

7. Appendix – Analysis results

7.1 Demography and baseline characteristics

Table 14.1.1: Disposition
Population: Randomised

	Arm	
	A (Experimental) N=99	B (Control) N=101
Number of subjects randomized	99 (100.0%)	101 (100.0%)
Number of subjects in treatment phase	99 (100.0%)	101 (100.0%)
Number of subjects completing the study	87 (87.9%)	91 (90.1%)
Number of subjects withdrawn from the study	11 (11.1%)	10 (9.9%)
Reason for premature discontinuation:		
Other	8 (8.1%)	6 (5.9%)
side effects	3* (3.0%)	0 (0.0%)
withdrawn informed consent	0 (0.0%)	4 (4.0%)

Note: Percentage based on number of randomized patients.

Other reason are: lost to follow-up, AF relapse, other diseases, refusing MRT

*2/3 of these patients had visits after discontinuation of study treatment (Switcher from Arm A to Arm B)

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Listing: Specification of other reasons for discontinuation
Population: Randomised

Arm	Site No.	Pat-ID	Specification for other reasons for discontinuation	ITT	PP
A (Experimental)	1	194	Studienabbruch bei Unverträglichkeit von Dabigatran.	yes	no
		208	Gesicherte Alzheimer-Krankheit mit spätem Beginn (R00.1/ G30.1 G)	yes	no
		8	53 Re-PVI	yes	no
		9	171 Hörsturz/Drehschwindel	yes	no
		199	Verärgerung wg. langer Wartezeit	yes	no
		13	44 2x täglich, regelmäßige Einnahme von Pradaxa ist nicht sicher gestellt.	yes	no
		73	Lost to follow up	yes	no
B (Control)	17	112	Pat. ist nicht bereit ins MRT zu gehen	yes	no
		1	4 MRT wurde abgebrochen	yes	no
		104	Patient wurde in den Kontrollarm randomisiert (kein Verzicht auf OAK seitens des Pat.) am 30.09.2017 Einverständniserklärung zurückgezogen.	yes	no
		5	67 Patient nicht mehr zu Visiten erschienen, keine Reaktion auf zahlreiche Anrufe und einen Brief	yes	no
		7	41 Rezidiv VHF	yes	no
		13	231 einmaliges VHF-Rezidiv	yes	no
	18	160	Rezidiv Vorhofflattern	yes	no

Table 14.1.1-2: Study population by site
Population: Randomised

Site	Population	Arm	
		A (Experimental) N=99	B (Control) N=101
Total	Randomized	99	101
	Safety	99	101
	ITT	99	101
	PP	82	87
01	Randomized	25	23
	Safety	25	23
	ITT	25	23
	PP	22	20
05	Randomized	7	9
	Safety	7	9
	ITT	7	9
	PP	6	6
07	Randomized	3	3
	Safety	3	3
	ITT	3	3
	PP	3	2
08	Randomized	6	6
	Safety	6	6

Site	Population	Arm	
		A (Experimental) N=99	B (Control) N=101
09	ITT	6	6
	PP	3	6
	Randomized	11	11
	Safety	11	11
	ITT	11	11
10	PP	9	9
	Randomized	2	1
	Safety	2	1
	ITT	2	1
	PP	1	1
11	Randomized	3	2
	Safety	3	2
	ITT	3	2
	PP	3	2
	Randomized	3	5
12	Safety	3	5
	ITT	3	5
	PP	2	5
	Randomized	16	17
	Safety	16	17

Site	Population	Arm	
		A (Experimental) N=99	B (Control) N=101
14	ITT	16	17
	PP	13	14
	Randomized	2	1
	Safety	2	1
	ITT	2	1
15	PP	2	1
	Randomized	0	2
	Safety	0	2
	ITT	0	2
	PP	0	2
16	Randomized	2	4
	Safety	2	4
	ITT	2	4
	PP	1	4
	Randomized	7	8
17	Safety	7	8
	ITT	7	8
	PP	6	8
	Randomized	2	3
	Safety	2	3

Site	Population	Arm	
		A (Experimental) N=99	B (Control) N=101
19	ITT	2	3
	PP	2	2
	Randomized	1	1
	Safety	1	1
	ITT	1	1
20	PP	1	1
	Randomized	3	1
	Safety	3	1
	ITT	3	1
	PP	3	0
21	Randomized	3	3
	Safety	3	3
	ITT	3	3
	PP	3	3
	Randomized	3	1
22	Safety	3	1
	ITT	3	1
	PP	2	1
	ITT	3	1

		Arm	
		A (Experimental)	B (Control)
Site	Population	N=99	N=101
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Safety population not involved treatment switcher. Including switchers mean: A – N=107, B – N=93			
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Table 14.1.2: Demography - quantitative parameter - ITT Population
Population: ITT

Variable	Arm	n	Mean	S.D.	Median	Range	95%-CI	P-value*
Age (years)								
	A (Experimental)	99	67.3	7.2	67.0	47- 81	(65.81 ; 68.69)	0.8629
	B (Control)	101	67.1	7.7	67.0	43- 82	(65.54 ; 68.60)	
	Total	200	67.2	7.5	67.0	43- 82	(66.12 ; 68.20)	
Height (cm)								
	A (Experimental)	99	173.5	9.1	173.0	** -192	(171.70 ; 175.32)	0.7665
	B (Control)	101	173.1	8.3	174.0	** -192	(171.49 ; 174.79)	
	Total	200	173.3	8.7	173.5	** -192	(172.11 ; 174.53)	
Weight (kg)								
	A (Experimental)	98	86.4	18.9	85.0	51-137	(82.65 ; 90.22)	0.2098
	B (Control)	101	89.7	17.3	88.0	50-138	(86.25 ; 93.07)	
	Total	199	88.1	18.1	87.0	50-138	(85.54 ; 90.60)	
BMI (kg/m^2)								
	A (Experimental)	98	28.7	6.1	27.4	19- 52	(27.49 ; 29.94)	0.1600
	B (Control)	101	29.8	4.8	29.8	19- 42	(28.86 ; 30.76)	

<i>Variable</i>	<i>Arm</i>	<i>n</i>	<i>Mean</i>	<i>S.D.</i>	<i>Median</i>	<i>Range</i>	<i>95%-CI</i>	<i>P-value*</i>
	Total	199	29.3	5.5	29.0	19- 52	(28.50 ; 30.04)	

*by Student's t-test
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Table 14.1.3: Demography - qualitative parameter - ITT Population
Population: ITT

Parameter - n (%)		Arm		Total N=200	p-Value*
		A (Experimental) N=99	B (Control) N=101		
Sex	male	56 (56.6%)	56 (55.4%)	112 (56.0%)	0.8876
	female	43 (43.4%)	45 (44.6%)	88 (44.0%)	
Cardinal point	NORDEN	9 (9.1%)	7 (6.9%)	16 (8.0%)	.
	OSTEN	16 (16.2%)	17 (16.8%)	33 (16.5%)	
	SÜDEN	34 (34.3%)	36 (35.6%)	70 (35.0%)	
	WESTEN	40 (40.4%)	41 (40.6%)	81 (40.5%)	
	Nordrhein-Westfalen	40 (40.4%)	41 (40.6%)	81 (40.5%)	
Federated state	Baden Württemberg	25 (25.3%)	28 (27.7%)	53 (26.5%)	.
	Rheinland-Pfalz	3 (3.0%)	2 (2.0%)	5 (2.5%)	
	Sachsen	16 (16.2%)	17 (16.8%)	33 (16.5%)	
	Bayern	6 (6.1%)	6 (5.9%)	12 (6.0%)	
	Niedersachsen	9 (9.1%)	7 (6.9%)	16 (8.0%)	

*by Fisher's exact test
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Table 14.1.4: Baseline characteristics - quantitative parameter - ITT Population
Population: ITT

Variable	Arm	n	Mean	S.D.	Median	Range	95%-CI	P-value*
CHA2DS2VASc Score								
	A (Experimental)	99	2.6	0.8	2.0	2- 5	(2.44 ; 2.77)	0.7346
	B (Control)	101	2.6	0.7	2.0	2- 4	(2.50 ; 2.79)	
						.		
	Total	200	2.6	0.8	2.0	2- 5	(2.52 ; 2.73)	
HAS-BLED-Score								
	A (Experimental)	59	1.3	0.7	1.0	0- 3	(1.15 ; 1.53)	0.2135
	B (Control)	58	1.5	0.7	2.0	0- 3	(1.33 ; 1.67)	
						.		
	Total	117	1.4	0.7	1.0	0- 3	(1.29 ; 1.55)	
ECG - Heart rate [bpm]								
	A (Experimental)	99	71.3	20.7	65.0	42-142	(67.18 ; 75.45)	0.6725
	B (Control)	100	70.0	22.7	63.5	39-180	(65.52 ; 74.50)	
						.		
	Total	199	70.7	21.7	65.0	39-180	(67.63 ; 73.69)	
TTE - LVEF [%]								
	A (Experimental)	80	58.0	9.4	60.0	10- 76	(55.87 ; 60.08)	0.8623

<i>Variable</i>	<i>Arm</i>	<i>n</i>	<i>Mean</i>	<i>S.D.</i>	<i>Median</i>	<i>Range</i>	<i>95%-CI</i>	<i>P-value*</i>
	B (Control)	84	57.7	8.6	60.0	35- 76	(55.86 ; 59.60)	
	Total	164	57.8	9.0	60.0	10- 76	(56.46 ; 59.24)	
TTE - Left atrial diameter [mm]								
	A (Experimental)	45	40.6	11.2	40.0	1- 74	(37.22 ; 43.94)	0.5000
	B (Control)	49	42.0	8.8	41.0	6- 67	(39.44 ; 44.52)	
	Total	94	41.3	10.0	41.0	1- 74	(39.26 ; 43.36)	
TTE - Left atrial volume [mL]								
	A (Experimental)	40	60.1	22.1	54.0	30-108	(53.01 ; 67.14)	0.2795
	B (Control)	43	66.5	31.4	65.0	16-156	(56.86 ; 76.21)	
	Total	83	63.4	27.4	60.0	16-156	(57.45 ; 69.40)	

*by Student's t-test

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Table 14.1.5: Baseline characteristics - qualitative parameter - ITT Population
Population: ITT

Parameter - n (%)		A (Experimental) N=99	B (Control) N=101	Total N=200	p-Value*
NYHA-class	missing	1 (1.0%)	2 (2.0%)	3 (1.5%)	0.6502
	I	18 (18.2%)	21 (20.8%)	39 (19.5%)	
	II	30 (30.3%)	30 (29.7%)	60 (30.0%)	
	III	13 (13.1%)	8 (7.9%)	21 (10.5%)	
	IV	0 (0.0%)	1 (1.0%)	1 (0.5%)	
	Not evaluated	37 (37.4%)	39 (38.6%)	76 (38.0%)	
EHRA-class	missing	4 (4.0%)	4 (4.0%)	8 (4.0%)	0.1048
	I	0 (0.0%)	6 (5.9%)	6 (3.0%)	
	II	30 (30.3%)	33 (32.7%)	63 (31.5%)	
	III	31 (31.3%)	33 (32.7%)	64 (32.0%)	
	IV	2 (2.0%)	1 (1.0%)	3 (1.5%)	
	Not evaluated	32 (32.3%)	24 (23.8%)	56 (28.0%)	
CHA2DS2VASc Score	2	58 (58.6%)	51 (50.5%)	109 (54.5%)	0.1551
	3	25 (25.3%)	35 (34.7%)	60 (30.0%)	
	4	13 (13.1%)	15 (14.9%)	28 (14.0%)	
	5	3 (3.0%)	0 (0.0%)	3 (1.5%)	
HAS-BLED-Score	missing	40 (40.4%)	43 (42.6%)	83 (41.5%)	0.5401
	0	7 (7.1%)	3 (3.0%)	10 (5.0%)	
	1	27 (27.3%)	25 (24.8%)	52 (26.0%)	
	2	23 (23.2%)	28 (27.7%)	51 (25.5%)	
	3	2 (2.0%)	2 (2.0%)	4 (2.0%)	

<i>Parameter - n (%)</i>		<i>A (Experimental) N=99</i>	<i>B (Control) N=101</i>	<i>Total N=200</i>	<i>p-Value*</i>
ECG - rhythm	atrial fibrillation	26 (26.3%)	29 (28.7%)	55 (27.5%)	0.7460
	atrial fibrillation, other	1 (1.0%)	0 (0.0%)	1 (0.5%)	
	missing	2 (2.0%)	2 (2.0%)	4 (2.0%)	
	other	2 (2.0%)	1 (1.0%)	3 (1.5%)	
	pacemaker	1 (1.0%)	0 (0.0%)	1 (0.5%)	
	sinus rhythm	67 (67.7%)	68 (67.3%)	135 (67.5%)	
	sinus rhythm, other	0 (0.0%)	1 (1.0%)	1 (0.5%)	
TTE - Aortic valve stenosis	ND/NA	19 (19.2%)	19 (18.8%)	38 (19.0%)	0.7241
	none	77 (77.8%)	78 (77.2%)	155 (77.5%)	
	mild	3 (3.0%)	4 (4.0%)	7 (3.5%)	
TTE - Aortic valve insufficiency	ND/NA	19 (19.2%)	19 (18.8%)	38 (19.0%)	0.3955
	none	61 (61.6%)	68 (67.3%)	129 (64.5%)	
	mild	18 (18.2%)	14 (13.9%)	32 (16.0%)	
	moderate	1 (1.0%)	0 (0.0%)	1 (0.5%)	
TTE - Mitral valve insufficiency	ND/NA	19 (19.2%)	20 (19.8%)	39 (19.5%)	0.5751
	none	17 (17.2%)	23 (22.8%)	40 (20.0%)	
	mild	54 (54.5%)	50 (49.5%)	104 (52.0%)	
	moderate	9 (9.1%)	8 (7.9%)	17 (8.5%)	
TTE - Tricuspid valve insufficiency	ND/NA	19 (19.2%)	20 (19.8%)	39 (19.5%)	0.7656
	none	30 (30.3%)	30 (29.7%)	60 (30.0%)	
	mild	47 (47.5%)	46 (45.5%)	93 (46.5%)	
	moderate	3 (3.0%)	4 (4.0%)	7 (3.5%)	

