, 4.7]	192	3 (1.6) [0.3, 4.5]				
>= 7	240	5 (2.1) [0.7, 4.8]	232	2 (0.9) [0.1, 3.1]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEEN_SSIE: Incidence of AESI mood change - non-severe by specific medical condition
SAF-S

	CR845		Placebo					
AESI mood change - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
E: Presence of specific medical conditions		n<10 for all subgroups						NE
No	358	6 (1.7) [0.6, 3.6]	359	3 (0.8) [0.2, 2.4]				
Yes	66	2 (3.0) [0.4, 10.5]	65	2 (3.1) [0.4, 10.7]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEEN_SSIF: Incidence of AESI mood change - non-severe by use of concomitant itch medication
SAF-S

	CR845		Placebo					
AESI mood change - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
F: Use of concomitant itch medication		n<10 for all subgroups						NE
No	265	4 (1.5) [0.4, 3.8]	261	4 (1.5) [0.4, 3.9]				
Yes	159	4 (2.5) [0.7, 6.3]	163	1 (0.6) [0.0, 3.4]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEU_SSIA: Incidence of AESI unusual feeling/sensation by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI unusual feeling/sensation	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
A: Age								0.314
< 65 years	281	10 (3.6) [1.7, 6.4]	289	6 (2.1) [0.8, 4.5]	1.714 [0.631, 4.653]	1.740 [0.624, 4.854]	1.5 [-1.6, 4.6]	0.284
>= 65 years	143	6 (4.2) [1.6, 8.9]	135	7 (5.2) [2.1, 10.4]	0.809 [0.279, 2.347]	0.801 [0.262, 2.446]	-1.0 [-6.7, 4.7]	0.697

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEU_SSIB: Incidence of AESI unusual feeling/sensation by sex
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI unusual feeling/sensation	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
B: Sex								0.791
Male	247	9 (3.6) [1.7, 6.8]	257	7 (2.7) [1.1, 5.5]	1.338 [0.506, 3.537]	1.351 [0.495, 3.684]	0.9 [-2.5, 4.4]	0.556
Female	177	7 (4.0) [1.6, 8.0]	167	6 (3.6) [1.3, 7.7]	1.101 [0.378, 3.208]	1.105 [0.364, 3.358]	0.4 [-4.2, 5.0]	0.861

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEU_SSIC: Incidence of AESI unusual feeling/sensation by race
SAF-S

	CR845		Placebo					
AESI unusual feeling/sensation	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
C: Race								0.679
Black/African American	135	8 (5.9) [2.6, 11.3]	113	4 (3.5) [1.0, 8.8]	1.674 [0.518, 5.415]	1.717 [0.503, 5.856]	2.4 [-3.7, 8.4]	0.384
White	253	8 (3.2) [1.4, 6.1]	262	8 (3.1) [1.3, 5.9]	1.036 [0.395, 2.717]	1.037 [0.383, 2.806]	0.1 [-3.3, 3.5]	0.943
Other	35	0 (0.0) [0.0, 10.0]	47	1 (2.1) [0.1, 11.3]	0.444 + [0.019, 10.595]	0.437 + [0.017, 11.041]	-2.1 [-8.7, 4.5]	1.000 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEU_SSID: Incidence of AESI unusual feeling/sensation by baseline WI-NRS
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI unusual feeling/sensation	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)								0.901
>= 4 to < 7	184	5 (2.7) [0.9, 6.2]	192	4 (2.1) [0.6, 5.2]	1.304 [0.356, 4.782]	1.313 [0.347, 4.967]	0.6 [-3.0, 4.3]	0.746 #
>= 7	240	11 (4.6) [2.3, 8.1]	232	9 (3.9) [1.8, 7.2]	1.181 [0.499, 2.798]	1.190 [0.484, 2.928]	0.7 [-3.3, 4.8]	0.705

