

Dossier zur Nutzenbewertung gemäß § 35a SGB V

Sebetralstat (Ekterly®)

Modul 4 A – Anhang 4-G

*Akutbehandlung von Attacken des hereditären Angioödems
(HAE) bei Erwachsenen und Jugendlichen ab 12 Jahren.*

Medizinischer Nutzen und
medizinischer Zusatznutzen,
Patientengruppen mit therapeutisch
bedeutsamem Zusatznutzen

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1 Binäre Analysen

1.1 Anzahl und Anteil der Attacken mit einem Beginn der Symptomverbesserung definiert als mindestens „ein wenig besser“ im PGI-C

1.1.1 Geschlecht

- PGI-C=Patient Global Impression of Change; CI=Confidence Interval
- Attack with beginning of symptom relief is defined as at least “a little better” (2 time points in a row without missing values in between) within 2, 4, 6, 8, 10, 12, 24, and 48 hours of the first IMP administration.
- Time to beginning of symptom relief is calculated as Date/time of first rating of “a little better” or higher (i.e. better or much better) which is immediately followed by another rating of “a little better” or higher (without possible missing values in between) – Date/time of first IMP administration.
- Attacks that did not have at least 2 post-baseline assessments within the analyzed period will be excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- †: p-value < 0.05.
- [1] P-value from Cochran-Mantel-Haenszel test.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS | SEX=MALE

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	19/29 (65.5)	8/25 (32.0)
RISK DIFFERENCE		
ESTIMATE	33.52	
EXACT 95% CI	(6.48, 57.05)	
RELATIVE RISK		
ESTIMATE	2.05	
EXACT 95% CI	(1.09, 4.75)	
ODDS RATIO		
ESTIMATE	4.04	
EXACT 95% CI	(1.14, 14.75)	
P-VALUE [1]	0.0150†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS | SEX=FEMALE

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	23/46 (50.0)	13/44 (29.5)
RISK DIFFERENCE		
ESTIMATE	20.45	
EXACT 95% CI	(-0.00, 40.38)	
RELATIVE RISK		
ESTIMATE	1.69	
EXACT 95% CI	(0.99, 3.17)	
ODDS RATIO		
ESTIMATE	2.38	
EXACT 95% CI	(0.92, 6.25)	
P-VALUE [1]	0.0490†	

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WITHIN 4 HOURS | SEX=MALE

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	25/30 (83.3)	11/25 (44.0)
RISK DIFFERENCE		
ESTIMATE	39.33	
EXACT 95% CI	(13.06, 61.63)	
RELATIVE RISK		
ESTIMATE	1.89	
EXACT 95% CI	(1.17, 3.46)	
ODDS RATIO		
ESTIMATE	6.36	
EXACT 95% CI	(1.60, 27.56)	
P-VALUE [1]	0.0025†	

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WITHIN 2 HOURS | SEX=FEMALE

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	33/48 (68.8)	22/48 (45.8)
RISK DIFFERENCE		
ESTIMATE	22.92	
EXACT 95% CI	(1.94, 42.44)	
RELATIVE RISK		
ESTIMATE	1.50	
EXACT 95% CI	(1.04, 2.29)	
ODDS RATIO		
ESTIMATE	2.60	
EXACT 95% CI	(1.05, 6.53)	
P-VALUE [1]	0.0240†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS | SEX=MALE

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	26/31 (83.9)	11/25 (44.0)
RISK DIFFERENCE		
ESTIMATE	39.87	
EXACT 95% CI	(14.22, 61.93)	
RELATIVE RISK		
ESTIMATE	1.91	
EXACT 95% CI	(1.17, 3.41)	
ODDS RATIO		
ESTIMATE	6.62	
EXACT 95% CI	(1.67, 28.57)	
P-VALUE [1]	0.0019†	

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WITHIN 6 HOURS | SEX=FEMALE

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	33/48 (68.8)	23/48 (47.9)
RISK DIFFERENCE		
ESTIMATE	20.83	
EXACT 95% CI	(-0.16, 40.51)	
RELATIVE RISK		
ESTIMATE	1.43	
EXACT 95% CI	(1.01, 2.13)	
ODDS RATIO		
ESTIMATE	2.39	
EXACT 95% CI	(0.96, 6.00)	
P-VALUE [1]	0.0395†	

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WITHIN 8 HOURS | SEX=MALE

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	26/31 (83.9)	12/25 (48.0)
RISK DIFFERENCE		
ESTIMATE	35.87	
EXACT 95% CI	(10.13, 58.56)	
RELATIVE RISK		
ESTIMATE	1.75	
EXACT 95% CI	(1.13, 3.10)	
ODDS RATIO		
ESTIMATE	5.63	
EXACT 95% CI	(1.42, 24.30)	
P-VALUE [1]	0.0046†	

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WITHIN 8 HOURS | SEX=FEMALE

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	34/48 (70.8)	28/48 (58.3)
RISK DIFFERENCE		
ESTIMATE	12.50	
EXACT 95% CI	(-8.51, 32.72)	
RELATIVE RISK		
ESTIMATE	1.21	
EXACT 95% CI	(0.90, 1.69)	
ODDS RATIO		
ESTIMATE	1.73	
EXACT 95% CI	(0.69, 4.43)	
P-VALUE [1]	0.2028	

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WITHIN 10 HOURS | SEX=MALE

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	27/31 (87.1)	12/25 (48.0)
RISK DIFFERENCE		
ESTIMATE	39.10	
EXACT 95% CI	(13.48, 61.31)	
RELATIVE RISK		
ESTIMATE	1.81	
EXACT 95% CI	(1.17, 3.17)	
ODDS RATIO		
ESTIMATE	7.31	
EXACT 95% CI	(1.72, 35.97)	
P-VALUE [1]	0.0017†	

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WITHIN 10 HOURS | SEX=FEMALE

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	36/48 (75.0)	29/48 (60.4)
RISK DIFFERENCE		
ESTIMATE	14.58	
EXACT 95% CI	(-6.44, 34.68)	
RELATIVE RISK		
ESTIMATE	1.24	
EXACT 95% CI	(0.93, 1.70)	
ODDS RATIO		
ESTIMATE	1.97	
EXACT 95% CI	(0.76, 5.20)	
P-VALUE [1]	0.1285	

1.1.2 Alter

- PGI-C=Patient Global Impression of Change; CI=Confidence Interval; NE=Not Evaluable
- Attack with beginning of symptom relief is defined as at least “a little better” (2 time points in a row without missing values in between) within 2, 4, 6, 8, 10, 12, 24, and 48 hours of the first IMP administration.
- Time to beginning of symptom relief is calculated as Date/time of first rating of “a little better” or higher (i.e. better or much better) which is immediately followed by another rating of “a little better” or higher (without possible missing values in between) – Date/time of first IMP administration.
- Attacks that did not have at least 2 post-baseline assessments within the analyzed period will be excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- †: p-value < 0.05.
- [1] P-value from Cochran-Mantel-Haenszel test.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS AGE GROUP= <18 YEARS		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/8 (50.0)	4/8 (50.0)
RISK DIFFERENCE		
ESTIMATE	0.00	
EXACT 95% CI	(-50.70, 50.70)	
RELATIVE RISK		
ESTIMATE	1.00	
EXACT 95% CI	(0.32, 3.17)	
ODDS RATIO		
ESTIMATE	1.00	
EXACT 95% CI	(0.10, 10.44)	
P-VALUE [1]	1.0000	

WITHIN 2 HOURS AGE GROUP= >=18 YEARS		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS AGE GROUP= >=18 YEARS		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	38/67 (56.7)	17/61 (27.9)
RISK DIFFERENCE		
ESTIMATE	28.85	
EXACT 95% CI	(11.61, 44.80)	
RELATIVE RISK		
ESTIMATE	2.04	
EXACT 95% CI	(1.27, 3.44)	
ODDS RATIO		
ESTIMATE	3.39	
EXACT 95% CI	(1.53, 7.63)	
P-VALUE [1]	0.0010†	

WITHIN 4 HOURS AGE GROUP= <18 YEARS		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	6/9 (66.7)	4/8 (50.0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS AGE GROUP= <18 YEARS		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
RISK DIFFERENCE		
ESTIMATE	16.67	
EXACT 95% CI	(-33.35, 60.45)	
RELATIVE RISK		
ESTIMATE	1.33	
EXACT 95% CI	(0.55, 4.52)	
ODDS RATIO		
ESTIMATE	2.00	
EXACT 95% CI	(0.19, 21.62)	
P-VALUE [1]	0.4990	

WITHIN 2 HOURS AGE GROUP= >=18 YEARS		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	52/69 (75.4)	29/65 (44.6)

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WITHIN 2 HOURS AGE GROUP= >=18 YEARS		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
RISK DIFFERENCE		
ESTIMATE	30.75	
EXACT 95% CI	(13.83, 46.13)	
RELATIVE RISK		
ESTIMATE	1.69	
EXACT 95% CI	(1.23, 2.47)	
ODDS RATIO		
ESTIMATE	3.80	
EXACT 95% CI	(1.72, 8.49)	
P-VALUE [1]	0.0003†	