<i>Parameter - n (%)</i>	<i>A (Experimental) N=99</i>	<i>B (Control) N=101</i>	<i>Total N=200</i>	<i>p-Value*</i>
severe	0 (0.0%)	1 (1.0%)	1 (0.5%)	

*by Chi square test

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Table: Selected anamnestic data - qualitative parameter - ITT Population
Population: ITT

Parameter - n (%)		A (Experimental) N=99	B (Control) N=101	Total N=200	p-Value*
Arterial hypertension	no	13 (13.1%)	12 (11.9%)	25 (12.5%)	0.8332
	yes	86 (86.9%)	89 (88.1%)	175 (87.5%)	
Coronary heart disease	no	83 (83.8%)	81 (80.2%)	164 (82.0%)	0.5821
	yes	16 (16.2%)	20 (19.8%)	36 (18.0%)	
CHD - if yes: specify	.	85 (85.9%)	81 (80.2%)	166 (83.0%)	.
	1-Gefäßerkrankung	7 (7.1%)	9 (8.9%)	16 (8.0%)	
	2-Gefäßerkrankung	5 (5.1%)	6 (5.9%)	11 (5.5%)	
	3-Gefäßerkrankung	2 (2.0%)	5 (5.0%)	7 (3.5%)	
Heart insufficiency	no	87 (87.9%)	90 (89.1%)	177 (88.5%)	0.8275
	yes	12 (12.1%)	11 (10.9%)	23 (11.5%)	
Pacemaker	no	96 (97.0%)	100 (99.0%)	196 (98.0%)	0.3662
	yes	3 (3.0%)	1 (1.0%)	4 (2.0%)	
PM - if yes - specify	.	96 (97.0%)	100 (99.0%)	196 (98.0%)	.
	2-Kammer	3 (3.0%)	1 (1.0%)	4 (2.0%)	
ICD	no	99 (100.0%)	101 (100.0%)	200 (100.0%)	0.3662
ICD - if yes - specify	.	99 (100.0%)	101 (100.0%)	200 (100.0%)	.
Peripheral arterial disease (pAVK)	no	95 (96.0%)	100 (99.0%)	195 (97.5%)	0.2094
	yes	4 (4.0%)	1 (1.0%)	5 (2.5%)	
COPD	no	89 (89.9%)	97 (96.0%)	186 (93.0%)	0.1030
	yes	10 (10.1%)	4 (4.0%)	14 (7.0%)	

<i>Parameter - n (%)</i>		<i>A (Experimental) N=99</i>	<i>B (Control) N=101</i>	<i>Total N=200</i>	<i>p-Value*</i>
OSAS	no	92 (92.9%)	93 (92.1%)	185 (92.5%)	1.0000
	yes	7 (7.1%)	8 (7.9%)	15 (7.5%)	
Diabetes mellitus	no	78 (78.8%)	81 (80.2%)	159 (79.5%)	0.8618
	yes	21 (21.2%)	20 (19.8%)	41 (20.5%)	
Diabetes - if yes - specify	.	78 (78.8%)	81 (80.2%)	159 (79.5%)	.
	nicht Insulin-abhängig	17 (17.2%)	15 (14.9%)	32 (16.0%)	
	Insulin-abhängig	4 (4.0%)	5 (5.0%)	9 (4.5%)	
Renal failure (GFR<60 mL/min)	no	93 (93.9%)	93 (92.1%)	186 (93.0%)	0.7830
	yes	6 (6.1%)	8 (7.9%)	14 (7.0%)	

*by Fisher's exact test
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Table: AF history - qualitative parameter - ITT Population
Population: ITT

Parameter - n (%)		A (Experimental) N=99	B (Control) N=101	Total N=200	p-Value*
current AF	missing	1 (1.0%)	1 (1.0%)	2 (1.0%)	0.7774
	no	44 (44.4%)	47 (46.5%)	91 (45.5%)	
	yes	54 (54.5%)	53 (52.5%)	107 (53.5%)	
AF classification	missing	3 (3.0%)	0 (0.0%)	3 (1.5%)	0.5815
	paroxysmal	65 (65.7%)	68 (67.3%)	133 (66.5%)	
	persistent	30 (30.3%)	33 (32.7%)	63 (31.5%)	
	permanent	1 (1.0%)	0 (0.0%)	1 (0.5%)	
Number of non-effective Antiarrhythmic agents	0	40 (40.4%)	37 (36.6%)	77 (38.5%)	0.9267
	1	48 (48.5%)	50 (49.5%)	98 (49.0%)	
	2	6 (6.1%)	6 (5.9%)	12 (6.0%)	

*current AF - by Fisher's exact test, others - by Chi square test
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Table: Procedural 1st ablation - quantitative parameter - ITT Population
Population: ITT

Variable	Arm	n	Mean	S.D.	Median	Range	95%-CI	P-value*
Transseptal duration (min)								
	A (Experimental)	93	80.5	52.5	78.0	5-306	(69.72 ; 91.33)	0.3626
	B (Control)	95	74.1	43.3	75.0	2-191	(65.30 ; 82.95)	
	Total	188	77.3	48.1	75.5	2-306	(70.38 ; 84.21)	
Total duration of procedure (min)								
	A (Experimental)	99	125.1	57.1	111.0	30-413	(113.70 ; 136.48)	0.2464
	B (Control)	100	116.8	41.7	110.0	51-240	(108.57 ; 125.11)	
	Total	199	120.9	50.0	110.0	30-413	(113.95 ; 127.94)	
Fluoroscopy time (min)								
	A (Experimental)	95	24.5	76.7	15.0	2-756	(8.89 ; 40.15)	0.3629
	B (Control)	100	17.0	25.4	13.0	1-251	(11.92 ; 22.00)	
	Total	195	20.6	56.5	14.0	1-756	(12.66 ; 28.63)	
Before Ablation - systolic BP (mmHg)								
	A (Experimental)	95	132.7	21.0	135.0	75-180	(128.46 ; 137.01)	0.5135

<i>Variable</i>	<i>Arm</i>	<i>n</i>	<i>Mean</i>	<i>S.D.</i>	<i>Median</i>	<i>Range</i>	<i>95%-CI</i>	<i>P-value*</i>
	B (Control)	92	134.8	21.1	134.0	85-195	(130.39 ; 139.11)	
	Total	187	133.7	21.0	135.0	75-195	(130.70 ; 136.76)	
Before Ablation - diastolic BP (mmHg)								
	A (Experimental)	95	75.0	14.8	75.0	35-115	(72.02 ; 78.06)	0.8566
	B (Control)	92	74.6	15.5	75.0	40-131	(71.44 ; 77.84)	
	Total	187	74.8	15.1	75.0	35-131	(72.67 ; 77.02)	
*by Student's t-test T_PVI.sas 07JUL22 08:04								

Table: Procedural 1st ablation - qualitative parameter - ITT Population
Population: ITT

Parameter - n (%)	A (Experimental) N=99	B (Control) N=101	Total N=200	p-Value*
Ablation mode	1 (1.0%)	0 (0.0%)	1 (0.5%)	0.8249
Anpressdruckmessung	0 (0.0%)	1 (1.0%)	1 (0.5%)	
Cryo-Ballon	13 (13.1%)	13 (12.9%)	26 (13.0%)	
Cryo-Ballon / ACHIEVE	11 (11.1%)	16 (15.8%)	27 (13.5%)	
Cryo-Ballon / ACHIEVE, Oesophagustemperatur	7 (7.1%)	9 (8.9%)	16 (8.0%)	
Cryo-Ballon / ACHIEVE, RF cooled tip	3 (3.0%)	1 (1.0%)	4 (2.0%)	
Cryo-Ballon / ACHIEVE, RF cooled tip, Anpressdruckmessung	1 (1.0%)	1 (1.0%)	2 (1.0%)	
Cryo-Ballon, Cryo-Ballon / ACHIEVE	3 (3.0%)	3 (3.0%)	6 (3.0%)	
Cryo-Ballon, Cryo-Ballon / ACHIEVE, Oesophagustemperatur	5 (5.1%)	2 (2.0%)	7 (3.5%)	
Cryo-Ballon, Cryo-Ballon / ACHIEVE, RF cooled tip	0 (0.0%)	2 (2.0%)	2 (1.0%)	
Cryo-Ballon, Oesophagustemperatur	14 (14.1%)	13 (12.9%)	27 (13.5%)	
Laser, Oesophagustemperatur	1 (1.0%)	0 (0.0%)	1 (0.5%)	
Oesophagustemperatur	13 (13.1%)	17 (16.8%)	30 (15.0%)	
RF cooled tip	12 (12.1%)	13 (12.9%)	25 (12.5%)	

Parameter - n (%)		A (Experimental) N=99	B (Control) N=101	Total N=200	p-Value*
3D mapping	RF cooled tip, Anpressdruckmessung	11 (11.1%)	7 (6.9%)	18 (9.0%)	0.7521
	RF cooled tip, Anpressdruckmessung, Oesophagustemperatur	3 (3.0%)	3 (3.0%)	6 (3.0%)	
	RF cooled tip, Oesophagustemperatur	1 (1.0%)	0 (0.0%)	1 (0.5%)	
	CARTO	26 (26.3%)	27 (26.7%)	53 (26.5%)	
	NAVX	28 (28.3%)	24 (23.8%)	52 (26.0%)	
	No 3D Mapping	45 (45.5%)	50 (49.5%)	95 (47.5%)	
Additional Ablation of cavotrikuspidal isthmus	no	89 (89.9%)	85 (84.2%)	174 (87.0%)	0.2275
	yes	10 (10.1%)	16 (15.8%)	26 (13.0%)	

*by Chi square test

T_PVI.sas 07JUL22 08:04

Procedural 2nd ablation was conducted in 6 patients (Pat. Nos. 80, 199 of Arm A and Pat. Nos. 85, 126, 154, 229 of Arm B).

Table: Procedural 2nd ablation - quantitative parameter - ITT Population
Population: ITT

Variable	Arm	n	Mean	S.D.	Median	Range	95%-CI	P-value*
Transseptal duration (min)								
	A (Experimental)	1	35.0		35.0	35- 35		
	B (Control)	4	91.5	80.3	87.5	7-184	(-36.26 ; 219.26)	
	Total	5	80.2	74.0	45.0	7-184	(-11.66 ; 172.06)	
Total duration of procedure (min)								
	A (Experimental)	2	84.5	29.0	84.5	64-105	(-176.0 ; 344.98)	0.2627
	B (Control)	4	179.0	95.3	197.5	55-266	(27.37 ; 330.63)	
	Total	6	147.5	89.4	130.0	55-266	(53.65 ; 241.35)	
Fluoroscopy time (min)								
	A (Experimental)	2	18.0	15.6	18.0	7- 29	(-121.8 ; 157.77)	0.4398
	B (Control)	3	10.0	5.0	10.0	5- 15	(-2.42 ; 22.42)	
	Total	5	13.2	9.6	10.0	5- 29	(1.28 ; 25.12)	
Before Ablation - systolic BP (mmHg)								
	A (Experimental)	2	138.0	12.7	138.0	129-147	(23.64 ; 252.36)	0.0747
	B (Control)	4	108.3	14.8	105.5	96-126	(84.63 ; 131.87)	

<i>Variable</i>	<i>Arm</i>	<i>n</i>	<i>Mean</i>	<i>S.D.</i>	<i>Median</i>	<i>Range</i>	<i>95%-CI</i>	<i>P-value*</i>
.								
	Total	6	118.2	20.0	120.5	96-147	(97.16 ; 139.17)	
Before Ablation - diastolic BP (mmHg)								
	A (Experimental)	2	86.5	29.0	86.5	66-107	(-174.0 ; 346.98)	0.2813
	B (Control)	4	66.5	13.4	64.5	53- 84	(45.21 ; 87.79)	
.								
	Total	6	73.2	19.5	67.5	53-107	(52.65 ; 93.68)	

*by Student's t-test
T_PVI.sas 07JUL22 08:04

Table: Procedural 2nd ablation - qualitative parameter - ITT Population
Population: ITT