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEU_SSIE: Incidence of AESI unusual feeling/sensation by specific medical condition
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI unusual feeling/sensation	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
E: Presence of specific medical conditions								0.329
No	358	11 (3.1) [1.5, 5.4]	359	11 (3.1) [1.5, 5.4]	1.003 [0.440, 2.283]	1.003 [0.429, 2.344]	0.0 [-2.8, 2.8]	0.995
Yes	66	5 (7.6) [2.5, 16.8]	65	2 (3.1) [0.4, 10.7]	2.462 [0.495, 12.240]	2.582 [0.483, 13.815]	4.5 [-4.7, 13.7]	0.440 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEU_SSIF: Incidence of AESI unusual feeling/sensation by use of concomitant itch medication
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI unusual feeling/sensation	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
F: Use of concomitant itch medication								0.729
No	265	9 (3.4) [1.6, 6.3]	261	8 (3.1) [1.3, 5.9]	1.108 [0.434, 2.828]	1.112 [0.422, 2.927]	0.3 [-3.1, 3.7]	0.830
Yes	159	7 (4.4) [1.8, 8.9]	163	5 (3.1) [1.0, 7.0]	1.435 [0.465, 4.428]	1.455 [0.452, 4.684]	1.3 [-3.4, 6.1]	0.528

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEUN_SSIA: Incidence of AESI unusual feeling/sensation - non-severe by age
SAF-S

AESI unusual feeling/sensation - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
A: Age								0.391
< 65 years	281	9 (3.2) [1.5, 6.0]	289	6 (2.1) [0.8, 4.5]	1.543 [0.556, 4.278]	1.561 [0.548, 4.443]	1.1 [-1.9, 4.1]	0.401
>= 65 years	143	6 (4.2) [1.6, 8.9]	135	7 (5.2) [2.1, 10.4]	0.809 [0.279, 2.347]	0.801 [0.262, 2.446]	-1.0 [-6.7, 4.7]	0.697

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEUN_SSIB: Incidence of AESI unusual feeling/sensation - non-severe by sex
SAF-S

AESI unusual feeling/sensation - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
B: Sex								0.918
Male	247	8 (3.2) [1.4, 6.3]	257	7 (2.7) [1.1, 5.5]	1.189 [0.438, 3.230]	1.195 [0.427, 3.348]	0.5 [-2.9, 3.9]	0.734
Female	177	7 (4.0) [1.6, 8.0]	167	6 (3.6) [1.3, 7.7]	1.101 [0.378, 3.208]	1.105 [0.364, 3.358]	0.4 [-4.2, 5.0]	0.861

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEUN_SSIC: Incidence of AESI unusual feeling/sensation - non-severe by race
SAF-S

AESI unusual feeling/sensation - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
C: Race								0.762	
Black/African American	135	7 (5.2) [2.1, 10.4]	113	4 (3.5) [1.0, 8.8]	1.465 [0.440, 4.877]	1.490 [0.425, 5.226]	1.6 [-4.2, 7.5]	0.532	
White	253	8 (3.2) [1.4, 6.1]	262	8 (3.1) [1.3, 5.9]	1.036 [0.395, 2.717]	1.037 [0.383, 2.806]	0.1 [-3.3, 3.5]	0.943	
Other	35	0 (0.0) [0.0, 10.0]	47	1 (2.1) [0.1, 11.3]	0.444 + [0.019, 10.595]	0.437 + [0.017, 11.041]	-2.1 [-8.7, 4.5]	1.000	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEUN_SSID: Incidence of AESI unusual feeling/sensation - non-severe by baseline WI-NRS
SAF-S

AESI unusual feeling/sensation - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
D: Baseline worst itching NRS score (WI-NRS)								0.808	
>= 4 to < 7	184	5 (2.7) [0.9, 6.2]	192	4 (2.1) [0.6, 5.2]	1.304 [0.356, 4.782]	1.313 [0.347, 4.967]	0.6 [-3.0, 4.3]	0.746	#
>= 7	240	10 (4.2) [2.0, 7.5]	232	9 (3.9) [1.8, 7.2]	1.074 [0.444, 2.595]	1.077 [0.430, 2.701]	0.3 [-3.7, 4.3]	0.874	

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEUN_SSIE: Incidence of AESI unusual feeling/sensation - non-severe by specific medical condition
SAF-S

AESI unusual feeling/sensation - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
E: Presence of specific medical conditions								0.283	
No	358	10 (2.8) [1.3, 5.1]	359	11 (3.1) [1.5, 5.4]	0.912 [0.392, 2.120]	0.909 [0.381, 2.168]	-0.3 [-3.0, 2.5]	0.830	
Yes	66	5 (7.6) [2.5, 16.8]	65	2 (3.1) [0.4, 10.7]	2.462 [0.495, 12.240]	2.582 [0.483, 13.815]	4.5 [-4.7, 13.7]	0.440	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AEUN_SSIF: Incidence of AESI unusual feeling/sensation - non-severe by use of concomitant itch medication
SAF-S