WITHIN 6 HOURS AGE GROUP= <18 YEARS		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	6/9 (66.7)	4/8 (50.0)
RISK DIFFERENCE		

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS AGE GROUP= <18 YEARS		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ESTIMATE	16.67	
EXACT 95% CI	(-33.35, 60.45)	
RELATIVE RISK		
ESTIMATE	1.33	
EXACT 95% CI	(0.55, 4.52)	
ODDS RATIO		
ESTIMATE	2.00	
EXACT 95% CI	(0.19, 21.62)	
P-VALUE [1]	0.4990	

WITHIN 6 HOURS AGE GROUP= >=18 YEARS		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	53/70 (75.7)	30/65 (46.2)
RISK DIFFERENCE		
ESTIMATE	29.56	

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WITHIN 6 HOURS AGE GROUP= >=18 YEARS		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
EXACT 95% CI	(12.79, 45.10)	
RELATIVE RISK		
ESTIMATE	1.64	
EXACT 95% CI	(1.21, 2.37)	
ODDS RATIO		
ESTIMATE	3.64	
EXACT 95% CI	(1.65, 8.11)	
P-VALUE [1]	0.0004†	

WITHIN 8 HOURS AGE GROUP= <18 YEARS		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	6/9 (66.7)	5/8 (62.5)
RISK DIFFERENCE		
ESTIMATE	4.17	
EXACT 95% CI	(-44.14, 49.71)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS AGE GROUP= <18 YEARS		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
RELATIVE RISK		
ESTIMATE	1.07	
EXACT 95% CI	(0.46, 2.62)	
ODDS RATIO		
ESTIMATE	1.20	
EXACT 95% CI	(0.11, 13.47)	
P-VALUE [1]	0.8618	

WITHIN 8 HOURS AGE GROUP= >=18 YEARS		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	54/70 (77.1)	35/65 (53.8)
RISK DIFFERENCE		
ESTIMATE	23.30	
EXACT 95% CI	(6.44, 39.33)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS AGE GROUP= >=18 YEARS		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
RELATIVE RISK		
ESTIMATE	1.43	
EXACT 95% CI	(1.07, 1.92)	
ODDS RATIO		
ESTIMATE	2.89	
EXACT 95% CI	(1.30, 6.53)	
P-VALUE [1]	0.0045†	

WITHIN 10 HOURS AGE GROUP= <18 YEARS		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	8/9 (88.9)	5/8 (62.5)
RISK DIFFERENCE		
ESTIMATE	26.39	
EXACT 95% CI	(-23.62, 66.38)	
RELATIVE RISK		

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS AGE GROUP= <18 YEARS		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ESTIMATE	1.42	
EXACT 95% CI	(0.77, 3.36)	
ODDS RATIO		
ESTIMATE	4.80	
EXACT 95% CI	(0.26, 282.79)	
P-VALUE [1]	0.2142	

WITHIN 10 HOURS AGE GROUP= >=18 YEARS		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	55/70 (78.6)	36/65 (55.4)
RISK DIFFERENCE		
ESTIMATE	23.19	
EXACT 95% CI	(6.26, 39.23)	
RELATIVE RISK		
ESTIMATE	1.42	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS AGE GROUP= >=18 YEARS		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
EXACT 95% CI	(1.07, 1.89)	
ODDS RATIO		
ESTIMATE	2.95	
EXACT 95% CI	(1.31, 6.77)	
P-VALUE [1]	0.0042†	

WITHIN 12 HOURS AGE GROUP= <18 YEARS		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	8/9 (88.9)	5/9 (55.6)
RISK DIFFERENCE		
ESTIMATE	33.33	
EXACT 95% CI	(-18.02, 73.31)	
RELATIVE RISK		
ESTIMATE	1.60	
EXACT 95% CI	(0.84, 3.93)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS AGE GROUP= <18 YEARS		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ODDS RATIO		
ESTIMATE	6.40	
EXACT 95% CI	(0.41, 353.65)	
P-VALUE [1]	0.1250	
WITHIN 12 HOURS AGE GROUP= >=18 YEARS		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	58/70 (82.9)	36/65 (55.4)
RISK DIFFERENCE		
ESTIMATE	27.47	
EXACT 95% CI	(10.58, 43.23)	
RELATIVE RISK		
ESTIMATE	1.50	
EXACT 95% CI	(1.16, 1.98)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS AGE GROUP= >=18 YEARS		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ODDS RATIO		
ESTIMATE	3.89	
EXACT 95% CI	(1.66, 9.42)	
P-VALUE [1]	0.0005†	
WITHIN 24 HOURS AGE GROUP= <18 YEARS		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	10/10 (100.0)	6/9 (66.7)
RISK DIFFERENCE		
ESTIMATE	33.33	
EXACT 95% CI	(-13.39, 70.07)	
RELATIVE RISK		
ESTIMATE	1.50	
EXACT 95% CI	(0.95, 3.34)	
ODDS RATIO		

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WITHIN 24 HOURS AGE GROUP= <18 YEARS		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ESTIMATE	NE	
EXACT 95% CI	NE	
P-VALUE [1]	0.0528	

WITHIN 24 HOURS AGE GROUP= >=18 YEARS		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	59/70 (84.3)	42/66 (63.6)
RISK DIFFERENCE		
ESTIMATE	20.65	
EXACT 95% CI	(3.72, 36.77)	
RELATIVE RISK		
ESTIMATE	1.32	
EXACT 95% CI	(1.05, 1.69)	
ODDS RATIO		
ESTIMATE	3.06	

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WITHIN 24 HOURS AGE GROUP= >=18 YEARS		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
EXACT 95% CI	(1.27, 7.67)	
P-VALUE [1]	0.0061†	

WITHIN 48 HOURS AGE GROUP= <18 YEARS		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	10/10 (100.0)	6/9 (66.7)
RISK DIFFERENCE		
ESTIMATE	33.33	
EXACT 95% CI	(-13.39, 70.07)	
RELATIVE RISK		
ESTIMATE	1.50	
EXACT 95% CI	(0.95, 3.34)	
ODDS RATIO		
ESTIMATE	NE	
EXACT 95% CI	NE	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | AGE GROUP= <18 YEARS

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)

P-VALUE [1]	0.0528	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS AGE GROUP= >=18 YEARS		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	59/70 (84.3)	44/66 (66.7)
RISK DIFFERENCE		
ESTIMATE	17.62	
EXACT 95% CI	(0.61, 33.87)	
RELATIVE RISK		
ESTIMATE	1.26	
EXACT 95% CI	(1.03, 1.58)	
ODDS RATIO		
ESTIMATE	2.68	
EXACT 95% CI	(1.10, 6.76)	
P-VALUE [1]	0.0170†	

1.1.3 Region (Variante 1)

- PGI-C=Patient Global Impression of Change; CI=Confidence Interval
- Attack with beginning of symptom relief is defined as at least “a little better” (2 time points in a row without missing values in between) within 2, 4, 6, 8, 10, 12, 24, and 48 hours of the first IMP administration.
- Time to beginning of symptom relief is calculated as Date/time of first rating of “a little better” or higher (i.e. better or much better) which is immediately followed by another rating of “a little better” or higher (without possible missing values in between) – Date/time of first IMP administration.
- Attacks that did not have at least 2 post-baseline assessments within the analyzed period will be excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- †: p-value < 0.05.
- [1] P-value from Cochran-Mantel-Haenszel test.