Parameter - n (%)		A (Experimental) N=99	B (Control) N=101	Total N=200	p-Value*
Ablation mode	Cryo-Ballon / ACHIEVE, RF cooled tip	1 (1.0%)	0 (0.0%)	1 (0.5%)	0.4409
	Cryo-Ballon, Cryo-Ballon / ACHIEVE	0 (0.0%)	1 (1.0%)	1 (0.5%)	
	Oesophagustemperatur	0 (0.0%)	1 (1.0%)	1 (0.5%)	
	RF cooled tip	1 (1.0%)	1 (1.0%)	2 (1.0%)	
	RF cooled tip, Anpressdruckmessung, Oesophagustemperatur	0 (0.0%)	1 (1.0%)	1 (0.5%)	
3D mapping	CARTO	0 (0.0%)	3 (3.0%)	3 (1.5%)	0.1534
	NAVX	1 (1.0%)	0 (0.0%)	1 (0.5%)	
	No 3D Mapping	1 (1.0%)	1 (1.0%)	2 (1.0%)	
Additional Ablation of cavotrikuspidal isthmus	no	1 (1.0%)	3 (3.0%)	4 (2.0%)	0.5403
	yes	1 (1.0%)	1 (1.0%)	2 (1.0%)	

*by Chi square test

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Table 14.1.8-1: Compliance by category - ITT population
Population: ITT

Visit	Parameter - n (%)		Arm	
			A (Experimental) N=99	B (Control) N=101
Visit 1 (3 months after Rand.)	Compliance category	missing	3 (3.0%)	101 (100.0%)
		good	89 (89.9%)	0 (0.0%)
		moderate	3 (3.0%)	0 (0.0%)
		poor	4 (4.0%)	0 (0.0%)
Visit 2 (9 months after Rand.)	Compliance category	missing	10 (10.1%)	98 (97.0%)
		good	76 (76.8%)	1 (1.0%)
		moderate	7 (7.1%)	0 (0.0%)
		poor	6 (6.1%)	2 (2.0%)
Visit 3 (12 months after Rand.)	Compliance category	missing	15 (15.2%)	96 (95.0%)
		good	70 (70.7%)	4 (4.0%)
		moderate	13 (13.1%)	1 (1.0%)
		poor	1 (1.0%)	0 (0.0%)

Percentage based on patients in the ITT population
Compliance in Arm B due to treatment switch.
good - > 80%, poor - < 50%, moderate - not good or poor
T_COMPLIANCE 07MAR22 13:30

Table 14.1.8-2: Number of switcher - ITT Population

Population: ITT

Parameter - n (%)		Arm	
		A (Experimental) N=99	B (Control) N=101
Switcher	yes	2 (2.0%)	10 (9.9%)
	no	97 (98.0%)	91 (90.1%)
T_SWITCHER.sas 18MAY22 08:50			

Table 14.1.8-3: Number of switcher per visit - ITT Population

Population: ITT

Visit	Parameter - n (%)		A (Experimental)	B (Control)
Visit 1 (3 months after Rand.)	Switcher	missing	96 (98.0%)	0 (0.0%)
		yes	2 (2.0%)	3 (3.2%)
		no	0 (0.0%)	90 (96.8%)
Visit 2 (9 months after Rand.)	Switcher	missing	93 (100.0%)	0 (0.0%)
		yes	0 (0.0%)	7 (7.8%)
		no	0 (0.0%)	83 (92.2%)
Visit 3 (12 months after Rand.)	Switcher	missing	90 (100.0%)	0 (0.0%)
		yes	0 (0.0%)	8 (8.7%)
		no	0 (0.0%)	84 (91.3%)

Percentage based on patients per visit in the ITT population.

Mutiple citations possible.

T_SWITCHER.sas 18MAY22 08:50

7.2 Efficacy - Primary endpoint

Table 14.2.1-1: Occurrence of new micro- and macro-embolic lesions 12 months after randomization – ITT population
Population: ITT

Parameter - n (%)	Arm		Total N=200	P-value
	A (Experimental) N=99	B (Control) N=101		
Occurrence of lesions after 12 months no	84 (84.8%)	90 (89.1%)	174 (87.0%)	0.4545
yes	15 (15.2%)	11 (10.9%)	26 (13.0%)	

Percentage based on patients in the ITT population

Missing values will be counted as failure (occurrence of lesion=YES).

p-value according to Cochran-Mantel Haenzel test stratified by site. Breslow-Day Statistic not computed--the data are too sparse.

T_MRT_Corelab 07MAR22 13:25

Table: Difference in occurrence of lesions
Population: ITT

Diff. in occurrence of lesions Arm A minus Arm B	95% CI*	CI Type
4.3 %	(-9.362 , 18.230)	Exact
	(-5.056 , 13.577)	Wald

*for occurrence of lesions YES.

Missing values will be counted as failure (occurrence of lesion=YES).

T_MRT_Corelab_CI.sas 17MAY22 12:05

Table 14.2.1-2: Occurrence of new micro- and macro-embolic lesions 12 months after randomization – PP population
Population: PP

		Arm			P-value
Parameter - n (%)		A (Experimental) N=82	B (Control) N=87	Total N=169	
Occurrence of lesions after 12 months	no	80 (97.6%)	87 (100.0%)	167 (98.8%)	0.1591
	yes	2 (2.4%)	0 (0.0%)	2 (1.2%)	

Percentage based on patients in the PP population

Missing values will be counted as failure (occurrence of lesion=YES).

p-value according to Cochran-Mantel Haenzel test stratified by site. Breslow-Day Statistic not computed--the data are too sparse.

T_MRT_Corelab 07MAR22 13:25

Table: Difference in occurrence of lesions
Population: PP

Diff. in occurrence of lesions Arm A minus Arm B	95% CI*	CI Type
2.4 %	(-12.734 , 17.464)	Exact
	(-0.900 , 5.778)	Wald

*for occurrence of lesions YES.

Missing values will be counted as failure (occurrence of lesion=YES).

T_MRT_Corelab_CI.sas 17MAY22 12:05

Table 14.2.1-1: Occurrence of new micro- and macro-embolic lesions 12 months after randomization – ITT population
Population: ITT

Parameter - n (%)	Arm		Total N=200	P-value
	A (Experimental) N=99	B (Control) N=101		
Occurrence of lesions after 12 months	missing	13 (13.1%)	24 (12.0%)	0.1517
	no	84 (84.8%)	174 (87.0%)	
	yes	2 (2.0%)	2 (1.0%)	

Percentage based on patients in the ITT population

Missing values due to premature discontinuation or MRT refuse at V3 will be ignored.

p-value according to Cochran-Mantel Haenzel test stratified by site. Breslow-Day Statistic not computed--the data are too sparse.

T_MRT_Corelab 07MAR22 13:25

Table: Difference in occurrence of lesions
Population: ITT

Diff. in occurrence of lesions Arm A minus Arm B	95% CI*	CI Type
2.3** %	(-12.590 , 17.207)	Exact
	(-0.860 , 5.511)	Wald

*for occurrence of lesions YES.

**2/86=2.3%

Missing values due to premature discontinuation or MRT refuse at V3 will be ignored.

T_MRT_Corelab_CI.sas 17MAY22 12:05

7.3 Efficacy - Secondary endpoints

- Location, size and number of new micro- and macro-embolic lesions

Listing 14.2.2-1: Location, size and number of new micro- and macro-embolic lesions on cerebral MRI
Population: Randomised

Arm	Site No.	Pat-ID	No. new lesions	No. unchanged lesions	Total Volume all lesions (ml)	Total Volume new lesions (ml)	ITT	PP
A (Experimental)	1	107	1	20	4.68	0.01	yes	yes
	13	211	2	0	0.04	0.04	yes	yes

Listing 14.2.2-2: New lesions
Population: Randomised

Arm	Site No.	Pat-ID	Lesion No.	Size (Volume in mL)	Side	Aterial blood stream area	ITT	PP
A (Experimental)	1	107	1	0.01	left	MCA	yes	yes
	13	211	1	0.02	right	MCA	yes	yes
			2	0.02	right	ACA	yes	yes

- Incidence of clinically evident cardio-embolic events

Table 14.2.3-1: Incidence of clinically evident cardio-embolic events -ITT population

Population: ITT

Visit	Parameter - n (%)		Arm	
			A (Experimental) N=99	B (Control) N=101
1	Stroke	no	98 (99.0%)	94 (93.1%)
	TIA	no	98 (99.0%)	94 (93.1%)
	Systemic embolism	no	98 (99.0%)	94 (93.1%)
	Cardio-embolic event	no	98 (99.0%)	94 (93.1%)
2	Stroke	no	94 (94.9%)	90 (89.1%)
	TIA	no	94 (94.9%)	90 (89.1%)
	Systemic embolism	no	94 (94.9%)	90 (89.1%)
	Cardio-embolic event	no	94 (94.9%)	90 (89.1%)
3	Stroke	no	90 (90.9%)	91 (90.1%)
	TIA	no	90 (90.9%)	91 (90.1%)
	Systemic embolism	no	90 (90.9%)	91 (90.1%)
	Cardio-embolic event	no	90 (90.9%)	91 (90.1%)

Percentage based on number of patients in the ITT population

T_SecEP 07MAR22 13:23

Table 14.2.3-2: Incidence of clinically evident cardio-embolic events -PP population
Population: PP

Visit	Parameter - n (%)		Arm	
			A (Experimental) N=82	B (Control) N=87
1	Stroke	no	82 (100.0%)	87 (100.0%)
	TIA	no	82 (100.0%)	87 (100.0%)
	Systemic embolism	no	82 (100.0%)	87 (100.0%)
	Cardio-embolic event	no	82 (100.0%)	87 (100.0%)
2	Stroke	no	82 (100.0%)	86 (98.9%)
	TIA	no	82 (100.0%)	86 (98.9%)
	Systemic embolism	no	82 (100.0%)	86 (98.9%)
	Cardio-embolic event	no	82 (100.0%)	86 (98.9%)
3	Stroke	no	82 (100.0%)	86 (98.9%)
	TIA	no	82 (100.0%)	86 (98.9%)
	Systemic embolism	no	82 (100.0%)	86 (98.9%)
	Cardio-embolic event	no	82 (100.0%)	86 (98.9%)

Percentage based on number of patients in the PP population

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- Incidence of clinically apparent neurological deficits

Table 14.2.4-1: Incidence of clinically apparent neurological deficits -ITT population
Population: ITT

Visit	Parameter - n (%)		Arm	
			A (Experimental) N=99	B (Control) N=101
1	Clinical apparent neurological deficits	no	98 (99.0%)	94 (93.1%)
		yes	0 (0.0%)	0 (0.0%)
2	Clinical apparent neurological deficits	no	94 (94.9%)	89 (88.1%)
		yes	0 (0.0%)	1 (1.0%)
3	Clinical apparent neurological deficits	no	90 (90.9%)	90 (89.1%)
		yes	0 (0.0%)	1 (1.0%)

Percentage based on number of patients in the ITT population
Multiple citation possible
T_SecEP 07MAR22 13:23

Table 14.2.4-2: Incidence of clinically apparent neurological deficits -PP population
Population: PP

Visit	Parameter - n (%)		Arm	
			A (Experimental) N=82	B (Control) N=87
1	Clinical apparent neurological deficits	no	82 (100.0%)	87 (100.0%)
		yes	0 (0.0%)	0 (0.0%)
2	Clinical apparent neurological deficits	no	82 (100.0%)	85 (97.7%)
		yes	0 (0.0%)	1 (1.1%)
3	Clinical apparent neurological deficits	no	82 (100.0%)	85 (97.7%)
		yes	0 (0.0%)	1 (1.1%)

Percentage based on number of patients in the PP population

Multiple citation possible

T_SecEP 07MAR22 13:23

Listing: Clinically apparent neurological deficits

	Site	Pat-ID	Visit	Clinical apparent neurological deficits	neurological deficit - Date	neurological deficit - mRS	neurological deficit- confirmation	EP - Comment - 1	EP - Comment - 2
A (Experimental)	1	208	2	yes	11/09/2019	.	Not confirmed	Kriterium des neurologischen Defizits nicht erfüllt	1. CEC am 12.06.2020: kein EP. 2. CEC am 11.06.2021: trotz zusätzlicher Infos weiterhin kein EP
B (Control)	1	26	2	yes	11/06/2020	.	Confirmed		Okulo Motorinsparese (??) neurologisch bestätigt, im CT keine Bedeutung, keine Thrombose

- Severeness of neurological deficits

There is only 1 patient in Arm B who had clinically apparent neurological deficits. Severeness was not judged (missing mRS assessment).