AESI unusual feeling/sensation - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
F: Use of concomitant itch medication								0.619
No	265	8 (3.0) [1.3, 5.9]	261	8 (3.1) [1.3, 5.9]	0.985 [0.375, 2.585]	0.984 [0.364, 2.663]	-0.0 [-3.4, 3.3]	0.975
Yes	159	7 (4.4) [1.8, 8.9]	163	5 (3.1) [1.0, 7.0]	1.435 [0.465, 4.428]	1.455 [0.452, 4.684]	1.3 [-3.4, 6.1]	0.528

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AER_SSIA: Incidence of AESI tachycardia/palpitation by age
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI tachycardia/palpitation	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
A: Age								0.352
< 65 years	281	4 (1.4) [0.4, 3.6]	289	8 (2.8) [1.2, 5.4]	0.514 [0.157, 1.689]	0.507 [0.151, 1.704]	-1.3 [-4.0, 1.4]	0.264
>= 65 years	143	3 (2.1) [0.4, 6.0]	135	2 (1.5) [0.2, 5.2]	1.416 [0.240, 8.344]	1.425 [0.234, 8.663]	0.6 [-3.2, 4.4]	1.000 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AER_SSIB: Incidence of AESI tachycardia/palpitation by sex
SAF-S

	CR845		Placebo					
AESI tachycardia/palpitation	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
B: Sex		n<10 for all subgroups						NE
Male	247	4 (1.6) [0.4, 4.1]	257	4 (1.6) [0.4, 3.9]				
Female	177	3 (1.7) [0.4, 4.9]	167	6 (3.6) [1.3, 7.7]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AER_SSIC: Incidence of AESI tachycardia/palpitation by race
SAF-S

	CR845		Placebo						
AESI tachycardia/palpitation	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
C: Race								0.720	
Black/African American	135	2 (1.5) [0.2, 5.2]	113	1 (0.9) [0.0, 4.8]	1.674 [0.154, 18.223]	1.684 [0.151, 18.819]	0.6 [-2.9, 4.1]	1.000	#
White	253	4 (1.6) [0.4, 4.0]	262	6 (2.3) [0.8, 4.9]	0.690 [0.197, 2.418]	0.685 [0.191, 2.458]	-0.7 [-3.5, 2.1]	0.752	#
Other	35	1 (2.9) [0.1, 14.9]	47	3 (6.4) [1.3, 17.5]	0.448 [0.049, 4.123]	0.431 [0.043, 4.333]	-3.5 [-14.9, 7.9]	0.632	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AER_SSID: Incidence of AESI tachycardia/palpitation by baseline WI-NRS
SAF-S

	CR845		Placebo					
AESI tachycardia/palpitation	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)		n<10 for all subgroups						NE
>= 4 to < 7	184	4 (2.2) [0.6, 5.5]	192	5 (2.6) [0.9, 6.0]				
>= 7	240	3 (1.3) [0.3, 3.6]	232	5 (2.2) [0.7, 5.0]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AER_SSIE: Incidence of AESI tachycardia/palpitation by specific medical condition
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI tachycardia/palpitation	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
E: Presence of specific medical conditions								0.749
No	358	6 (1.7) [0.6, 3.6]	359	8 (2.2) [1.0, 4.3]	0.752 [0.264, 2.146]	0.748 [0.257, 2.178]	-0.6 [-2.9, 1.8]	0.593
Yes	66	1 (1.5) [0.0, 8.2]	65	2 (3.1) [0.4, 10.7]	0.492 [0.046, 5.299]	0.485 [0.043, 5.479]	-1.6 [-8.2, 5.1]	0.619 #

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AER_SSIF: Incidence of AESI tachycardia/palpitation by use of concomitant itch medication
SAF-S

	CR845		Placebo					
		n (%)		n (%)	RR	OR	RD	
AESI tachycardia/palpitation	N	[95 % CI]	N	[95 % CI]	[95 % CI]	[95 % CI]	[95 % CI]	p-value
F: Use of concomitant itch medication		n<10 for all subgroups						NE
No	265	3 (1.1) [0.2, 3.3]	261	6 (2.3) [0.8, 4.9]				
Yes	159	4 (2.5) [0.7, 6.3]	163	4 (2.5) [0.7, 6.2]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AERN_SSIA: Incidence of AESI tachycardia/palpitation - non-severe by age
SAF-S