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WITHIN 2 HOURS REGION 1=US		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	16/23 (69.6)	4/17 (23.5)
RISK DIFFERENCE		
ESTIMATE	46.04	
EXACT 95% CI	(14.81, 70.59)	
RELATIVE RISK		
ESTIMATE	2.96	
EXACT 95% CI	(1.23, 10.91)	
ODDS RATIO		
ESTIMATE	7.43	
EXACT 95% CI	(1.49, 41.00)	
P-VALUE [1]	0.0045†	

WITHIN 2 HOURS REGION 1=ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS REGION 1=ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	26/52 (50.0)	17/52 (32.7)
RISK DIFFERENCE		
ESTIMATE	17.31	
EXACT 95% CI	(-2.85, 36.45)	
RELATIVE RISK		
ESTIMATE	1.53	
EXACT 95% CI	(0.94, 2.67)	
ODDS RATIO		
ESTIMATE	2.06	
EXACT 95% CI	(0.87, 4.93)	
P-VALUE [1]	0.0745	

WITHIN 4 HOURS REGION 1=US		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	19/24 (79.2)	8/20 (40.0)

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WITHIN 4 HOURS REGION 1=US		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
RISK DIFFERENCE		
ESTIMATE	39.17	
EXACT 95% CI	(9.30, 63.92)	
RELATIVE RISK		
ESTIMATE	1.98	
EXACT 95% CI	(1.12, 4.43)	
ODDS RATIO		
ESTIMATE	5.70	
EXACT 95% CI	(1.28, 27.12)	
P-VALUE [1]	0.0086†	

WITHIN 4 HOURS REGION 1=ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	39/54 (72.2)	25/53 (47.2)

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WITHIN 4 HOURS REGION 1=ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
RISK DIFFERENCE		
ESTIMATE	25.05	
EXACT 95% CI	(5.48, 42.58)	
RELATIVE RISK		
ESTIMATE	1.53	
EXACT 95% CI	(1.07, 2.26)	
ODDS RATIO		
ESTIMATE	2.91	
EXACT 95% CI	(1.21, 7.06)	
P-VALUE [1]	0.0085†	

WITHIN 6 HOURS REGION 1=US		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	19/24 (79.2)	9/20 (45.0)
RISK DIFFERENCE		

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WITHIN 6 HOURS REGION 1=US		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ESTIMATE	34.17	
EXACT 95% CI	(4.25, 59.64)	
RELATIVE RISK		
ESTIMATE	1.76	
EXACT 95% CI	(1.07, 3.40)	
ODDS RATIO		
ESTIMATE	4.64	
EXACT 95% CI	(1.05, 21.92)	
P-VALUE [1]	0.0204†	

WITHIN 6 HOURS REGION 1=ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	40/55 (72.7)	25/53 (47.2)
RISK DIFFERENCE		
ESTIMATE	25.56	

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WITHIN 6 HOURS REGION 1=ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
EXACT 95% CI	(6.26, 42.92)	
RELATIVE RISK		
ESTIMATE	1.54	
EXACT 95% CI	(1.09, 2.28)	
ODDS RATIO		
ESTIMATE	2.99	
EXACT 95% CI	(1.25, 7.23)	
P-VALUE [1]	0.0069†	

WITHIN 8 HOURS REGION 1=US		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	19/24 (79.2)	12/20 (60.0)
RISK DIFFERENCE		
ESTIMATE	19.17	
EXACT 95% CI	(-10.98, 46.94)	

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WITHIN 8 HOURS REGION 1=US		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
RELATIVE RISK		
ESTIMATE	1.32	
EXACT 95% CI	(0.88, 2.34)	
ODDS RATIO		
ESTIMATE	2.53	
EXACT 95% CI	(0.56, 12.14)	
P-VALUE [1]	0.1702	

WITHIN 8 HOURS REGION 1=ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	41/55 (74.5)	28/53 (52.8)
RISK DIFFERENCE		
ESTIMATE	21.72	
EXACT 95% CI	(2.43, 39.05)	

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WITHIN 8 HOURS REGION 1=ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
RELATIVE RISK		
ESTIMATE	1.41	
EXACT 95% CI	(1.04, 1.97)	
ODDS RATIO		
ESTIMATE	2.61	
EXACT 95% CI	(1.08, 6.42)	
P-VALUE [1]	0.0194†	

WITHIN 10 HOURS REGION 1=US		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	19/24 (79.2)	12/20 (60.0)
RISK DIFFERENCE		
ESTIMATE	19.17	
EXACT 95% CI	(-10.98, 46.94)	
RELATIVE RISK		

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WITHIN 10 HOURS REGION 1=US		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ESTIMATE	1.32	
EXACT 95% CI	(0.88, 2.34)	
ODDS RATIO		
ESTIMATE	2.53	
EXACT 95% CI	(0.56, 12.14)	
P-VALUE [1]	0.1702	

WITHIN 10 HOURS REGION 1=ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	44/55 (80.0)	29/53 (54.7)
RISK DIFFERENCE		
ESTIMATE	25.28	
EXACT 95% CI	(6.19, 42.49)	
RELATIVE RISK		
ESTIMATE	1.46	

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WITHIN 10 HOURS REGION 1=ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
EXACT 95% CI	(1.09, 2.01)	
ODDS RATIO		
ESTIMATE	3.31	
EXACT 95% CI	(1.31, 8.62)	
P-VALUE [1]	0.0052†	

WITHIN 12 HOURS REGION 1=US		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	20/24 (83.3)	12/20 (60.0)
RISK DIFFERENCE		
ESTIMATE	23.33	
EXACT 95% CI	(-6.92, 50.63)	
RELATIVE RISK		
ESTIMATE	1.39	
EXACT 95% CI	(0.94, 2.52)	

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WITHIN 12 HOURS REGION 1=US		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ODDS RATIO		
ESTIMATE	3.33	
EXACT 95% CI	(0.69, 18.07)	
P-VALUE [1]	0.0871	

WITHIN 12 HOURS REGION 1=ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	46/55 (83.6)	29/54 (53.7)
RISK DIFFERENCE		
ESTIMATE	29.93	
EXACT 95% CI	(10.81, 46.37)	
RELATIVE RISK		
ESTIMATE	1.56	
EXACT 95% CI	(1.18, 2.15)	

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WITHIN 12 HOURS REGION 1=ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ODDS RATIO		
ESTIMATE	4.41	
EXACT 95% CI	(1.68, 12.16)	
P-VALUE [1]	0.0008†	
WITHIN 24 HOURS REGION 1=US		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	21/24 (87.5)	14/20 (70.0)
RISK DIFFERENCE		
ESTIMATE	17.50	
EXACT 95% CI	(-12.81, 45.50)	
RELATIVE RISK		
ESTIMATE	1.25	
EXACT 95% CI	(0.91, 1.98)	
ODDS RATIO		

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WITHIN 24 HOURS REGION 1=US		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ESTIMATE	3.00	
EXACT 95% CI	(0.52, 21.12)	
P-VALUE [1]	0.1566	

WITHIN 24 HOURS REGION 1=ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	48/56 (85.7)	34/55 (61.8)
RISK DIFFERENCE		
ESTIMATE	23.90	
EXACT 95% CI	(4.90, 40.74)	
RELATIVE RISK		
ESTIMATE	1.39	
EXACT 95% CI	(1.08, 1.83)	
ODDS RATIO		
ESTIMATE	3.71	

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WITHIN 24 HOURS REGION 1=ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
EXACT 95% CI	(1.36, 10.75)	
P-VALUE [1]	0.0043†	

WITHIN 48 HOURS REGION 1=US		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	21/24 (87.5)	14/20 (70.0)
RISK DIFFERENCE		
ESTIMATE	17.50	
EXACT 95% CI	(-12.81, 45.50)	
RELATIVE RISK		
ESTIMATE	1.25	
EXACT 95% CI	(0.91, 1.98)	
ODDS RATIO		
ESTIMATE	3.00	
EXACT 95% CI	(0.52, 21.12)	

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WITHIN 48 HOURS REGION 1=US		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE [1]	0.1566	
WITHIN 48 HOURS REGION 1=ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	48/56 (85.7)	36/55 (65.5)
RISK DIFFERENCE		
ESTIMATE	20.26	
EXACT 95% CI	(1.25, 37.37)	
RELATIVE RISK		
ESTIMATE	1.31	
EXACT 95% CI	(1.05, 1.69)	
ODDS RATIO		
ESTIMATE	3.17	
EXACT 95% CI	(1.15, 9.26)	

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WITHIN 48 HOURS REGION 1=ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE [1]	0.0133†	

1.1.4 Region (Variante 2)

- Time to beginning of symptom relief is calculated as Date/time of first rating of “a little better” or higher (i.e. better or much better) which is immediately followed by another rating of “a little better” or higher (without possible missing values in between) – Date/time of first IMP administration.
- Attacks that did not have at least 2 post-baseline assessments within the analyzed period will be excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- †: p-value < 0.05.
- [1] P-value from Cochran-Mantel-Haenszel test.