- Incidence of other thrombotic or thrombo-embolic events

Table 14.2.6-1: Incidence of other thrombotic or thrombo-embolic events -ITT Population
Population: ITT

Visit	Parameter - n (%)		Arm	
			A (Experimental) N=99	B (Control) N=101
1	Myocardial infarction	no	98 (99.0%)	94 (93.1%)
	Deep vein thrombosis	no	98 (99.0%)	94 (93.1%)
	Pulmonary embolism	no	98 (99.0%)	94 (93.1%)
	Thrombo-embolic event	no	98 (99.0%)	94 (93.1%)
2	Myocardial infarction	no	94 (94.9%)	90 (89.1%)
	Deep vein thrombosis	no	94 (94.9%)	90 (89.1%)
	Pulmonary embolism	no	94 (94.9%)	90 (89.1%)
	Thrombo-embolic event	no	94 (94.9%)	90 (89.1%)
3	Myocardial infarction	no	90 (90.9%)	91 (90.1%)
	Deep vein thrombosis	no	90 (90.9%)	91 (90.1%)
	Pulmonary embolism	no	90 (90.9%)	91 (90.1%)
	Thrombo-embolic event	no	90 (90.9%)	91 (90.1%)

Percentage based on number of patients in the ITT population

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Table 14.2.6-2: Incidence of other thrombotic or thrombo-embolic events -PP Population
Population: PP

Visit	Parameter - n (%)		Arm	
			A (Experimental) N=82	B (Control) N=87
1	Myocardial infarction	no	82 (100.0%)	87 (100.0%)
	Deep vein thrombosis	no	82 (100.0%)	87 (100.0%)
	Pulmonary embolism	no	82 (100.0%)	87 (100.0%)
	Thrombo-embolic event	no	82 (100.0%)	87 (100.0%)
2	Myocardial infarction	no	82 (100.0%)	86 (98.9%)
	Deep vein thrombosis	no	82 (100.0%)	86 (98.9%)
	Pulmonary embolism	no	82 (100.0%)	86 (98.9%)
	Thrombo-embolic event	no	82 (100.0%)	86 (98.9%)
3	Myocardial infarction	no	82 (100.0%)	86 (98.9%)
	Deep vein thrombosis	no	82 (100.0%)	86 (98.9%)
	Pulmonary embolism	no	82 (100.0%)	86 (98.9%)
	Thrombo-embolic event	no	82 (100.0%)	86 (98.9%)

Percentage based on number of patients in the PP population

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- Life-threatening/major/minor bleedings

Table 14.2.7-1: Bleeding - ITT population
Population: ITT

Visit	Parameter - n (%)		Arm	
			A (Experimental) N=99	B (Control) N=101
1	Bleeding	no	97 (98.0%)	93 (92.1%)
		yes	1 (1.0%)	1 (1.0%)
2	Bleeding	no	92 (92.9%)	90 (89.1%)
		yes	2 (2.0%)	0 (0.0%)
3	Bleeding	no	88 (88.9%)	90 (89.1%)
		yes	2 (2.0%)	1 (1.0%)

Percentage based on number of patients in the ITT population
Multiple citation possible
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Table 14.2.7-3: Bleeding - PP population
Population: PP

Visit	Parameter - n (%)		Arm	
			A (Experimental) N=82	B (Control) N=87
1	Bleeding	no	81 (98.8%)	86 (98.9%)
		yes	1 (1.2%)	1 (1.1%)
2	Bleeding	no	80 (97.6%)	86 (98.9%)
		yes	2 (2.4%)	0 (0.0%)
3	Bleeding	no	80 (97.6%)	85 (97.7%)
		yes	2 (2.4%)	1 (1.1%)

Percentage based on number of patients in the PP population

Multiple citation possible

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Listing: Bleeding

Bleeding										
	Site	Pat-ID	Visit	Bleeding	Bleeding Date	Bleeding grade	Bleeding confirmation	EP - Comment - 1	EP - Comment - 2	
(Experimental)	A	5	70	3	yes	11/05/2018	minor	Confirmed	Patient berichtet über vermehrtes Zahnfleischbluten an Zahnimplantaten	Gingivabluten, Endpunkte bestätigt. VHF durch Patienten bestätigt
			71	1	yes	15/10/2017	minor	Confirmed	Patient berichtet von vermehrtem Zahnfleischbluten, deshalb wurde die Dosis reduziert.	Gingivabluten, Babigatrandosis erhöht

	Site	Pat-ID	Visit	Bleeding	Bleeding Date	Bleeding grade	Bleeding confirmation	EP - Comment - 1	EP - Comment - 2
B (Control)	8	54	1	yes	18/09/2017	minor	Confirmed		Keine Unterlagen, Endpunkt nicht bestätigt (CEC 11.06.2020). Endpunkt doch bestätigt durch Augenschein Visite 25.09.2017 (CEC 11.06.2021)

- Hemorrhagic cerebral infarctions

Table 14.2.8-1: Hemorrhagic cerebral infarctions - ITT population
Population: ITT

Visit	Parameter - n (%)		Arm	
			A (Experimental) N=99	B (Control) N=101
1	Hemorrhagic cerebral infarctions	no	98 (99.0%)	94 (93.1%)
2	Hemorrhagic cerebral infarctions	no	94 (94.9%)	90 (89.1%)
3	Hemorrhagic cerebral infarctions	no	90 (90.9%)	91 (90.1%)

Percentage based on number of patients in the ITT population

Multiple citation possible

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Table 14.2.8-2: Hemorrhagic cerebral infarctions -PP population
Population: PP

Visit	Parameter - n (%)		Arm	
			A (Experimental) N=82	B (Control) N=87
1	Hemorrhagic cerebral infarctions	no	82 (100.0%)	87 (100.0%)
2	Hemorrhagic cerebral infarctions	no	82 (100.0%)	86 (98.9%)
3	Hemorrhagic cerebral infarctions	no	82 (100.0%)	86 (98.9%)

Percentage based on number of patients in the PP population

Multiple citation possible

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- All-cause mortality

Table 14.2.9-1: All-cause mortality - ITT population

Population: ITT

Visit	Parameter - n (%)		Arm	
			A (Experimental) N=99	B (Control) N=101
1	Death	no	98 (99.0%)	94 (93.1%)
2	Death	no	94 (94.9%)	90 (89.1%)
3	Death	no	90 (90.9%)	91 (90.1%)

Percentage based on number of patients in the ITT population

Multiple citation possible

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Table 14.2.9-2: All-cause mortality - PP population

Population: PP

Visit	Parameter - n (%)		Arm	
			A (Experimental) N=82	B (Control) N=87
1	Death	no	82 (100.0%)	87 (100.0%)
2	Death	no	82 (100.0%)	86 (98.9%)
3	Death	no	82 (100.0%)	86 (98.9%)

Percentage based on number of patients in the PP population

Multiple citation possible

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- Cardiovascular mortality

No patient died during the trial.

- Cardio-embolic events subgroup analyses

No cardio-embolic events occurred during the trial.

- QoL-EQ-5D

Table 14.2.12-1: QoL-EQ-5D - ITT population

Population: ITT

<i>Visit</i>	<i>Arm</i>	<i>n</i>	<i>Mean</i>	<i>S.D.</i>	<i>Range</i>	<i>Median</i>	<i>95%-CI</i>	<i>P-value*</i>
Randomisation	A (Experimental)	96	76.1	17.1	5-100	80.0	(72.59 ; 79.53)	0.1888
	B (Control)	99	81.2	13.8	20-100	85.0	(78.46 ; 83.98)	
Visit 3 (12 months after Rand.)	A (Experimental)	89	77.1	18.5	5-101	80.0	(73.17 ; 80.97)	
	B (Control)	91	79.3	15.6	30-100	80.0	(76.10 ; 82.58)	
Changes from day 0					.			
Visit 3 (12 months after Rand.)	A (Experimental)	89	3.0	20.7	-40- 90	0.0	(-1.36 ; 7.36)	0.1888
	B (Control)	91	-0.7	16.9	-50- 95	0.0	(-4.24 ; 2.81)	

*by Student's t-test

T_MOCA_QoL.sas 07JUL22 08:04

Table 14.2.12-2: QoL-EQ-5D - PP Population
Population: PP

<i>Visit</i>	<i>Arm</i>	<i>n</i>	<i>Mean</i>	<i>S.D.</i>	<i>Range</i>	<i>Median</i>	<i>95%-CI</i>	<i>P-value*</i>
Randomisation	A (Experimental)	79	77.2	16.9	5-100	80.0	(73.39 ; 80.97)	0.2213
	B (Control)	86	82.0	12.8	40-100	85.0	(79.26 ; 84.74)	
Visit 3 (12 months after Rand.)	A (Experimental)	82	77.4	18.5	5-101	80.0	(73.32 ; 81.46)	
	B (Control)	86	80.2	14.9	30-100	80.0	(76.99 ; 83.36)	
Changes from day 0					.			
Visit 3 (12 months after Rand.)	A (Experimental)	82	3.0	21.5	-40- 90	0.0	(-1.69 ; 7.77)	
	B (Control)	86	-0.7	17.2	-50- 95	0.0	(-4.34 ; 3.01)	

*by Student's t-test
T_MOCA_QoL.sas 07JUL22 08:04

- MOCA test

Table 14.2.13-1: MOCA test - ITT population
Population: ITT

<i>Visit</i>	<i>Arm</i>	<i>n</i>	<i>Mean</i>	<i>S.D.</i>	<i>Range</i>	<i>Median</i>	<i>95%-CI</i>	<i>P-value*</i>
Randomisation	A (Experimental)	95	25.2	3.5	12- 30	26.0	(24.46 ; 25.90)	0.5145
	B (Control)	96	25.7	3.5	16- 31	26.0	(24.95 ; 26.36)	
Visit 3 (12 months after Rand.)	A (Experimental)	84	26.0	3.3	17- 30	27.0	(25.33 ; 26.77)	
	B (Control)	87	26.5	2.8	17- 30	27.0	(25.93 ; 27.13)	
Changes from day 0					.			
Visit 3 (12 months after Rand.)	A (Experimental)	84	1.2	5.2	-11- 28	1.0	(0.08 ; 2.32)	
	B (Control)	87	0.8	3.2	-8- 8	1.0	(0.08 ; 1.46)	

*by Student's t-test

T_MOCA_QoL.sas 07JUL22 08:04

Table 14.2.13-2: MOCA test - PP Population
Population: PP

<i>Visit</i>	<i>Arm</i>	<i>n</i>	<i>Mean</i>	<i>S.D.</i>	<i>Range</i>	<i>Median</i>	<i>95%-CI</i>	<i>P-value*</i>
Randomisation	A (Experimental)	79	25.3	3.3	16- 30	25.0	(24.55 ; 26.01)	0.3795
	B (Control)	83	25.8	3.3	17- 31	26.0	(25.04 ; 26.48)	
Visit 3 (12 months after Rand.)	A (Experimental)	79	26.0	3.3	17- 30	27.0	(25.29 ; 26.76)	
	B (Control)	82	26.5	2.9	17- 30	27.0	(25.89 ; 27.15)	
Changes from day 0					.			
Visit 3 (12 months after Rand.)	A (Experimental)	79	1.4	5.1	-8- 28	1.0	(0.23 ; 2.53)	
	B (Control)	82	0.8	3.3	-8- 8	1.0	(0.06 ; 1.50)	

*by Student's t-test
T_MOCA_QoL.sas 07JUL22 08:04

7.4 Safety

- Adverse Events

Table 14.3.2-1: Overview of AEs - SAF population
Population: Safety

Number of treated subjects - n (%)	Arm		p-Value*
	A (Experimental) N=107	B (Control) N=93	
with any AE	72 (67.3%)	46 (49.5%)	0.0106
with drug-related AE	6 (5.6%)	3 (3.2%)	0.5078
With severe AE	10 (9.3%)	8 (8.6%)	0.8546
with SAE	34 (31.8%)	18 (19.4%)	0.0458

Note: Calculation of percentages based on number of patients in SP

*by Chi-Square test. If any category has a cell count less than 5, then the Fisher exact test will be used

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Table 14.3.2-2: Incidence of AEs by SOC and PT - SAF population
Population: Safety

System Organ Class	Preferred term	Arm		P-Value* (Chi-Square/Fisher Exact)
		A (Experimental) N= 107	B (Control) N= 93	
Allgemeine Erkrankungen und Beschwerden am Verabreichungsort	Total	9 (8.4%)	3 (3.2%)	0.1458
	Brustkorbbeschwerden	1 (0.9%)	0 (0.0%)	1.0000
	Brustkorbschmerz	2 (1.9%)	0 (0.0%)	0.4999
	Chemische Unverträglichkeit von Medikamenten	1 (0.9%)	0 (0.0%)	1.0000
	Ermüdung	1 (0.9%)	0 (0.0%)	1.0000
	Granulom	0 (0.0%)	1 (1.1%)	0.4650
	Oedem peripher	2 (1.9%)	2 (2.2%)	1.0000
	Schmerzen an der Punktionsstelle	1 (0.9%)	0 (0.0%)	1.0000
	Unerwünschte Arzneimittelwirkung	1 (0.9%)	0 (0.0%)	1.0000
	Zyste	1 (0.9%)	0 (0.0%)	1.0000
Augenerkrankungen	Total	1 (0.9%)	3 (3.2%)	0.3396
	Augenblutung	0 (0.0%)	1 (1.1%)	0.4650
	Doppeltsehen	0 (0.0%)	1 (1.1%)	0.4650
	Entropium	1 (0.9%)	0 (0.0%)	1.0000
	Makulaoedem	0 (0.0%)	1 (1.1%)	0.4650
Chirurgische und medizinische Eingriffe	Total	9 (8.4%)	6 (6.5%)	0.5997
	Cholezystektomie	1 (0.9%)	0 (0.0%)	1.0000