AESI tachycardia/palpitation - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
A: Age								0.352	
< 65 years	281	4 (1.4) [0.4, 3.6]	289	8 (2.8) [1.2, 5.4]	0.514 [0.157, 1.689]	0.507 [0.151, 1.704]	-1.3 [-4.0, 1.4]	0.264	
>= 65 years	143	3 (2.1) [0.4, 6.0]	135	2 (1.5) [0.2, 5.2]	1.416 [0.240, 8.344]	1.425 [0.234, 8.663]	0.6 [-3.2, 4.4]	1.000	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AERN_SSIB: Incidence of AESI tachycardia/palpitation - non-severe by sex
SAF-S

AESI tachycardia/palpitation - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
B: Sex		n<10 for all subgroups						NE
Male	247	4 (1.6) [0.4, 4.1]	257	4 (1.6) [0.4, 3.9]				
Female	177	3 (1.7) [0.4, 4.9]	167	6 (3.6) [1.3, 7.7]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AERN_SSIC: Incidence of AESI tachycardia/palpitation - non-severe by race
SAF-S

	CR845		Placebo						
AESI tachycardia/palpitation - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
C: Race								0.720	
Black/African American	135	2 (1.5) [0.2, 5.2]	113	1 (0.9) [0.0, 4.8]	1.674 [0.154, 18.223]	1.684 [0.151, 18.819]	0.6 [-2.9, 4.1]	1.000	#
White	253	4 (1.6) [0.4, 4.0]	262	6 (2.3) [0.8, 4.9]	0.690 [0.197, 2.418]	0.685 [0.191, 2.458]	-0.7 [-3.5, 2.1]	0.752	#
Other	35	1 (2.9) [0.1, 14.9]	47	3 (6.4) [1.3, 17.5]	0.448 [0.049, 4.123]	0.431 [0.043, 4.333]	-3.5 [-14.9, 7.9]	0.632	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AERN_SSID: Incidence of AESI tachycardia/palpitation - non-severe by baseline WI-NRS
SAF-S

AESI tachycardia/palpitation - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
D: Baseline worst itching NRS score (WI-NRS)		n<10 for all subgroups						NE
>= 4 to < 7	184	4 (2.2) [0.6, 5.5]	192	5 (2.6) [0.9, 6.0]				
>= 7	240	3 (1.3) [0.3, 3.6]	232	5 (2.2) [0.7, 5.0]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AERN_SSIE: Incidence of AESI tachycardia/palpitation - non-severe by specific medical condition
SAF-S

AESI tachycardia/palpitation - non-severe	CR845 N	CR845 n (%) [95 % CI]	Placebo N	Placebo n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value	
E: Presence of specific medical conditions								0.749	
No	358	6 (1.7) [0.6, 3.6]	359	8 (2.2) [1.0, 4.3]	0.752 [0.264, 2.146]	0.748 [0.257, 2.178]	-0.6 [-2.9, 1.8]	0.593	
Yes	66	1 (1.5) [0.0, 8.2]	65	2 (3.1) [0.4, 10.7]	0.492 [0.046, 5.299]	0.485 [0.043, 5.479]	-1.6 [-8.2, 5.1]	0.619	#

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022

Table IT2AERN_SSIF: Incidence of AESI tachycardia/palpitation - non-severe by use of concomitant itch medication
SAF-S

	CR845		Placebo					
AESI tachycardia/palpitation - non-severe	N	n (%) [95 % CI]	N	n (%) [95 % CI]	RR [95 % CI]	OR [95 % CI]	RD [95 % CI]	p-value
F: Use of concomitant itch medication		n<10 for all subgroups						NE
No	265	3 (1.1) [0.2, 3.3]	261	6 (2.3) [0.8, 4.9]				
Yes	159	4 (2.5) [0.7, 6.3]	163	4 (2.5) [0.7, 6.2]				

Note: SAF-S = Week 12 Safety Set.
N = total number of patients in analysis set. n = number of patients with events during double blind treatment period.
95% CI = 95% confidence interval (percentages: Clopper-Pearson, RR/OR: Wald, RD: Newcombe method).
p-value = Cochran Q test for heterogeneity / Chi-square test, a # indicates that exact test of Fisher was used instead. * = significant treatment effect. i = significant Cochran Q.
AESI = adverse event of special interest. RR = relative risk. OR = odds ratio. RD = risk difference. + = adding of 0.5 to each cell. NE = not evaluable. Cochran Q test is only performed if there are at least 10 patients with events in a subgroup.
Source Data: aae_i, created on: 17FEB2022