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WITHIN 2 HOURS REGION 2=NORTH AMERICA		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	16/23 (69.6)	4/17 (23.5)
RISK DIFFERENCE		
ESTIMATE	46.04	
EXACT 95% CI	(14.81, 70.59)	
RELATIVE RISK		
ESTIMATE	2.96	
EXACT 95% CI	(1.23, 10.91)	
ODDS RATIO		
ESTIMATE	7.43	
EXACT 95% CI	(1.49, 41.00)	
P-VALUE [1]	0.0045†	

WITHIN 2 HOURS REGION 2=EUROPE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS REGION 2=EUROPE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	18/39 (46.2)	13/41 (31.7)
RISK DIFFERENCE		
ESTIMATE	14.45	
EXACT 95% CI	(-8.15, 35.25)	
RELATIVE RISK		
ESTIMATE	1.46	
EXACT 95% CI	(0.82, 2.83)	
ODDS RATIO		
ESTIMATE	1.85	
EXACT 95% CI	(0.68, 5.08)	
P-VALUE [1]	0.1877	

WITHIN 2 HOURS REGION 2=ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	8/13 (61.5)	4/11 (36.4)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS REGION 2=ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
RISK DIFFERENCE		
ESTIMATE	25.17	
EXACT 95% CI	(-16.66, 61.13)	
RELATIVE RISK		
ESTIMATE	1.69	
EXACT 95% CI	(0.71, 6.77)	
ODDS RATIO		
ESTIMATE	2.80	
EXACT 95% CI	(0.41, 20.26)	
P-VALUE [1]	0.2289	
WITHIN 4 HOURS REGION 2=NORTH AMERICA		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	19/24 (79.2)	8/20 (40.0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS REGION 2=NORTH AMERICA		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
RISK DIFFERENCE		
ESTIMATE	39.17	
EXACT 95% CI	(9.30, 63.92)	
RELATIVE RISK		
ESTIMATE	1.98	
EXACT 95% CI	(1.12, 4.43)	
ODDS RATIO		
ESTIMATE	5.70	
EXACT 95% CI	(1.28, 27.12)	
P-VALUE [1]	0.0086†	

WITHIN 4 HOURS REGION 2=EUROPE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	27/40 (67.5)	20/42 (47.6)
RISK DIFFERENCE		

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS REGION 2=EUROPE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ESTIMATE	19.88	
EXACT 95% CI	(-1.85, 40.79)	
RELATIVE RISK		
ESTIMATE	1.42	
EXACT 95% CI	(0.97, 2.19)	
ODDS RATIO		
ESTIMATE	2.28	
EXACT 95% CI	(0.85, 6.19)	
P-VALUE [1]	0.0706	

WITHIN 4 HOURS REGION 2=ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	12/14 (85.7)	5/11 (45.5)
RISK DIFFERENCE		
ESTIMATE	40.26	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS REGION 2=ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
EXACT 95% CI	(0.17, 71.90)	
RELATIVE RISK		
ESTIMATE	1.89	
EXACT 95% CI	(1.01, 5.81)	
ODDS RATIO		
ESTIMATE	7.20	
EXACT 95% CI	(0.82, 88.91)	
P-VALUE [1]	0.0358†	

WITHIN 6 HOURS REGION 2=NORTH AMERICA		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	19/24 (79.2)	9/20 (45.0)
RISK DIFFERENCE		
ESTIMATE	34.17	
EXACT 95% CI	(4.25, 59.64)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS REGION 2=NORTH AMERICA		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
RELATIVE RISK		
ESTIMATE	1.76	
EXACT 95% CI	(1.07, 3.40)	
ODDS RATIO		
ESTIMATE	4.64	
EXACT 95% CI	(1.05, 21.92)	
P-VALUE [1]	0.0204†	

WITHIN 6 HOURS REGION 2=EUROPE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	27/40 (67.5)	20/42 (47.6)
RISK DIFFERENCE		
ESTIMATE	19.88	
EXACT 95% CI	(-1.85, 40.79)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS REGION 2=EUROPE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
RELATIVE RISK		
ESTIMATE	1.42	
EXACT 95% CI	(0.97, 2.19)	
ODDS RATIO		
ESTIMATE	2.28	
EXACT 95% CI	(0.85, 6.19)	
P-VALUE [1]	0.0706	

WITHIN 2 HOURS REGION 2=ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	13/15 (86.7)	5/11 (45.5)
RISK DIFFERENCE		
ESTIMATE	41.21	
EXACT 95% CI	(2.03, 72.33)	
RELATIVE RISK		

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS REGION 2=ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ESTIMATE	1.91	
EXACT 95% CI	(1.02, 6.47)	
ODDS RATIO		
ESTIMATE	7.80	
EXACT 95% CI	(0.89, 95.56)	
P-VALUE [1]	0.0274†	

WITHIN 8 HOURS REGION 2=NORTH AMERICA		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	19/24 (79.2)	12/20 (60.0)
RISK DIFFERENCE		
ESTIMATE	19.17	
EXACT 95% CI	(-10.98, 46.94)	
RELATIVE RISK		
ESTIMATE	1.32	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS REGION 2=NORTH AMERICA		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
EXACT 95% CI	(0.88, 2.34)	
ODDS RATIO		
ESTIMATE	2.53	
EXACT 95% CI	(0.56, 12.14)	
P-VALUE [1]	0.1702	

WITHIN 8 HOURS REGION 2=EUROPE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	28/40 (70.0)	22/42 (52.4)
RISK DIFFERENCE		
ESTIMATE	17.62	
EXACT 95% CI	(-3.77, 38.66)	
RELATIVE RISK		
ESTIMATE	1.34	
EXACT 95% CI	(0.93, 2.03)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS REGION 2=EUROPE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ODDS RATIO		
ESTIMATE	2.12	
EXACT 95% CI	(0.78, 5.84)	
P-VALUE [1]	0.1042	
WITHIN 2 HOURS REGION 2=ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	13/15 (86.7)	6/11 (54.5)
RISK DIFFERENCE		
ESTIMATE	32.12	
EXACT 95% CI	(-7.46, 65.10)	
RELATIVE RISK		
ESTIMATE	1.59	
EXACT 95% CI	(0.94, 3.99)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS REGION 2=ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ODDS RATIO		
ESTIMATE	5.42	
EXACT 95% CI	(0.61, 67.68)	
P-VALUE [1]	0.0736	

WITHIN 10 HOURS REGION 2=NORTH AMERICA		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	19/24 (79.2)	12/20 (60.0)
RISK DIFFERENCE		
ESTIMATE	19.17	
EXACT 95% CI	(-10.98, 46.94)	
RELATIVE RISK		
ESTIMATE	1.32	
EXACT 95% CI	(0.88, 2.34)	
ODDS RATIO		

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS REGION 2=NORTH AMERICA		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ESTIMATE	2.53	
EXACT 95% CI	(0.56, 12.14)	
P-VALUE [1]	0.1702	

WITHIN 10 HOURS REGION 2=EUROPE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	31/40 (77.5)	22/42 (52.4)
RISK DIFFERENCE		
ESTIMATE	25.12	
EXACT 95% CI	(3.96, 45.44)	
RELATIVE RISK		
ESTIMATE	1.48	
EXACT 95% CI	(1.06, 2.16)	
ODDS RATIO		
ESTIMATE	3.13	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS REGION 2=EUROPE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
EXACT 95% CI	(1.10, 9.27)	
P-VALUE [1]	0.0181†	

WITHIN 10 HOURS REGION 2=ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	13/15 (86.7)	7/11 (63.6)
RISK DIFFERENCE		
ESTIMATE	23.03	
EXACT 95% CI	(-16.51, 57.32)	
RELATIVE RISK		
ESTIMATE	1.36	
EXACT 95% CI	(0.85, 2.80)	
ODDS RATIO		
ESTIMATE	3.71	
EXACT 95% CI	(0.39, 48.31)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS REGION 2=ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE [1]	0.1769	
WITHIN 12 HOURS REGION 2=NORTH AMERICA		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	20/24 (83.3)	12/20 (60.0)
RISK DIFFERENCE		
ESTIMATE	23.33	
EXACT 95% CI	(-6.92, 50.63)	
RELATIVE RISK		
ESTIMATE	1.39	
EXACT 95% CI	(0.94, 2.52)	
ODDS RATIO		
ESTIMATE	3.33	
EXACT 95% CI	(0.69, 18.07)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS REGION 2=NORTH AMERICA		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE [1]	0.0871	
WITHIN 12 HOURS REGION 2=EUROPE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	33/40 (82.5)	22/42 (52.4)
RISK DIFFERENCE		
ESTIMATE	30.12	
EXACT 95% CI	(8.97, 49.87)	
RELATIVE RISK		
ESTIMATE	1.58	
EXACT 95% CI	(1.11, 2.31)	
ODDS RATIO		
ESTIMATE	4.29	
EXACT 95% CI	(1.41, 13.89)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS REGION 2=EUROPE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE [1]	0.0039†	
WITHIN 2 HOURS REGION 2=ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	13/15 (86.7)	7/12 (58.3)
RISK DIFFERENCE		
ESTIMATE	28.33	
EXACT 95% CI	(-10.35, 61.26)	
RELATIVE RISK		
ESTIMATE	1.49	
EXACT 95% CI	(0.91, 3.07)	
ODDS RATIO		
ESTIMATE	4.64	
EXACT 95% CI	(0.54, 57.35)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS REGION 2=ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE [1]	0.1014	
WITHIN 24 HOURS REGION 2=NORTH AMERICA		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	21/24 (87.5)	14/20 (70.0)
RISK DIFFERENCE		
ESTIMATE	17.50	
EXACT 95% CI	(-12.81, 45.50)	
RELATIVE RISK		
ESTIMATE	1.25	
EXACT 95% CI	(0.91, 1.98)	
ODDS RATIO		
ESTIMATE	3.00	
EXACT 95% CI	(0.52, 21.12)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS REGION 2=NORTH AMERICA		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE [1]	0.1566	
WITHIN 24 HOURS REGION 2=EUROPE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	35/41 (85.4)	25/43 (58.1)
RISK DIFFERENCE		
ESTIMATE	27.23	
EXACT 95% CI	(6.04, 46.86)	
RELATIVE RISK		
ESTIMATE	1.47	
EXACT 95% CI	(1.09, 2.09)	
ODDS RATIO		
ESTIMATE	4.20	
EXACT 95% CI	(1.33, 14.60)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS REGION 2=EUROPE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE [1]	0.0061†	
WITHIN 24 HOURS REGION 2=ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	13/15 (86.7)	9/12 (75.0)
RISK DIFFERENCE		
ESTIMATE	11.67	
EXACT 95% CI	(-26.98, 47.86)	
RELATIVE RISK		
ESTIMATE	1.16	
EXACT 95% CI	(0.75, 2.13)	
ODDS RATIO		
ESTIMATE	2.17	
EXACT 95% CI	(0.20, 30.09)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS REGION 2=ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE [1]	0.4467	
WITHIN 48 HOURS REGION 2=NORTH AMERICA		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	21/24 (87.5)	14/20 (70.0)
RISK DIFFERENCE		
ESTIMATE	17.50	
EXACT 95% CI	(-12.81, 45.50)	
RELATIVE RISK		
ESTIMATE	1.25	
EXACT 95% CI	(0.91, 1.98)	
ODDS RATIO		
ESTIMATE	3.00	
EXACT 95% CI	(0.52, 21.12)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS REGION 2=NORTH AMERICA		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE [1]	0.1566	
WITHIN 48 HOURS REGION 2=EUROPE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	35/41 (85.4)	27/43 (62.8)
RISK DIFFERENCE		
ESTIMATE	22.58	
EXACT 95% CI	(1.18, 42.52)	
RELATIVE RISK		
ESTIMATE	1.36	
EXACT 95% CI	(1.04, 1.86)	
ODDS RATIO		
ESTIMATE	3.46	
EXACT 95% CI	(1.08, 12.12)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS REGION 2=EUROPE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE [1]	0.0194†	
WITHIN 48 HOURS REGION 2=ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	13/15 (86.7)	9/12 (75.0)
RISK DIFFERENCE		
ESTIMATE	11.67	
EXACT 95% CI	(-26.98, 47.86)	
RELATIVE RISK		
ESTIMATE	1.16	
EXACT 95% CI	(0.75, 2.13)	
ODDS RATIO		
ESTIMATE	2.17	
EXACT 95% CI	(0.20, 30.09)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS REGION 2=ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE [1]	0.4467	