System Organ Class	Preferred term	Arm		P-Value* (Chi-Square/Fisher Exact)
		A (Experimental) N= 107	B (Control) N= 93	
	Dentaloperation	0 (0.0%)	1 (1.1%)	0.4650
	Einsetzen eines Herzschrittmachers	0 (0.0%)	1 (1.1%)	0.4650
	Gelenkplastik	1 (0.9%)	0 (0.0%)	1.0000
	Intraokulaeres Linsenimplantat	1 (0.9%)	0 (0.0%)	1.0000
	Katarakt-Operation	1 (0.9%)	1 (1.1%)	1.0000
	Katheterablation	1 (0.9%)	0 (0.0%)	1.0000
	Krankenhausaufenthalt	1 (0.9%)	0 (0.0%)	1.0000
	Operation zur Wiederherstellung des Fingers	0 (0.0%)	1 (1.1%)	0.4650
	Operativer Eingriff	2 (1.9%)	0 (0.0%)	0.4999
	Transurethrale Blasenresektion	0 (0.0%)	1 (1.1%)	0.4650
	Varizenoperation	1 (0.9%)	0 (0.0%)	1.0000
	Zahnwurzelentfernung	0 (0.0%)	1 (1.1%)	0.4650
	Total	0 (0.0%)	3 (3.2%)	0.0988
	Hypothyreose	0 (0.0%)	2 (2.2%)	0.2150
Endokrine Erkrankungen	Struma	0 (0.0%)	1 (1.1%)	0.4650
Erkrankungen der Atemwege, des Brustraums und Mediastinums	Total	9 (8.4%)	5 (5.4%)	0.4015
	Asthma	0 (0.0%)	1 (1.1%)	0.4650
	Belastungsdyspnoe	1 (0.9%)	2 (2.2%)	0.5984
	Diaphragmalaehmung	1 (0.9%)	0 (0.0%)	1.0000

System Organ Class	Preferred term	Arm		P-Value* (Chi-Square/Fisher Exact)
		A (Experimental) N= 107	B (Control) N= 93	
Erkrankungen der Geschlechtsorgane und der Brustdrüse	Dyspnoe	1 (0.9%)	1 (1.1%)	1.0000
	Epistaxis	3 (2.8%)	0 (0.0%)	0.2499
	Pleuraerguss	1 (0.9%)	1 (1.1%)	1.0000
	Pulmonale arterielle Hypertonie	1 (0.9%)	0 (0.0%)	1.0000
	Schlafapnoe-Syndrom	1 (0.9%)	2 (2.2%)	0.5984
	Total	1 (0.9%)	0 (0.0%)	1.0000
Erkrankungen der Haut und des Unterhautgewebes	Krümmung des Penis	1 (0.9%)	0 (0.0%)	1.0000
	Total	3 (2.8%)	1 (1.1%)	0.6249
	Akne	1 (0.9%)	0 (0.0%)	1.0000
	Ausschlag	0 (0.0%)	1 (1.1%)	0.4650
	Kalter Schweiss	1 (0.9%)	0 (0.0%)	1.0000
	Psoriasis	1 (0.9%)	0 (0.0%)	1.0000
Erkrankungen der Nieren und Harnwege	Total	5 (4.7%)	1 (1.1%)	0.2186
	Nichtinfektiöse Zystitis	1 (0.9%)	1 (1.1%)	1.0000
	Nierenfunktionsbeeinträchtigung	2 (1.9%)	0 (0.0%)	0.4999
	Nierenversagen	2 (1.9%)	0 (0.0%)	0.4999
Erkrankungen des Gastrointestinaltrakts	Total	10 (9.3%)	6 (6.5%)	0.4518
	Bauch aufgetrieben	1 (0.9%)	0 (0.0%)	1.0000
	Chronische Gastritis	1 (0.9%)	0 (0.0%)	1.0000
	Diarrhoe	2 (1.9%)	0 (0.0%)	0.4999

System Organ Class	Preferred term	Arm		P-Value* (Chi-Square/Fisher Exact)
		A (Experimental) N= 107	B (Control) N= 93	
Erkrankungen des Immunsystems	Dyspepsie	1 (0.9%)	0 (0.0%)	1.0000
	Erosive Gastritis	0 (0.0%)	1 (1.1%)	0.4650
	Gastritis	2 (1.9%)	1 (1.1%)	1.0000
	Gastrooesophageale Refluxerkrankung	0 (0.0%)	1 (1.1%)	0.4650
	Leistenbruch	2 (1.9%)	0 (0.0%)	0.4999
	Oesophagitis	1 (0.9%)	0 (0.0%)	1.0000
	Pankreatitis	0 (0.0%)	1 (1.1%)	0.4650
	Parotisvergroesserung	0 (0.0%)	1 (1.1%)	0.4650
	Schmerzen Oberbauch	0 (0.0%)	2 (2.2%)	0.2150
	Stuhl weich	1 (0.9%)	0 (0.0%)	1.0000
	Uebelkeit	1 (0.9%)	0 (0.0%)	1.0000
	Total	0 (0.0%)	1 (1.1%)	0.4650
	Ueberempfindlichkeit	0 (0.0%)	1 (1.1%)	0.4650
Erkrankungen des Nervensystems	Total	10 (9.3%)	7 (7.5%)	0.6455
	Demenz vom Alzheimertyp	1 (0.9%)	0 (0.0%)	1.0000
	Hypoaesthesie	0 (0.0%)	1 (1.1%)	0.4650
	Karpaltunnelsyndrom	1 (0.9%)	0 (0.0%)	1.0000
	Kopfschmerzen	2 (1.9%)	0 (0.0%)	0.4999
	Myasthenia gravis	0 (0.0%)	1 (1.1%)	0.4650
	Neuralgie	1 (0.9%)	0 (0.0%)	1.0000

System Organ Class	Preferred term	Arm		P-Value* (Chi-Square/Fisher Exact)
		A (Experimental) N= 107	B (Control) N= 93	
Erkrankungen des Ohrs und des Labyrinths	Schwindel orthostatisch	0 (0.0%)	1 (1.1%)	0.4650
	Schwindelgefuehl	3 (2.8%)	2 (2.2%)	1.0000
	Stenose der Arteria carotis	1 (0.9%)	0 (0.0%)	1.0000
	Synkope	2 (1.9%)	2 (2.2%)	1.0000
	Zerebrale Mikroembolie	1 (0.9%)	0 (0.0%)	1.0000
	Total	1 (0.9%)	1 (1.1%)	1.0000
	Hoersturz	1 (0.9%)	0 (0.0%)	1.0000
	Lagerungsvertigo	0 (0.0%)	1 (1.1%)	0.4650
	Tinnitus	1 (0.9%)	0 (0.0%)	1.0000
	Vertigo	1 (0.9%)	0 (0.0%)	1.0000
Gefaesserkrankungen	Total	6 (5.6%)	5 (5.4%)	0.9430
	Haematom	1 (0.9%)	1 (1.1%)	1.0000
	Hitzewallung	0 (0.0%)	1 (1.1%)	0.4650
	Hypertensive Krise	2 (1.9%)	1 (1.1%)	1.0000
	Hypertensiver Notfall	0 (0.0%)	1 (1.1%)	0.4650
	Hypertonie	0 (0.0%)	1 (1.1%)	0.4650
	Hypotonie	1 (0.9%)	0 (0.0%)	1.0000
	Kreislaufkollaps	1 (0.9%)	0 (0.0%)	1.0000
	Lymphoedem	0 (0.0%)	1 (1.1%)	0.4650
	Periphere Venenerkrankung	1 (0.9%)	0 (0.0%)	1.0000

System Organ Class	Preferred term	Arm		P-Value* (Chi-Square/Fisher Exact)
		A (Experimental) N= 107	B (Control) N= 93	
Gutartige, boesartige und nicht spezifizierte Neubildungen (einschl. Zysten und Polypen)	Total	2 (1.9%)	5 (5.4%)	0.2539
	Basalzellkarzinom	0 (0.0%)	1 (1.1%)	0.4650
	Boesartiges Melanom	0 (0.0%)	1 (1.1%)	0.4650
	Enchondromatose	0 (0.0%)	1 (1.1%)	0.4650
	Karzinom der Bronchien	0 (0.0%)	1 (1.1%)	0.4650
	Lipom der Brustdruese	1 (0.9%)	0 (0.0%)	1.0000
	Prostatakarzinom	1 (0.9%)	1 (1.1%)	1.0000
Herzerkrankungen	Total	38 (35.5%)	10 (10.8%)	<0.0001
	Aortenklappeninsuffizienz	1 (0.9%)	0 (0.0%)	1.0000
	Bradyarrhythmie	0 (0.0%)	1 (1.1%)	0.4650
	Bradykardie	1 (0.9%)	0 (0.0%)	1.0000
	Diastolische Dysfunktion	1 (0.9%)	0 (0.0%)	1.0000
	Herzinsuffizienz	3 (2.8%)	0 (0.0%)	0.2499
	Mitralklappeninsuffizienz	1 (0.9%)	0 (0.0%)	1.0000
	Myokarditis	1 (0.9%)	0 (0.0%)	1.0000
	Palpitationen	5 (4.7%)	3 (3.2%)	0.7265
	Perikarderguss	2 (1.9%)	0 (0.0%)	0.4999
	Sinusbradykardie	0 (0.0%)	1 (1.1%)	0.4650
	Supraventrikulaere Extrasystolen	1 (0.9%)	0 (0.0%)	1.0000
	Tachyarrhythmia	1 (0.9%)	0 (0.0%)	1.0000

System Organ Class	Preferred term	Arm		P-Value* (Chi-Square/Fisher Exact)
		A (Experimental) N= 107	B (Control) N= 93	
Infektionen und parasitäre Erkrankungen	Tachykardie	2 (1.9%)	0 (0.0%)	0.4999
	Tachykardie ventrikulär	1 (0.9%)	0 (0.0%)	1.0000
	Trikuspidalklappeninsuffizienz	2 (1.9%)	0 (0.0%)	0.4999
	Vorhofflattern	5 (4.7%)	0 (0.0%)	0.0624
	Vorhofflimmern	27 (25.2%)	7 (7.5%)	0.0009
	Total	9 (8.4%)	11 (11.8%)	0.4218
	Bakterielle Infektion	0 (0.0%)	1 (1.1%)	0.4650
	Bronchitis	1 (0.9%)	1 (1.1%)	1.0000
	Erysipel	0 (0.0%)	1 (1.1%)	0.4650
	Gastrointestinalinfektion	0 (0.0%)	1 (1.1%)	0.4650
	Grippe	3 (2.8%)	1 (1.1%)	0.6249
	Harnwegsinfektion	0 (0.0%)	1 (1.1%)	0.4650
	Herpes zoster	0 (0.0%)	2 (2.2%)	0.2150
	Konjunktivitis	1 (0.9%)	0 (0.0%)	1.0000
	Nasopharyngitis	1 (0.9%)	0 (0.0%)	1.0000
	Pneumonie	2 (1.9%)	1 (1.1%)	1.0000
	Sinusitis	0 (0.0%)	2 (2.2%)	0.2150
	Zahnfistel	0 (0.0%)	1 (1.1%)	0.4650
	Zystitis	2 (1.9%)	0 (0.0%)	0.4999
	Total	0 (0.0%)	1 (1.1%)	0.4650
Leber- und Gallenerkrankungen				

System Organ Class	Preferred term	Arm		P-Value* (Chi-Square/Fisher Exact)
		A (Experimental) N= 107	B (Control) N= 93	
Psychiatrische Erkrankungen	Leberzyste	0 (0.0%)	1 (1.1%)	0.4650
	Total	2 (1.9%)	1 (1.1%)	1.0000
	Depression	0 (0.0%)	1 (1.1%)	0.4650
	Panikattacke	2 (1.9%)	0 (0.0%)	0.4999
Skelettmuskulatur-, Bindegewebs- und Knochenerkrankungen	Total	7 (6.5%)	4 (4.3%)	0.5488
	Arthralgie	0 (0.0%)	1 (1.1%)	0.4650
	Bandscheibenprotrusion	1 (0.9%)	0 (0.0%)	1.0000
	Bursitis	1 (0.9%)	0 (0.0%)	1.0000
	Haematom des Muskels	0 (0.0%)	1 (1.1%)	0.4650
	Osteoarthritis	2 (1.9%)	1 (1.1%)	1.0000
	Rueckenschmerzen	0 (0.0%)	1 (1.1%)	0.4650
	Schleimbeutelkrankung	1 (0.9%)	0 (0.0%)	1.0000
	Schmerz in einer Extremität	1 (0.9%)	0 (0.0%)	1.0000
	Schmerzen des Muskel- und Skelettsystems	1 (0.9%)	0 (0.0%)	1.0000
	Spinalstenose	1 (0.9%)	0 (0.0%)	1.0000
Stoffwechsel- und Ernährungsstörungen	Total	3 (2.8%)	1 (1.1%)	0.6249
	Dehydration	1 (0.9%)	0 (0.0%)	1.0000
	Gicht	2 (1.9%)	1 (1.1%)	1.0000
Untersuchungen	Total	6 (5.6%)	2 (2.2%)	0.2889
	Arthroskopie	1 (0.9%)	0 (0.0%)	1.0000