1.1.5 Prophylaxe-Status (Variante 1)

- PGI-C=Patient Global Impression of Change; CI=Confidence Interval
- Attack with beginning of symptom relief is defined as at least “a little better” (2 time points in a row without missing values in between) within 2, 4, 6, 8, 10, 12, 24, and 48 hours of the first IMP administration.
- Time to beginning of symptom relief is calculated as Date/time of first rating of “a little better” or higher (i.e. better or much better) which is immediately followed by another rating of “a little better” or higher (without possible missing values in between) – Date/time of first IMP administration.
- Attacks that did not have at least 2 post-baseline assessments within the analyzed period will be excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- †: p-value < 0.05.
- [1] P-value from Cochran-Mantel-Haenszel test.

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WITHIN 2 HOURS PROPHYLACTIC TREATMENT STATUS 1=ON PROPHYLACTIC TREATMENT		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	8/17 (47.1)	3/15 (20.0)
RISK DIFFERENCE		
ESTIMATE	27.06	
EXACT 95% CI	(-7.05, 57.99)	
RELATIVE RISK		
ESTIMATE	2.35	
EXACT 95% CI	(0.81, 12.89)	
ODDS RATIO		
ESTIMATE	3.56	
EXACT 95% CI	(0.60, 25.83)	
P-VALUE [1]	0.1134	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS PROPHYLACTIC TREATMENT STATUS 1=ON DEMAND		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	34/58 (58.6)	18/54 (33.3)
RISK DIFFERENCE		
ESTIMATE	25.29	
EXACT 95% CI	(6.72, 42.74)	
RELATIVE RISK		
ESTIMATE	1.76	
EXACT 95% CI	(1.08, 3.01)	
ODDS RATIO		
ESTIMATE	2.83	
EXACT 95% CI	(1.23, 6.59)	
P-VALUE [1]	0.0076†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

 WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 1=ON
 PROPHYLACTIC TREATMENT

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	14/18 (77.8)	8/18 (44.4)
RISK DIFFERENCE		
ESTIMATE	33.33	
EXACT 95% CI	(-1.94, 62.89)	
RELATIVE RISK		
ESTIMATE	1.75	
EXACT 95% CI	(1.00, 3.62)	
ODDS RATIO		
ESTIMATE	4.38	
EXACT 95% CI	(0.85, 24.85)	
P-VALUE [1]	0.0431†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS PROPHYLACTIC TREATMENT STATUS 1=ON DEMAND		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	44/60 (73.3)	25/55 (45.5)
RISK DIFFERENCE		
ESTIMATE	27.88	
EXACT 95% CI	(9.57, 44.72)	
RELATIVE RISK		
ESTIMATE	1.61	
EXACT 95% CI	(1.13, 2.45)	
ODDS RATIO		
ESTIMATE	3.30	
EXACT 95% CI	(1.41, 7.78)	
P-VALUE [1]	0.0024†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS PROPHYLACTIC TREATMENT STATUS 1=ON PROPHYLACTIC TREATMENT		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	14/18 (77.8)	9/18 (50.0)
RISK DIFFERENCE		
ESTIMATE	27.78	
EXACT 95% CI	(-7.56, 58.36)	
RELATIVE RISK		
ESTIMATE	1.56	
EXACT 95% CI	(0.93, 3.05)	
ODDS RATIO		
ESTIMATE	3.50	
EXACT 95% CI	(0.68, 19.88)	
P-VALUE [1]	0.0871	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS PROPHYLACTIC TREATMENT STATUS 1=ON DEMAND		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	45/61 (73.8)	25/55 (45.5)
RISK DIFFERENCE		
ESTIMATE	28.32	
EXACT 95% CI	(10.18, 45.07)	
RELATIVE RISK		
ESTIMATE	1.62	
EXACT 95% CI	(1.13, 2.42)	
ODDS RATIO		
ESTIMATE	3.38	
EXACT 95% CI	(1.45, 7.95)	
P-VALUE [1]	0.0019†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

 WITHIN 8 HOURS | PROPHYLACTIC TREATMENT STATUS 1=ON
 PROPHYLACTIC TREATMENT

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	14/18 (77.8)	12/18 (66.7)
RISK DIFFERENCE		
ESTIMATE	11.11	
EXACT 95% CI	(-23.80, 44.13)	
RELATIVE RISK		
ESTIMATE	1.17	
EXACT 95% CI	(0.73, 1.91)	
ODDS RATIO		
ESTIMATE	1.75	
EXACT 95% CI	(0.32, 10.43)	
P-VALUE [1]	0.4631	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS PROPHYLACTIC TREATMENT STATUS 1=ON DEMAND		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	46/61 (75.4)	28/55 (50.9)
RISK DIFFERENCE		
ESTIMATE	24.50	
EXACT 95% CI	(6.45, 41.59)	
RELATIVE RISK		
ESTIMATE	1.48	
EXACT 95% CI	(1.07, 2.12)	
ODDS RATIO		
ESTIMATE	2.96	
EXACT 95% CI	(1.26, 7.04)	
P-VALUE [1]	0.0063†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS PROPHYLACTIC TREATMENT STATUS 1=ON PROPHYLACTIC TREATMENT		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	14/18 (77.8)	13/18 (72.2)
RISK DIFFERENCE		
ESTIMATE	5.56	
EXACT 95% CI	(-29.03, 39.19)	
RELATIVE RISK		
ESTIMATE	1.08	
EXACT 95% CI	(0.70, 1.74)	
ODDS RATIO		
ESTIMATE	1.35	
EXACT 95% CI	(0.23, 8.33)	
P-VALUE [1]	0.7043	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS PROPHYLACTIC TREATMENT STATUS 1=ON DEMAND		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	49/61 (80.3)	28/55 (50.9)
RISK DIFFERENCE		
ESTIMATE	29.42	
EXACT 95% CI	(11.44, 46.15)	
RELATIVE RISK		
ESTIMATE	1.58	
EXACT 95% CI	(1.17, 2.27)	
ODDS RATIO		
ESTIMATE	3.94	
EXACT 95% CI	(1.61, 9.85)	
P-VALUE [1]	0.0009†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

 WITHIN 12 HOURS | PROPHYLACTIC TREATMENT STATUS 1=ON
 PROPHYLACTIC TREATMENT

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	15/18 (83.3)	13/18 (72.2)
RISK DIFFERENCE		
ESTIMATE	11.11	
EXACT 95% CI	(-23.80, 44.13)	
RELATIVE RISK		
ESTIMATE	1.15	
EXACT 95% CI	(0.77, 1.84)	
ODDS RATIO		
ESTIMATE	1.92	
EXACT 95% CI	(0.30, 14.58)	
P-VALUE [1]	0.4292	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS PROPHYLACTIC TREATMENT STATUS 1=ON DEMAND		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	51/61 (83.6)	28/56 (50.0)
RISK DIFFERENCE		
ESTIMATE	33.61	
EXACT 95% CI	(15.89, 49.96)	
RELATIVE RISK		
ESTIMATE	1.67	
EXACT 95% CI	(1.25, 2.42)	
ODDS RATIO		
ESTIMATE	5.10	
EXACT 95% CI	(2.02, 13.40)	
P-VALUE [1]	0.0001†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS PROPHYLACTIC TREATMENT STATUS 1=ON PROPHYLACTIC TREATMENT		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	16/18 (88.9)	13/18 (72.2)
RISK DIFFERENCE		
ESTIMATE	16.67	
EXACT 95% CI	(-18.49, 48.97)	
RELATIVE RISK		
ESTIMATE	1.23	
EXACT 95% CI	(0.84, 1.91)	
ODDS RATIO		
ESTIMATE	3.08	
EXACT 95% CI	(0.40, 36.23)	
P-VALUE [1]	0.2129	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS PROPHYLACTIC TREATMENT STATUS 1=ON DEMAND		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	53/62 (85.5)	35/57 (61.4)
RISK DIFFERENCE		
ESTIMATE	24.08	
EXACT 95% CI	(6.01, 40.91)	
RELATIVE RISK		
ESTIMATE	1.39	
EXACT 95% CI	(1.08, 1.86)	
ODDS RATIO		
ESTIMATE	3.70	
EXACT 95% CI	(1.42, 10.15)	
P-VALUE [1]	0.0029†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS PROPHYLACTIC TREATMENT STATUS 1=ON PROPHYLACTIC TREATMENT		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	16/18 (88.9)	13/18 (72.2)
RISK DIFFERENCE		
ESTIMATE	16.67	
EXACT 95% CI	(-18.49, 48.97)	
RELATIVE RISK		
ESTIMATE	1.23	
EXACT 95% CI	(0.84, 1.91)	
ODDS RATIO		
ESTIMATE	3.08	
EXACT 95% CI	(0.40, 36.23)	
P-VALUE [1]	0.2129	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS PROPHYLACTIC TREATMENT STATUS 1=ON DEMAND		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	53/62 (85.5)	37/57 (64.9)
RISK DIFFERENCE		
ESTIMATE	20.57	
EXACT 95% CI	(2.44, 37.56)	
RELATIVE RISK		
ESTIMATE	1.32	
EXACT 95% CI	(1.05, 1.70)	
ODDS RATIO		
ESTIMATE	3.18	
EXACT 95% CI	(1.21, 8.80)	
P-VALUE [1]	0.0093†	