System Organ Class	Preferred term	Arm		P-Value* (Chi-Square/Fisher Exact)
		A (Experimental) N= 107	B (Control) N= 93	
Verletzung, Vergiftung und durch Eingriffe bedingte Komplikationen	Auswurffraktion verkleinert	0 (0.0%)	1 (1.1%)	0.4650
	C-reaktives Protein anomal	1 (0.9%)	0 (0.0%)	1.0000
	Endoskopie des oberen Gastrointestinaltrakts	1 (0.9%)	0 (0.0%)	1.0000
	Glykolisiertes Haemoglobin erhoeht	1 (0.9%)	0 (0.0%)	1.0000
	Leberfunktionstest anomal	1 (0.9%)	0 (0.0%)	1.0000
	N-terminales Prohormon von BNP	0 (0.0%)	1 (1.1%)	0.4650
	N-terminales Prohormon von BNP erhoeht	1 (0.9%)	1 (1.1%)	1.0000
	Natriuretisches Peptid Typ B erhoeht	0 (0.0%)	1 (1.1%)	0.4650
	Total	10 (9.3%)	9 (9.7%)	0.9364
	Arthropodenbiss	1 (0.9%)	0 (0.0%)	1.0000
	Baenderzerrung	0 (0.0%)	1 (1.1%)	0.4650
	Blutung nach einem Eingriff	1 (0.9%)	0 (0.0%)	1.0000
	Fraktur der Hand	1 (0.9%)	1 (1.1%)	1.0000
	Fraktur des Fusses	1 (0.9%)	1 (1.1%)	1.0000
	Fraktur des Schluesselbeins	1 (0.9%)	0 (0.0%)	1.0000
	Fraktur einer oberen Extremitaet	1 (0.9%)	0 (0.0%)	1.0000
	Fraktur eines Brustwirbels	1 (0.9%)	0 (0.0%)	1.0000
	Frakturen von Gesichtsknochen	1 (0.9%)	0 (0.0%)	1.0000

System Organ Class	Preferred term	Arm		P-Value* (Chi-Square/Fisher Exact)
		A (Experimental) N= 107	B (Control) N= 93	
	Gestoerte Wundheilung an der Inzisionsstelle	1 (0.9%)	0 (0.0%)	1.0000
	Haematurie nach einem Eingriff	0 (0.0%)	1 (1.1%)	0.4650
	Hauteinriss	0 (0.0%)	1 (1.1%)	0.4650
	Humerusfraktur	0 (0.0%)	2 (2.2%)	0.2150
	Nervenverletzung	0 (0.0%)	1 (1.1%)	0.4650
	Serom	0 (0.0%)	1 (1.1%)	0.4650
	Sturz	2 (1.9%)	1 (1.1%)	1.0000
	Vaskulaeres Pseudoaneurysma	1 (0.9%)	0 (0.0%)	1.0000
	Verkehrsunfall	1 (0.9%)	0 (0.0%)	1.0000

Note: Calculation of percentages based on number of patients in SP

Note: A patient with more than one AE within a PT was counted once in PT

*If any category has a cell count less than 5, then the Fisher exact test will be used

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Table 14.3.1-3: Incidence of AEs by maximum severity - SAF Population
Population: Safety

System Organ Class	Preferred term	Severity	Arm	
			A (Experimental) N= 107	B (Control) N= 93
Allgemeine Erkrankungen und Beschwerden am Verabreichungsort	Total	mild	4 (3.7%)	3 (3.2%)
		moderate	5 (4.7%)	0 (0.0%)
	Brustkorbbeschwerden	moderate	1 (0.9%)	0 (0.0%)
	Brustkorbschmerz	mild	1 (0.9%)	0 (0.0%)
		moderate	1 (0.9%)	0 (0.0%)
	Chemische Unverträglichkeit von Medikamenten	mild	1 (0.9%)	0 (0.0%)
	Ermüdung	mild	1 (0.9%)	0 (0.0%)
	Granulom	mild	0 (0.0%)	1 (1.1%)
	Oedem peripher	mild	1 (0.9%)	2 (2.2%)
		moderate	1 (0.9%)	0 (0.0%)
	Schmerzen an der Punktionsstelle	mild	1 (0.9%)	0 (0.0%)
	Unerwünschte Arzneimittelwirkung	moderate	1 (0.9%)	0 (0.0%)
	Zyste	moderate	1 (0.9%)	0 (0.0%)
Augenerkrankungen	Total	mild	0 (0.0%)	2 (2.2%)
		severe	1 (0.9%)	1 (1.1%)
	Augenblutung	mild	0 (0.0%)	1 (1.1%)
	Doppeltsehen	mild	0 (0.0%)	1 (1.1%)

System Organ Class	Preferred term	Severity	Arm	
			A (Experimental) N= 107	B (Control) N= 93
Chirurgische und medizinische Eingriffe	Entropium	severe	1 (0.9%)	0 (0.0%)
	Makulaoedem	severe	0 (0.0%)	1 (1.1%)
	Total	mild	2 (1.9%)	3 (3.2%)
		moderate	6 (5.6%)	2 (2.2%)
		severe	1 (0.9%)	1 (1.1%)
	Cholezystektomie	moderate	1 (0.9%)	0 (0.0%)
	Dentaloperation	mild	0 (0.0%)	1 (1.1%)
	Einsetzen eines Herzschrittmachers	severe	0 (0.0%)	1 (1.1%)
	Gelenkplastik	severe	1 (0.9%)	0 (0.0%)
	Intraokulaeres Linsenimplantat	moderate	1 (0.9%)	0 (0.0%)
	Katarakt-Operation	moderate	1 (0.9%)	1 (1.1%)
	Katheterablation	mild	1 (0.9%)	0 (0.0%)
	Krankenhausaufenthalt	mild	1 (0.9%)	0 (0.0%)
	Operation zur Wiederherstellung des Fingers	mild	0 (0.0%)	1 (1.1%)
	Operativer Eingriff	moderate	2 (1.9%)	0 (0.0%)
	Transurethrale Blasenresektion	moderate	0 (0.0%)	1 (1.1%)
	Varizenoperation	moderate	1 (0.9%)	0 (0.0%)
	Zahnwurzelentfernung	mild	0 (0.0%)	1 (1.1%)
Endokrine Erkrankungen	Total	mild	0 (0.0%)	3 (3.2%)
	Hypothyreose	mild	0 (0.0%)	2 (2.2%)

System Organ Class	Preferred term	Severity	Arm	
			A (Experimental) N= 107	B (Control) N= 93
Erkrankungen der Atemwege, des Brustraums und Mediastinums	Struma	mild	0 (0.0%)	1 (1.1%)
	Total	mild	5 (4.7%)	2 (2.2%)
		moderate	4 (3.7%)	1 (1.1%)
		severe	0 (0.0%)	2 (2.2%)
	Asthma	mild	0 (0.0%)	1 (1.1%)
	Belastungsdyspnoe	mild	0 (0.0%)	2 (2.2%)
		moderate	1 (0.9%)	0 (0.0%)
	Diaphragmalaehmung	moderate	1 (0.9%)	0 (0.0%)
	Dyspnoe	mild	1 (0.9%)	0 (0.0%)
		moderate	0 (0.0%)	1 (1.1%)
	Epistaxis	mild	3 (2.8%)	0 (0.0%)
	Pleuraerguss	mild	0 (0.0%)	1 (1.1%)
		moderate	1 (0.9%)	0 (0.0%)
	Pulmonale arterielle Hypertonie	moderate	1 (0.9%)	0 (0.0%)
	Schlafapnoe-Syndrom	mild	1 (0.9%)	0 (0.0%)
Erkrankungen der Geschlechtsorgane und der Brustdruese		severe	0 (0.0%)	2 (2.2%)
	Total	moderate	1 (0.9%)	0 (0.0%)
	Krue mmung des Penis	moderate	1 (0.9%)	0 (0.0%)
Erkrankungen der Haut und des Unterhautgewebes	Total	mild	2 (1.9%)	0 (0.0%)
		moderate	1 (0.9%)	0 (0.0%)

System Organ Class	Preferred term	Severity	Arm	
			A (Experimental) N= 107	B (Control) N= 93
Erkrankungen der Nieren und Harnwege		severe	0 (0.0%)	1 (1.1%)
	Akne	mild	1 (0.9%)	0 (0.0%)
	Ausschlag	severe	0 (0.0%)	1 (1.1%)
	Kalter Schweiss	moderate	1 (0.9%)	0 (0.0%)
	Psoriasis	mild	1 (0.9%)	0 (0.0%)
	Total	mild	3 (2.8%)	0 (0.0%)
		moderate	2 (1.9%)	1 (1.1%)
	Nichtinfektiöse Zystitis	moderate	1 (0.9%)	1 (1.1%)
	Nierenfunktionsbeeinträchtigung	mild	2 (1.9%)	0 (0.0%)
	Nierenversagen	mild	1 (0.9%)	0 (0.0%)
Erkrankungen des Gastrointestinaltrakts		moderate	1 (0.9%)	0 (0.0%)
	Total	mild	8 (7.5%)	4 (4.3%)
		moderate	2 (1.9%)	1 (1.1%)
		severe	0 (0.0%)	1 (1.1%)
	Bauch aufgetrieben	mild	1 (0.9%)	0 (0.0%)
	Chronische Gastritis	mild	1 (0.9%)	0 (0.0%)
	Diarrhoe	mild	2 (1.9%)	0 (0.0%)
	Dyspepsie	mild	1 (0.9%)	0 (0.0%)
	Erosive Gastritis	mild	0 (0.0%)	1 (1.1%)
	Gastritis	mild	2 (1.9%)	1 (1.1%)

System Organ Class	Preferred term	Severity	Arm	
			A (Experimental) N= 107	B (Control) N= 93
	Gastrooesophageale Refluxerkrankung	severe	0 (0.0%)	1 (1.1%)
	Leistenbruch	moderate	2 (1.9%)	0 (0.0%)
	Oesophagitis	mild	1 (0.9%)	0 (0.0%)
	Pankreatitis	mild	0 (0.0%)	1 (1.1%)
	Parotisvergroesserung	moderate	0 (0.0%)	1 (1.1%)
	Schmerzen Oberbauch	mild	0 (0.0%)	2 (2.2%)
	Stuhl weich	mild	1 (0.9%)	0 (0.0%)
	Uebelkeit	mild	1 (0.9%)	0 (0.0%)
	Total	mild	0 (0.0%)	1 (1.1%)
	Ueberempfindlichkeit	mild	0 (0.0%)	1 (1.1%)
Erkrankungen des Immunsystems				
Erkrankungen des Nervensystems	Total	mild	3 (2.8%)	3 (3.2%)
		moderate	6 (5.6%)	4 (4.3%)
		severe	1 (0.9%)	0 (0.0%)
	Demenz vom Alzheimertyp	moderate	1 (0.9%)	0 (0.0%)
	Hypoaesthesie	moderate	0 (0.0%)	1 (1.1%)
	Karpaltunnelsyndrom	moderate	1 (0.9%)	0 (0.0%)
	Kopfschmerzen	mild	1 (0.9%)	0 (0.0%)
		severe	1 (0.9%)	0 (0.0%)
	Myasthenia gravis	moderate	0 (0.0%)	1 (1.1%)
	Neuralgie	moderate	1 (0.9%)	0 (0.0%)

System Organ Class	Preferred term	Severity	Arm	
			A (Experimental) N= 107	B (Control) N= 93
Erkrankungen des Ohrs und des Labyrinths	Schwindel orthostatisch	mild	0 (0.0%)	1 (1.1%)
	Schwindelgefuehl	mild	1 (0.9%)	1 (1.1%)
		moderate	2 (1.9%)	1 (1.1%)
	Stenose der Arteria carotis	mild	1 (0.9%)	0 (0.0%)
	Synkope	mild	1 (0.9%)	1 (1.1%)
		moderate	1 (0.9%)	1 (1.1%)
	Zerebrale Mikroembolie	mild	1 (0.9%)	0 (0.0%)
	Total	mild	0 (0.0%)	1 (1.1%)
		severe	1 (0.9%)	0 (0.0%)
	Hoersturz	severe	1 (0.9%)	0 (0.0%)
	Lagerungsvertigo	mild	0 (0.0%)	1 (1.1%)
	Tinnitus	severe	1 (0.9%)	0 (0.0%)
Gefaesserkrankungen	Vertigo	severe	1 (0.9%)	0 (0.0%)
	Total	mild	5 (4.7%)	4 (4.3%)
		moderate	1 (0.9%)	1 (1.1%)
	Haematom	mild	1 (0.9%)	1 (1.1%)
	Hitzewallung	mild	0 (0.0%)	1 (1.1%)
	Hypertensive Krise	mild	1 (0.9%)	1 (1.1%)
		moderate	1 (0.9%)	0 (0.0%)
	Hypertensiver Notfall	mild	0 (0.0%)	1 (1.1%)

System Organ Class	Preferred term	Severity	Arm	
			A (Experimental) N= 107	B (Control) N= 93
Gutartige, boesartige und nicht spezifizierte Neubildungen (einschl. Zysten und Polypen)	Hypertonie	mild	0 (0.0%)	1 (1.1%)
	Hypotonie	mild	1 (0.9%)	0 (0.0%)
	Kreislaufkollaps	mild	1 (0.9%)	0 (0.0%)
	Lymphoedem	moderate	0 (0.0%)	1 (1.1%)
	Periphere Venenerkrankung	mild	1 (0.9%)	0 (0.0%)
	Total	mild	1 (0.9%)	0 (0.0%)
		moderate	0 (0.0%)	4 (4.3%)
		severe	1 (0.9%)	1 (1.1%)
	Basalzellkarzinom	moderate	0 (0.0%)	1 (1.1%)
	Boesartiges Melanom	moderate	0 (0.0%)	1 (1.1%)
	Enchondromatose	moderate	0 (0.0%)	1 (1.1%)
	Karzinom der Bronchien	moderate	0 (0.0%)	1 (1.1%)
	Lipom der Brustdruese	mild	1 (0.9%)	0 (0.0%)
	Prostatakarzinom	severe	1 (0.9%)	1 (1.1%)
Herzerkrankungen	Total	mild	15 (14.0%)	9 (9.7%)
		moderate	19 (17.8%)	1 (1.1%)
		severe	4 (3.7%)	0 (0.0%)
	Aortenklappeninsuffizienz	mild	1 (0.9%)	0 (0.0%)
	Bradyarrhythmie	mild	0 (0.0%)	1 (1.1%)
	Bradykardie	mild	1 (0.9%)	0 (0.0%)

System Organ Class	Preferred term	Severity	Arm	
			A (Experimental) N= 107	B (Control) N= 93
	Diastolische Dysfunktion	mild	1 (0.9%)	0 (0.0%)
	Herzinsuffizienz	mild	1 (0.9%)	0 (0.0%)
		moderate	2 (1.9%)	0 (0.0%)
	Mitralklappeninsuffizienz	mild	1 (0.9%)	0 (0.0%)
	Myokarditis	moderate	1 (0.9%)	0 (0.0%)
	Palpitationen	mild	3 (2.8%)	3 (3.2%)
		moderate	2 (1.9%)	0 (0.0%)
	Perikarderguss	mild	1 (0.9%)	0 (0.0%)
		severe	1 (0.9%)	0 (0.0%)
	Sinusbradykardie	mild	0 (0.0%)	1 (1.1%)
	Supraventrikuläre Extrasystolen	moderate	1 (0.9%)	0 (0.0%)
	Tachyarrhythmia	moderate	1 (0.9%)	0 (0.0%)
	Tachykardie	mild	2 (1.9%)	0 (0.0%)
	Tachykardie ventrikulär	moderate	1 (0.9%)	0 (0.0%)
	Trikuspidalklappeninsuffizienz	mild	1 (0.9%)	0 (0.0%)
		moderate	1 (0.9%)	0 (0.0%)
	Vorhofflattern	mild	2 (1.9%)	0 (0.0%)
		moderate	3 (2.8%)	0 (0.0%)
	Vorhofflimmern	mild	10 (9.3%)	6 (6.5%)
		moderate	14 (13.1%)	1 (1.1%)

System Organ Class	Preferred term	Severity	Arm	
			A (Experimental) N= 107	B (Control) N= 93
Infektionen und parasitäre Erkrankungen	Total	severe	3 (2.8%)	0 (0.0%)
		mild	2 (1.9%)	6 (6.5%)
		moderate	7 (6.5%)	5 (5.4%)
	Bakterielle Infektion	mild	0 (0.0%)	1 (1.1%)
	Bronchitis	mild	1 (0.9%)	1 (1.1%)
	Erysipel	moderate	0 (0.0%)	1 (1.1%)
	Gastrointestinalinfektion	mild	0 (0.0%)	1 (1.1%)
	Grippe	mild	1 (0.9%)	0 (0.0%)
	Harnwegsinfektion	moderate	2 (1.9%)	1 (1.1%)
		moderate	0 (0.0%)	1 (1.1%)
		mild	0 (0.0%)	1 (1.1%)
	Herpes zoster	mild	0 (0.0%)	1 (1.1%)
	Konjunktivitis	moderate	0 (0.0%)	1 (1.1%)
		moderate	1 (0.9%)	0 (0.0%)
		moderate	1 (0.9%)	0 (0.0%)
	Nasopharyngitis	moderate	1 (0.9%)	0 (0.0%)
	Pneumonie	moderate	2 (1.9%)	1 (1.1%)
	Sinusitis	mild	0 (0.0%)	1 (1.1%)
		moderate	0 (0.0%)	1 (1.1%)
	Zahnfistel	mild	0 (0.0%)	1 (1.1%)
	Zystitis	moderate	2 (1.9%)	0 (0.0%)
Leber- und Gallenerkrankungen	Total	mild	0 (0.0%)	1 (1.1%)

System Organ Class	Preferred term	Severity	Arm	
			A (Experimental) N= 107	B (Control) N= 93
Psychiatrische Erkrankungen	Leberzyste	mild	0 (0.0%)	1 (1.1%)
	Total	mild	2 (1.9%)	0 (0.0%)
		moderate	0 (0.0%)	1 (1.1%)
	Depression	moderate	0 (0.0%)	1 (1.1%)
Skelettmuskulatur-, Bindegewebs- und Knochenerkrankungen	Panikattacke	mild	2 (1.9%)	0 (0.0%)
	Total	mild	3 (2.8%)	3 (3.2%)
		moderate	4 (3.7%)	1 (1.1%)
	Arthralgie	mild	0 (0.0%)	1 (1.1%)
	Bandscheibenprotrusion	moderate	1 (0.9%)	0 (0.0%)
	Bursitis	mild	1 (0.9%)	0 (0.0%)
	Haematom des Muskels	mild	0 (0.0%)	1 (1.1%)
	Osteoarthritis	mild	1 (0.9%)	0 (0.0%)
		moderate	1 (0.9%)	1 (1.1%)
	Rueckenschmerzen	mild	0 (0.0%)	1 (1.1%)
	Schleimbeutelkrankung	mild	1 (0.9%)	0 (0.0%)
	Schmerz in einer Extremität	moderate	1 (0.9%)	0 (0.0%)
	Schmerzen des Muskel- und Skelettsystems	moderate	1 (0.9%)	0 (0.0%)
	Spinalstenose	mild	1 (0.9%)	0 (0.0%)
Stoffwechsel- und Ernährungsstörungen	Total	mild	1 (0.9%)	1 (1.1%)
		moderate	2 (1.9%)	0 (0.0%)

System Organ Class	Preferred term	Severity	Arm	
			A (Experimental) N= 107	B (Control) N= 93
Untersuchungen	Dehydration	mild	1 (0.9%)	0 (0.0%)
	Gicht	mild	0 (0.0%)	1 (1.1%)
		moderate	2 (1.9%)	0 (0.0%)
	Total	mild	4 (3.7%)	0 (0.0%)
		moderate	2 (1.9%)	1 (1.1%)
		severe	0 (0.0%)	1 (1.1%)
	Arthroskopie	mild	1 (0.9%)	0 (0.0%)
	Auswurfraction verkleinert	severe	0 (0.0%)	1 (1.1%)
	C-reaktives Protein anomal	mild	1 (0.9%)	0 (0.0%)
	Endoskopie des oberen Gastrointestinaltrakts	mild	1 (0.9%)	0 (0.0%)
	Glykolisiertes Haemoglobin erhoeht	moderate	1 (0.9%)	0 (0.0%)
	Leberfunktionstest anomal	mild	1 (0.9%)	0 (0.0%)
	N-terminales Prohormon von BNP	moderate	0 (0.0%)	1 (1.1%)
	N-terminales Prohormon von BNP erhoeht	moderate	1 (0.9%)	0 (0.0%)
		severe	0 (0.0%)	1 (1.1%)
	Natriuretisches Peptid Typ B erhoeht	moderate	0 (0.0%)	1 (1.1%)
Verletzung, Vergiftung und durch Eingriffe bedingte Komplikationen	Total	mild	3 (2.8%)	2 (2.2%)
		moderate	5 (4.7%)	5 (5.4%)
		severe	2 (1.9%)	2 (2.2%)

System Organ Class	Preferred term	Severity	Arm	
			A (Experimental) N= 107	B (Control) N= 93
	Arthropodenbiss	mild	1 (0.9%)	0 (0.0%)
	Baenderzerrung	moderate	0 (0.0%)	1 (1.1%)
	Blutung nach einem Eingriff	mild	1 (0.9%)	0 (0.0%)
	Fraktur der Hand	moderate	1 (0.9%)	1 (1.1%)
	Fraktur des Fusses	mild	1 (0.9%)	0 (0.0%)
		severe	0 (0.0%)	1 (1.1%)
	Fraktur des Schluesselbeins	moderate	1 (0.9%)	0 (0.0%)
	Fraktur einer oberen Extremitaet	severe	1 (0.9%)	0 (0.0%)
	Fraktur eines Brustwirbels	severe	1 (0.9%)	0 (0.0%)
	Frakturen von Gesichtsknochen	mild	1 (0.9%)	0 (0.0%)
	Gestoerte Wundheilung an der Inzisionsstelle	moderate	1 (0.9%)	0 (0.0%)
	Haematurie nach einem Eingriff	mild	0 (0.0%)	1 (1.1%)
	Hauteinriss	moderate	0 (0.0%)	1 (1.1%)
	Humerusfraktur	moderate	0 (0.0%)	1 (1.1%)
		severe	0 (0.0%)	1 (1.1%)
	Nervenverletzung	mild	0 (0.0%)	1 (1.1%)
	Serom	moderate	0 (0.0%)	1 (1.1%)
	Sturz	mild	0 (0.0%)	1 (1.1%)
		moderate	1 (0.9%)	0 (0.0%)
		severe	1 (0.9%)	0 (0.0%)

System Organ Class	Preferred term	Severity	Arm	
			A (Experimental) N= 107	B (Control) N= 93
	Vaskulaeres Pseudoaneurysma	moderate	1 (0.9%)	0 (0.0%)
	Verkehrsunfall	moderate	1 (0.9%)	0 (0.0%)

Calculation of percentages based on number of patients in SP

A patient with more than one AE within a PT was counted once in PT

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Table 14.3.1-4: Incidence of drug-related AEs - SAF Population
Population: Safety

System Organ Class	Preferred term	Arm		P-Value* (Chi-Square/Fisher Exact)
		A (Experimental) N= 107	B (Control) N= 93	
Allgemeine Erkrankungen und Beschwerden am Verabreichungsort	Total	2 (1.9%)	0 (0.0%)	0.4999
	Chemische Unverträglichkeit von Medikamenten	1 (0.9%)	0 (0.0%)	1.0000
	Unerwünschte Arzneimittelwirkung	1 (0.9%)	0 (0.0%)	1.0000
Erkrankungen der Atemwege, des Brustraums und Mediastinums	Total	1 (0.9%)	0 (0.0%)	1.0000
	Epistaxis	1 (0.9%)	0 (0.0%)	1.0000
Erkrankungen des Gastrointestinaltrakts	Total	2 (1.9%)	2 (2.2%)	1.0000
	Bauch aufgetrieben	1 (0.9%)	0 (0.0%)	1.0000
	Diarrhoe	1 (0.9%)	0 (0.0%)	1.0000
	Schmerzen Oberbauch	0 (0.0%)	2 (2.2%)	0.2150
	Stuhl weich	1 (0.9%)	0 (0.0%)	1.0000
Herzerkrankungen	Total	0 (0.0%)	1 (1.1%)	0.4650
	Vorhofflimmern	0 (0.0%)	1 (1.1%)	0.4650
Verletzung, Vergiftung und durch Eingriffe bedingte Komplikationen	Total	1 (0.9%)	0 (0.0%)	1.0000
	Blutung nach einem Eingriff	1 (0.9%)	0 (0.0%)	1.0000

		Arm		
System Organ Class	Preferred term	A (Experimental) N= 107	B (Control) N= 93	P-Value* (Chi-Square/Fisher Exact)
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Calculation of percentages based on number of patients in SP				
A patient with more than one AE within a PT was counted once in PT				
Relation to study drug was judged with YES				
*If any category has a cell count less than 5, then the Fisher exact test will be used				
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Table 14.3.1-5: SAE - SAF Population
Population: Safety

System Organ Class	Preferred term	Arm		P-Value* (Chi-Square/Fisher Exact)
		A (Experimental) N= 107	B (Control) N= 93	
Allgemeine Erkrankungen und Beschwerden am Verabreichungsort	Total	2 (1.9%)	0 (0.0%)	0.4999
	Brustkorbbeschwerden	1 (0.9%)	0 (0.0%)	1.0000
	Brustkorbschmerz	1 (0.9%)	0 (0.0%)	1.0000
Augenerkrankungen	Total	1 (0.9%)	1 (1.1%)	1.0000
	Doppeltsehen	0 (0.0%)	1 (1.1%)	0.4650
	Entropium	1 (0.9%)	0 (0.0%)	1.0000
Chirurgische und medizinische Eingriffe	Total	5 (4.7%)	2 (2.2%)	0.4530
	Cholezystektomie	1 (0.9%)	0 (0.0%)	1.0000
	Einsetzen eines Herzschrittmachers	0 (0.0%)	1 (1.1%)	0.4650
	Gelenkplastik	1 (0.9%)	0 (0.0%)	1.0000
	Katheterablation	1 (0.9%)	0 (0.0%)	1.0000
	Operativer Eingriff	2 (1.9%)	0 (0.0%)	0.4999
	Transurethrale Blasenresektion	0 (0.0%)	1 (1.1%)	0.4650
Endokrine Erkrankungen	Total	0 (0.0%)	1 (1.1%)	0.4650
	Struma	0 (0.0%)	1 (1.1%)	0.4650
Erkrankungen der Atemwege, des Brustraums und Mediastinums	Total	2 (1.9%)	1 (1.1%)	1.0000
	Dyspnoe	0 (0.0%)	1 (1.1%)	0.4650
	Pleuraerguss	1 (0.9%)	0 (0.0%)	1.0000