1.1.6 Prophylaxe-Status (Variante 2)

- PGI-C=Patient Global Impression of Change; CI=Confidence Interval; NE=Not Evaluable
- Attack with beginning of symptom relief is defined as at least “a little better” (2 time points in a row without missing values in between) within 2, 4, 6, 8, 10, 12, 24, and 48 hours of the first IMP administration.
- Time to beginning of symptom relief is calculated as Date/time of first rating of “a little better” or higher (i.e. better or much better) which is immediately followed by another rating of “a little better” or higher (without possible missing values in between) – Date/time of first IMP administration.
- Attacks that did not have at least 2 post-baseline assessments within the analyzed period will be excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- †: p-value < 0.05.
- [1] P-value from Cochran-Mantel-Haenszel test.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS PROPHYLACTIC TREATMENT STATUS 2 = ON KALLIKREIN		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/12 (33.3)	2/11 (18.2)
RISK DIFFERENCE		
ESTIMATE	15.15	
EXACT 95% CI	(-23.46, 53.76)	
RELATIVE RISK		
ESTIMATE	1.83	
EXACT 95% CI	(0.39, 13.23)	
ODDS RATIO		
ESTIMATE	2.25	
EXACT 95% CI	(0.23, 30.26)	
P-VALUE [1]	0.4188	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS PROPHYLACTIC TREATMENT STATUS 2 = ON OTHER		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/5 (80.0)	1/4 (25.0)
RISK DIFFERENCE		
ESTIMATE	55.00	
EXACT 95% CI	(-17.95, 93.71)	
RELATIVE RISK		
ESTIMATE	3.20	
EXACT 95% CI	(0.66, 92.34)	
ODDS RATIO		
ESTIMATE	12.00	
EXACT 95% CI	(0.31, 782.99)	
P-VALUE [1]	0.1198	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	34/58 (58.6)	18/54 (33.3)
RISK DIFFERENCE		
ESTIMATE	25.29	
EXACT 95% CI	(6.72, 42.74)	
RELATIVE RISK		
ESTIMATE	1.76	
EXACT 95% CI	(1.08, 3.01)	
ODDS RATIO		
ESTIMATE	2.83	
EXACT 95% CI	(1.23, 6.59)	
P-VALUE [1]	0.0076†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS PROPHYLACTIC TREATMENT STATUS 2 = ON KALLIKREIN		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/13 (69.2)	6/14 (42.9)
RISK DIFFERENCE		
ESTIMATE	26.37	
EXACT 95% CI	(-12.70, 60.68)	
RELATIVE RISK		
ESTIMATE	1.62	
EXACT 95% CI	(0.79, 3.95)	
ODDS RATIO		
ESTIMATE	3.00	
EXACT 95% CI	(0.49, 19.82)	
P-VALUE [1]	0.1763	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS PROPHYLACTIC TREATMENT STATUS 2 = ON OTHER		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/5 (100.0)	2/4 (50.0)
RISK DIFFERENCE		
ESTIMATE	50.00	
EXACT 95% CI	(-20.86, 93.24)	
RELATIVE RISK		
ESTIMATE	2.00	
EXACT 95% CI	(0.83, 14.80)	
ODDS RATIO		
ESTIMATE	NE	
EXACT 95% CI	NE	
P-VALUE [1]	0.0910	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	44/60 (73.3)	25/55 (45.5)
RISK DIFFERENCE		
ESTIMATE	27.88	
EXACT 95% CI	(9.57, 44.72)	
RELATIVE RISK		
ESTIMATE	1.61	
EXACT 95% CI	(1.13, 2.45)	
ODDS RATIO		
ESTIMATE	3.30	
EXACT 95% CI	(1.41, 7.78)	
P-VALUE [1]	0.0024†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS PROPHYLACTIC TREATMENT STATUS 2 = ON KALLIKREIN		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/13 (69.2)	7/14 (50.0)
RISK DIFFERENCE		
ESTIMATE	19.23	
EXACT 95% CI	(-19.21, 54.90)	
RELATIVE RISK		
ESTIMATE	1.38	
EXACT 95% CI	(0.70, 3.20)	
ODDS RATIO		
ESTIMATE	2.25	
EXACT 95% CI	(0.37, 14.80)	
P-VALUE [1]	0.3187	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS PROPHYLACTIC TREATMENT STATUS 2 = ON OTHER		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/5 (100.0)	2/4 (50.0)
RISK DIFFERENCE		
ESTIMATE	50.00	
EXACT 95% CI	(-20.86, 93.24)	
RELATIVE RISK		
ESTIMATE	2.00	
EXACT 95% CI	(0.83, 14.80)	
ODDS RATIO		
ESTIMATE	NE	
EXACT 95% CI	NE	
P-VALUE [1]	0.0910	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	45/61 (73.8)	25/55 (45.5)
RISK DIFFERENCE		
ESTIMATE	28.32	
EXACT 95% CI	(10.18, 45.07)	
RELATIVE RISK		
ESTIMATE	1.62	
EXACT 95% CI	(1.13, 2.42)	
ODDS RATIO		
ESTIMATE	3.38	
EXACT 95% CI	(1.45, 7.95)	
P-VALUE [1]	0.0019†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS PROPHYLACTIC TREATMENT STATUS 2 = ON KALLIKREIN		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/13 (69.2)	10/14 (71.4)
RISK DIFFERENCE		
ESTIMATE	-2.20	
EXACT 95% CI	(-37.57, 36.18)	
RELATIVE RISK		
ESTIMATE	0.97	
EXACT 95% CI	(0.53, 1.76)	
ODDS RATIO		
ESTIMATE	0.90	
EXACT 95% CI	(0.13, 6.47)	
P-VALUE [1]	0.9024	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS PROPHYLACTIC TREATMENT STATUS 2 = ON OTHER		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/5 (100.0)	2/4 (50.0)
RISK DIFFERENCE		
ESTIMATE	50.00	
EXACT 95% CI	(-20.86, 93.24)	
RELATIVE RISK		
ESTIMATE	2.00	
EXACT 95% CI	(0.83, 14.80)	
ODDS RATIO		
ESTIMATE	NE	
EXACT 95% CI	NE	
P-VALUE [1]	0.0910	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	46/61 (75.4)	28/55 (50.9)
RISK DIFFERENCE		
ESTIMATE	24.50	
EXACT 95% CI	(6.45, 41.59)	
RELATIVE RISK		
ESTIMATE	1.48	
EXACT 95% CI	(1.07, 2.12)	
ODDS RATIO		
ESTIMATE	2.96	
EXACT 95% CI	(1.26, 7.04)	
P-VALUE [1]	0.0063†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS PROPHYLACTIC TREATMENT STATUS 2 = ON KALLIKREIN		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/13 (69.2)	11/14 (78.6)
RISK DIFFERENCE		
ESTIMATE	-9.34	
EXACT 95% CI	(-43.34, 29.48)	
RELATIVE RISK		
ESTIMATE	0.88	
EXACT 95% CI	(0.47, 1.46)	
ODDS RATIO		
ESTIMATE	0.61	
EXACT 95% CI	(0.07, 4.81)	
P-VALUE [1]	0.5871	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS PROPHYLACTIC TREATMENT STATUS 2 = ON OTHER		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/5 (100.0)	2/4 (50.0)
RISK DIFFERENCE		
ESTIMATE	50.00	
EXACT 95% CI	(-20.86, 93.24)	
RELATIVE RISK		
ESTIMATE	2.00	
EXACT 95% CI	(0.83, 14.80)	
ODDS RATIO		
ESTIMATE	NE	
EXACT 95% CI	NE	
P-VALUE [1]	0.0910	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	49/61 (80.3)	28/55 (50.9)
RISK DIFFERENCE		
ESTIMATE	29.42	
EXACT 95% CI	(11.44, 46.15)	
RELATIVE RISK		
ESTIMATE	1.58	
EXACT 95% CI	(1.17, 2.27)	
ODDS RATIO		
ESTIMATE	3.94	
EXACT 95% CI	(1.61, 9.85)	
P-VALUE [1]	0.0009†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS PROPHYLACTIC TREATMENT STATUS 2 = ON KALLIKREIN		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	10/13 (76.9)	11/14 (78.6)
RISK DIFFERENCE		
ESTIMATE	-1.65	
EXACT 95% CI	(-36.28, 36.26)	
RELATIVE RISK		
ESTIMATE	0.98	
EXACT 95% CI	(0.59, 1.59)	
ODDS RATIO		
ESTIMATE	0.91	
EXACT 95% CI	(0.10, 8.48)	
P-VALUE [1]	0.9195	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS PROPHYLACTIC TREATMENT STATUS 2 = ON OTHER		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/5 (100.0)	2/4 (50.0)
RISK DIFFERENCE		
ESTIMATE	50.00	
EXACT 95% CI	(-20.86, 93.24)	
RELATIVE RISK		
ESTIMATE	2.00	
EXACT 95% CI	(0.83, 14.80)	
ODDS RATIO		
ESTIMATE	NE	
EXACT 95% CI	NE	
P-VALUE [1]	0.0910	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	51/61 (83.6)	28/56 (50.0)
RISK DIFFERENCE		
ESTIMATE	33.61	
EXACT 95% CI	(15.89, 49.96)	
RELATIVE RISK		
ESTIMATE	1.67	
EXACT 95% CI	(1.25, 2.42)	
ODDS RATIO		
ESTIMATE	5.10	
EXACT 95% CI	(2.02, 13.40)	
P-VALUE [1]	0.0001†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS PROPHYLACTIC TREATMENT STATUS 2 = ON KALLIKREIN		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	11/13 (84.6)	11/14 (78.6)
RISK DIFFERENCE		
ESTIMATE	6.04	
EXACT 95% CI	(-29.52, 42.82)	
RELATIVE RISK		
ESTIMATE	1.08	
EXACT 95% CI	(0.67, 1.76)	
ODDS RATIO		
ESTIMATE	1.50	
EXACT 95% CI	(0.14, 21.00)	
P-VALUE [1]	0.6918	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS PROPHYLACTIC TREATMENT STATUS 2 = ON OTHER		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/5 (100.0)	2/4 (50.0)
RISK DIFFERENCE		
ESTIMATE	50.00	
EXACT 95% CI	(-20.86, 93.24)	
RELATIVE RISK		
ESTIMATE	2.00	
EXACT 95% CI	(0.83, 14.80)	
ODDS RATIO		
ESTIMATE	NE	
EXACT 95% CI	NE	
P-VALUE [1]	0.0910	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	53/62 (85.5)	35/57 (61.4)
RISK DIFFERENCE		
ESTIMATE	24.08	
EXACT 95% CI	(6.01, 40.91)	
RELATIVE RISK		
ESTIMATE	1.39	
EXACT 95% CI	(1.08, 1.86)	
ODDS RATIO		
ESTIMATE	3.70	
EXACT 95% CI	(1.42, 10.15)	
P-VALUE [1]	0.0029†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS PROPHYLACTIC TREATMENT STATUS 2 = ON KALLIKREIN		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	11/13 (84.6)	11/14 (78.6)
RISK DIFFERENCE		
ESTIMATE	6.04	
EXACT 95% CI	(-29.52, 42.82)	
RELATIVE RISK		
ESTIMATE	1.08	
EXACT 95% CI	(0.67, 1.76)	
ODDS RATIO		
ESTIMATE	1.50	
EXACT 95% CI	(0.14, 21.00)	
P-VALUE [1]	0.6918	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS PROPHYLACTIC TREATMENT STATUS 2 = ON OTHER		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/5 (100.0)	2/4 (50.0)
RISK DIFFERENCE		
ESTIMATE	50.00	
EXACT 95% CI	(-20.86, 93.24)	
RELATIVE RISK		
ESTIMATE	2.00	
EXACT 95% CI	(0.83, 14.80)	
ODDS RATIO		
ESTIMATE	NE	
EXACT 95% CI	NE	
P-VALUE [1]	0.0910	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	53/62 (85.5)	37/57 (64.9)
RISK DIFFERENCE		
ESTIMATE	20.57	
EXACT 95% CI	(2.44, 37.56)	
RELATIVE RISK		
ESTIMATE	1.32	
EXACT 95% CI	(1.05, 1.70)	
ODDS RATIO		
ESTIMATE	3.18	
EXACT 95% CI	(1.21, 8.80)	
P-VALUE [1]	0.0093†	

1.1.7 Attacken-Schwere (PGI-S) zu Baseline

- PGI-C=Patient Global Impression of Change; CI=Confidence Interval
- Attack with beginning of symptom relief is defined as at least “a little better” (2 time points in a row without missing values in between) within 2, 4, 6, 8, 10, 12, 24, and 48 hours of the first IMP administration.
- Time to beginning of symptom relief is calculated as Date/time of first rating of “a little better” or higher (i.e. better or much better) which is immediately followed by another rating of “a little better” or higher (without possible missing values in between) – Date/time of first IMP administration.
- Attacks that did not have at least 2 post-baseline assessments within the analyzed period will be excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- †: p-value < 0.05.
- [1] P-value from Cochran-Mantel-Haenszel test.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS ATTACK SEVERITY AT BASELINE PGI-S = NONE OR MILD		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	17/31 (54.8)	8/32 (25.0)
RISK DIFFERENCE		
ESTIMATE	29.84	
EXACT 95% CI	(4.12, 51.93)	
RELATIVE RISK		
ESTIMATE	2.19	
EXACT 95% CI	(1.09, 5.08)	
ODDS RATIO		
ESTIMATE	3.64	
EXACT 95% CI	(1.11, 12.29)	
P-VALUE [1]	0.0164†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS ATTACK SEVERITY AT BASELINE PGI-S = MODERATE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	16/30 (53.3)	10/25 (40.0)
RISK DIFFERENCE		
ESTIMATE	13.33	
EXACT 95% CI	(-13.55, 38.87)	
RELATIVE RISK		
ESTIMATE	1.33	
EXACT 95% CI	(0.74, 2.66)	
ODDS RATIO		
ESTIMATE	1.71	
EXACT 95% CI	(0.52, 5.77)	
P-VALUE [1]	0.3285	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS ATTACK SEVERITY AT BASELINE PGI-S = SEVERE OR VERY SEVERE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/14 (64.3)	3/12 (25.0)
RISK DIFFERENCE		
ESTIMATE	39.29	
EXACT 95% CI	(-0.39, 70.77)	
RELATIVE RISK		
ESTIMATE	2.57	
EXACT 95% CI	(0.97, 12.44)	
ODDS RATIO		
ESTIMATE	5.40	
EXACT 95% CI	(0.77, 43.44)	
P-VALUE [1]	0.0495†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS ATTACK SEVERITY AT BASELINE PGI-S = NONE OR MILD		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	25/33 (75.8)	15/33 (45.5)
RISK DIFFERENCE		
ESTIMATE	30.30	
EXACT 95% CI	(4.85, 52.94)	
RELATIVE RISK		
ESTIMATE	1.67	
EXACT 95% CI	(1.09, 2.87)	
ODDS RATIO		
ESTIMATE	3.75	
EXACT 95% CI	(1.17, 12.41)	
P-VALUE [1]	0.0124†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
MODERATE