System Organ Class	Preferred term	Arm		P-Value* (Chi-Square/Fisher Exact)
		A (Experimental) N= 107	B (Control) N= 93	
Erkrankungen der Geschlechtsorgane und der Brustdruese	Schlafapnoe-Syndrom	1 (0.9%)	0 (0.0%)	1.0000
	Total	1 (0.9%)	0 (0.0%)	1.0000
	Krümmung des Penis	1 (0.9%)	0 (0.0%)	1.0000
Erkrankungen der Haut und des Unterhautgewebes	Total	0 (0.0%)	1 (1.1%)	0.4650
	Ausschlag	0 (0.0%)	1 (1.1%)	0.4650
Erkrankungen der Nieren und Harnwege	Total	1 (0.9%)	0 (0.0%)	1.0000
	Nierenversagen	1 (0.9%)	0 (0.0%)	1.0000
Erkrankungen des Gastrointestinaltrakts	Total	4 (3.7%)	3 (3.2%)	1.0000
	Diarrhoe	1 (0.9%)	0 (0.0%)	1.0000
	Gastritis	1 (0.9%)	0 (0.0%)	1.0000
	Gastrooesophageale Refluxerkrankung	0 (0.0%)	1 (1.1%)	0.4650
	Leistenbruch	2 (1.9%)	0 (0.0%)	0.4999
	Pankreatitis	0 (0.0%)	1 (1.1%)	0.4650
	Parotisvergrößerung	0 (0.0%)	1 (1.1%)	0.4650
	Total	3 (2.8%)	1 (1.1%)	0.6249
	Demenz vom Alzheimer-Typ	1 (0.9%)	0 (0.0%)	1.0000
Erkrankungen des Nervensystems	Kopfschmerzen	1 (0.9%)	0 (0.0%)	1.0000
	Myasthenia gravis	0 (0.0%)	1 (1.1%)	0.4650
	Synkope	1 (0.9%)	0 (0.0%)	1.0000
	Total	0 (0.0%)	1 (1.1%)	0.4650

System Organ Class	Preferred term	Arm		P-Value* (Chi-Square/Fisher Exact)
		A (Experimental) N= 107	B (Control) N= 93	
Gefaesserkrankungen	Lagerungsvertigo	0 (0.0%)	1 (1.1%)	0.4650
	Total	0 (0.0%)	1 (1.1%)	0.4650
	Hypertensive Krise	0 (0.0%)	1 (1.1%)	0.4650
	Hypertensiver Notfall	0 (0.0%)	1 (1.1%)	0.4650
Gutartige, boesartige und nicht spezifizierte Neubildungen (einschl. Zysten und Polypen)	Total	1 (0.9%)	3 (3.2%)	0.3396
	Boesartiges Melanom	0 (0.0%)	1 (1.1%)	0.4650
	Karzinom der Bronchien	0 (0.0%)	1 (1.1%)	0.4650
	Prostatakarzinom	1 (0.9%)	1 (1.1%)	1.0000
Herzerkrankungen	Total	18 (16.8%)	2 (2.2%)	0.0006
	Herzinsuffizienz	2 (1.9%)	0 (0.0%)	0.4999
	Myokarditis	1 (0.9%)	0 (0.0%)	1.0000
	Palpitationen	2 (1.9%)	0 (0.0%)	0.4999
	Perikarderguss	1 (0.9%)	0 (0.0%)	1.0000
	Supraventrikulaere Extrasystolen	1 (0.9%)	0 (0.0%)	1.0000
	Tachyarrhythmia	1 (0.9%)	0 (0.0%)	1.0000
	Tachykardie	1 (0.9%)	0 (0.0%)	1.0000
	Vorhofflattern	3 (2.8%)	0 (0.0%)	0.2499
	Vorhofflimmern	10 (9.3%)	2 (2.2%)	0.0384
	Total	2 (1.9%)	2 (2.2%)	1.0000
	Erysipel	0 (0.0%)	1 (1.1%)	0.4650

System Organ Class	Preferred term	Arm		P-Value* (Chi-Square/Fisher Exact)
		A (Experimental) N= 107	B (Control) N= 93	
Skelettmuskulatur-, Bindegewebs- und Knochenerkrankungen	Grippe	1 (0.9%)	0 (0.0%)	1.0000
	Harnwegsinfektion	0 (0.0%)	1 (1.1%)	0.4650
	Pneumonie	1 (0.9%)	0 (0.0%)	1.0000
	Total	1 (0.9%)	2 (2.2%)	0.5984
	Haematom des Muskels	0 (0.0%)	1 (1.1%)	0.4650
	Osteoarthritis	1 (0.9%)	1 (1.1%)	1.0000
Stoffwechsel- und Ernährungsstörungen	Total	1 (0.9%)	0 (0.0%)	1.0000
	Dehydratation	1 (0.9%)	0 (0.0%)	1.0000
Untersuchungen	Total	1 (0.9%)	0 (0.0%)	1.0000
	Arthroskopie	1 (0.9%)	0 (0.0%)	1.0000
Verletzung, Vergiftung und durch Eingriffe bedingte Komplikationen	Total	3 (2.8%)	6 (6.5%)	0.3082
	Fraktur des Fusses	0 (0.0%)	1 (1.1%)	0.4650
	Fraktur einer oberen Extremität	1 (0.9%)	0 (0.0%)	1.0000
	Fraktur eines Brustwirbels	1 (0.9%)	0 (0.0%)	1.0000
	Frakturen von Gesichtsknochen	1 (0.9%)	0 (0.0%)	1.0000
	Gestörte Wundheilung an der Inzisionsstelle	1 (0.9%)	0 (0.0%)	1.0000
	Haematurie nach einem Eingriff	0 (0.0%)	1 (1.1%)	0.4650
	Hauteinriss	0 (0.0%)	1 (1.1%)	0.4650
	Humerusfraktur	0 (0.0%)	2 (2.2%)	0.2150
	Serom	0 (0.0%)	1 (1.1%)	0.4650

		Arm		
		A (Experimental) N= 107	B (Control) N= 93	P-Value* (Chi-Square/Fisher Exact)
System Organ Class	Preferred term			
<hr/>				
Calculation of percentages based on number of patients in SP				
A patient with more than one AE within a PT was counted once in PT				
*If any category has a cell count less than 5, then the Fisher exact test will be used				
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- Selected laboratory data

Table 14.3.6: Selected laboratory data - SAF Population
Population: Safety

Variable	Visit	Arm	n	Mean	S.D.	Median	Range	95%-CI
Serum creatinine [mg/dL]	Randomisation	A (Experimental)	104	0.9	0.2	0.9	1- 2	(0.90 ; 0.99)
		B (Control)	91	0.9	0.2	0.9	0- 2	(0.87 ; 0.96)
	Visit 1	A (Experimental)	101	0.9	0.2	0.9	1- 2	(0.91 ; 0.99)
		B (Control)	82	2.1	10.6	0.9	1- 97	(-0.23 ; 4.43)
	Visit 2	A (Experimental)	99	1.8	8.1	0.9	1- 81	(0.21 ; 3.43)
		B (Control)	82	0.9	0.2	0.9	1- 2	(0.88 ; 0.97)
	Visit 3	A (Experimental)	97	0.9	0.2	0.9	1- 2	(0.88 ; 0.96)
		B (Control)	84	0.9	0.2	0.9	1- 2	(0.86 ; 0.94)
	Changes from day 0						.	
	Visit 1	A (Experimental)	101	0.0	0.2	0.0	-1- 1	(-0.01 ; 0.07)
		B (Control)	82	1.2	10.6	0.0	-0- 96	(-1.12 ; 3.53)
	Visit 2	A (Experimental)	99	0.9	8.1	0.0	-1- 80	(-0.70 ; 2.52)
		B (Control)	82	0.0	0.2	0.0	-0- 1	(-0.00 ; 0.09)
	Visit 3	A (Experimental)	97	0.0	0.2	0.0	-1- 1	(-0.04 ; 0.05)
		B (Control)	84	0.0	0.2	-0.0	-0- 1	(-0.02 ; 0.06)

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Table 14.3.6: Selected laboratory data - SAF Population
Population: Safety

Variable	Visit	Arm	n	Mean	S.D.	Median	Range	95%-CI
GFR [mL/min]	Randomisation	A (Experimental)	102	71.7	16.1	70.0	44- 120	(68.59 ; 74.91)
		B (Control)	89	74.5	16.2	70.0	42- 108	(71.13 ; 77.95)
	Visit 1	A (Experimental)	102	70.4	15.0	70.0	41- 121	(67.49 ; 73.38)
		B (Control)	82	74.2	16.7	70.0	39- 137	(70.52 ; 77.84)
	Visit 2	A (Experimental)	98	71.1	15.0	70.0	33- 112	(68.14 ; 74.13)
		B (Control)	80	74.7	16.0	70.0	37- 126	(71.12 ; 78.23)
	Visit 3	A (Experimental)	96	72.6	14.8	70.0	35- 115	(69.63 ; 75.61)
		B (Control)	84	74.4	16.0	70.0	37- 132	(70.95 ; 77.87)
	Changes from day 0							
	Visit 1	A (Experimental)	102	2.8	15.0	0.0	-22- 73	(-0.19 ; 5.71)
		B (Control)	82	3.0	17.2	0.0	-39- 95	(-0.74 ; 6.84)
	Visit 2	A (Experimental)	98	2.8	17.1	0.0	-42- 72	(-0.66 ; 6.20)
		B (Control)	80	3.0	18.8	0.0	-39- 91	(-1.15 ; 7.21)
	Visit 3	A (Experimental)	96	5.0	18.2	0.0	-39- 73	(1.36 ; 8.72)
		B (Control)	84	2.6	18.8	0.0	-39- 91	(-1.47 ; 6.67)

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Table 14.3.6: Selected laboratory data - SAF Population
Population: Safety

Variable	Visit	Arm	n	Mean	S.D.	Median	Range	95%-CI
CRP [mg/L]	Randomisation	A (Experimental)	99	2.5	3.6	1.0	0- 19	(1.76 ; 3.18)
		B (Control)	87	2.1	2.8	1.2	0- 19	(1.47 ; 2.68)
	Visit 1	A (Experimental)	93	1.9	2.3	1.0	0- 9	(1.39 ; 2.34)
		B (Control)	77	1.7	2.2	0.9	0- 13	(1.21 ; 2.22)
	Visit 2	A (Experimental)	87	2.7	5.3	1.2	0- 41	(1.61 ; 3.88)
		B (Control)	74	1.9	2.5	1.0	0- 13	(1.33 ; 2.49)
	Visit 3	A (Experimental)	90	2.0	2.6	1.1	0- 17	(1.44 ; 2.55)
		B (Control)	76	2.0	2.6	0.9	0- 13	(1.37 ; 2.57)
	Changes from day 0							
	Visit 1	A (Experimental)	93	-0.5	3.0	0.0	-14- 9	(-1.12 ; 0.11)
		B (Control)	77	-0.0	2.1	0.0	-9- 12	(-0.48 ; 0.45)
	Visit 2	A (Experimental)	87	0.3	5.7	0.0	-16- 40	(-0.93 ; 1.50)
		B (Control)	74	0.2	1.7	0.0	-3- 9	(-0.18 ; 0.61)
	Visit 3	A (Experimental)	90	-0.4	3.7	0.0	-14- 16	(-1.15 ; 0.40)
		B (Control)	76	0.3	2.0	0.0	-4- 9	(-0.12 ; 0.78)

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Table 14.3.6: Selected laboratory data - SAF Population
Population: Safety

Variable	Visit	Arm	n	Mean	S.D.	Median	Range	95%-CI
NTproBNP [pg/mL]	Randomisation	A (Experimental)	89	291.9	382.4	179.0	10- 2315	(211.31 ; 372.41)
		B (Control)	79	226.1	191.4	183.0	19- 863	(183.21 ; 268.95)
	Visit 1	A (Experimental)	88	279.1	338.4	150.0	5- 2039	(207.42 ; 350.81)
		B (Control)	73	238.7	258.1	164.0	23- 1571	(178.46 ; 298.89)
	Visit 2	A (Experimental)	84	351.8	656.7	185.0	10- 4797	(209.26 ; 494.31)
		B (Control)	71	213.6	186.6	131.0	21- 798	(169.39 ; 257.71)
	Visit 3	A (Experimental)	89	342.3	607.8	176.0	11- 4329	(214.30 ; 470.39)
		B (Control)	76	298.8	702.5	164.5	20- 6050	(138.29 ; 459.34)
	Changes from day 0						.	
	Visit 1	A (Experimental)	88	9.1	223.1	0.5	-691- 665	(-38.19 ; 56.36)
		B (Control)	73	31.2	202.0	5.0	-159- 1571	(-15.89 ; 78.38)
	Visit 2	A (Experimental)	84	114.0	387.2	25.9	-279- 2482	(29.93 ; 197.99)
		B (Control)	71	21.1	117.2	16.0	-235- 352	(-6.60 ; 48.88)
	Visit 3	A (Experimental)	89	95.9	531.6	5.0	-687- 3290	(-16.03 ; 207.93)
		B (Control)	76	105.9	699.8	11.5	-189- 6050	(-54.00 ; 265.82)

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