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	22/31 (71.0)	15/28 (53.6)
RISK DIFFERENCE		
ESTIMATE	17.40	
EXACT 95% CI	(-8.68, 41.22)	
RELATIVE RISK		
ESTIMATE	1.32	
EXACT 95% CI	(0.88, 2.24)	
ODDS RATIO		
ESTIMATE	2.12	
EXACT 95% CI	(0.64, 7.14)	
P-VALUE [1]	0.1713	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS ATTACK SEVERITY AT BASELINE PGI-S = SEVERE OR VERY SEVERE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	11/14 (78.6)	3/12 (25.0)
RISK DIFFERENCE		
ESTIMATE	53.57	
EXACT 95% CI	(14.20, 81.02)	
RELATIVE RISK		
ESTIMATE	3.14	
EXACT 95% CI	(1.26, 12.50)	
ODDS RATIO		
ESTIMATE	11.00	
EXACT 95% CI	(1.37, 100.58)	
P-VALUE [1]	0.0074†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS ATTACK SEVERITY AT BASELINE PGI-S = NONE OR MILD		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	25/33 (75.8)	15/33 (45.5)
RISK DIFFERENCE		
ESTIMATE	30.30	
EXACT 95% CI	(4.85, 52.94)	
RELATIVE RISK		
ESTIMATE	1.67	
EXACT 95% CI	(1.09, 2.87)	
ODDS RATIO		
ESTIMATE	3.75	
EXACT 95% CI	(1.17, 12.41)	
P-VALUE [1]	0.0124†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS ATTACK SEVERITY AT BASELINE PGI-S = MODERATE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	23/32 (71.9)	15/28 (53.6)
RISK DIFFERENCE		
ESTIMATE	18.30	
EXACT 95% CI	(-7.32, 42.16)	
RELATIVE RISK		
ESTIMATE	1.34	
EXACT 95% CI	(0.90, 2.30)	
ODDS RATIO		
ESTIMATE	2.21	
EXACT 95% CI	(0.67, 7.44)	
P-VALUE [1]	0.1455	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
SEVERE OR VERY SEVERE

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	11/14 (78.6)	4/12 (33.3)
RISK DIFFERENCE		
ESTIMATE	45.24	
EXACT 95% CI	(5.16, 75.15)	
RELATIVE RISK		
ESTIMATE	2.36	
EXACT 95% CI	(1.06, 12.37)	
ODDS RATIO		
ESTIMATE	7.33	
EXACT 95% CI	(0.99, 61.61)	
P-VALUE [1]	0.0225†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS ATTACK SEVERITY AT BASELINE PGI-S = NONE OR MILD		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	25/33 (75.8)	19/33 (57.6)
RISK DIFFERENCE		
ESTIMATE	18.18	
EXACT 95% CI	(-7.41, 42.09)	
RELATIVE RISK		
ESTIMATE	1.32	
EXACT 95% CI	(0.92, 1.97)	
ODDS RATIO		
ESTIMATE	2.30	
EXACT 95% CI	(0.72, 7.67)	
P-VALUE [1]	0.1200	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS ATTACK SEVERITY AT BASELINE PGI-S = MODERATE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	24/32 (75.0)	17/28 (60.7)
RISK DIFFERENCE		
ESTIMATE	14.29	
EXACT 95% CI	(-11.23, 38.70)	
RELATIVE RISK		
ESTIMATE	1.24	
EXACT 95% CI	(0.86, 1.91)	
ODDS RATIO		
ESTIMATE	1.94	
EXACT 95% CI	(0.56, 6.82)	
P-VALUE [1]	0.2393	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS ATTACK SEVERITY AT BASELINE PGI-S = SEVERE OR VERY SEVERE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	11/14 (78.6)	4/12 (33.3)
RISK DIFFERENCE		
ESTIMATE	45.24	
EXACT 95% CI	(5.16, 75.15)	
RELATIVE RISK		
ESTIMATE	2.36	
EXACT 95% CI	(1.06, 12.37)	
ODDS RATIO		
ESTIMATE	7.33	
EXACT 95% CI	(0.99, 61.61)	
P-VALUE [1]	0.0225†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS ATTACK SEVERITY AT BASELINE PGI-S = NONE OR MILD		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	27/33 (81.8)	20/33 (60.6)
RISK DIFFERENCE		
ESTIMATE	21.21	
EXACT 95% CI	(-4.38, 44.84)	
RELATIVE RISK		
ESTIMATE	1.35	
EXACT 95% CI	(0.97, 1.97)	
ODDS RATIO		
ESTIMATE	2.93	
EXACT 95% CI	(0.84, 10.94)	
P-VALUE [1]	0.0590	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS ATTACK SEVERITY AT BASELINE PGI-S = MODERATE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	25/32 (78.1)	17/28 (60.7)
RISK DIFFERENCE		
ESTIMATE	17.41	
EXACT 95% CI	(-8.22, 41.58)	
RELATIVE RISK		
ESTIMATE	1.29	
EXACT 95% CI	(0.91, 2.00)	
ODDS RATIO		
ESTIMATE	2.31	
EXACT 95% CI	(0.65, 8.48)	
P-VALUE [1]	0.1454	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

 WITHIN 10 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
 SEVERE OR VERY SEVERE

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	11/14 (78.6)	4/12 (33.3)
RISK DIFFERENCE		
ESTIMATE	45.24	
EXACT 95% CI	(5.16, 75.15)	
RELATIVE RISK		
ESTIMATE	2.36	
EXACT 95% CI	(1.06, 12.37)	
ODDS RATIO		
ESTIMATE	7.33	
EXACT 95% CI	(0.99, 61.61)	
P-VALUE [1]	0.0225†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS ATTACK SEVERITY AT BASELINE PGI-S = NONE OR MILD		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	29/33 (87.9)	20/34 (58.8)
RISK DIFFERENCE		
ESTIMATE	29.06	
EXACT 95% CI	(6.08, 51.10)	
RELATIVE RISK		
ESTIMATE	1.49	
EXACT 95% CI	(1.09, 2.17)	
ODDS RATIO		
ESTIMATE	5.08	
EXACT 95% CI	(1.30, 23.75)	
P-VALUE [1]	0.0078†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS ATTACK SEVERITY AT BASELINE PGI-S = MODERATE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	26/32 (81.3)	17/28 (60.7)
RISK DIFFERENCE		
ESTIMATE	20.54	
EXACT 95% CI	(-5.17, 44.44)	
RELATIVE RISK		
ESTIMATE	1.34	
EXACT 95% CI	(0.96, 2.09)	
ODDS RATIO		
ESTIMATE	2.80	
EXACT 95% CI	(0.76, 10.94)	
P-VALUE [1]	0.0808	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

 WITHIN 12 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
 SEVERE OR VERY SEVERE

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	11/14 (78.6)	4/12 (33.3)
RISK DIFFERENCE		
ESTIMATE	45.24	
EXACT 95% CI	(5.16, 75.15)	
RELATIVE RISK		
ESTIMATE	2.36	
EXACT 95% CI	(1.06, 12.37)	
ODDS RATIO		
ESTIMATE	7.33	
EXACT 95% CI	(0.99, 61.61)	
P-VALUE [1]	0.0225†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS ATTACK SEVERITY AT BASELINE PGI-S = NONE OR MILD		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	30/33 (90.9)	23/34 (67.6)
RISK DIFFERENCE		
ESTIMATE	23.26	
EXACT 95% CI	(-0.03, 45.77)	
RELATIVE RISK		
ESTIMATE	1.34	
EXACT 95% CI	(1.05, 1.86)	
ODDS RATIO		
ESTIMATE	4.78	
EXACT 95% CI	(1.07, 29.10)	
P-VALUE [1]	0.0201†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS ATTACK SEVERITY AT BASELINE PGI-S = MODERATE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	27/33 (81.8)	18/28 (64.3)
RISK DIFFERENCE		
ESTIMATE	17.53	
EXACT 95% CI	(-7.85, 41.13)	
RELATIVE RISK		
ESTIMATE	1.27	
EXACT 95% CI	(0.93, 1.91)	
ODDS RATIO		
ESTIMATE	2.50	
EXACT 95% CI	(0.67, 9.83)	
P-VALUE [1]	0.1239	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS ATTACK SEVERITY AT BASELINE PGI-S = SEVERE OR VERY SEVERE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	12/14 (85.7)	7/13 (53.8)
RISK DIFFERENCE		
ESTIMATE	31.87	
EXACT 95% CI	(-8.03, 63.37)	
RELATIVE RISK		
ESTIMATE	1.59	
EXACT 95% CI	(0.94, 3.41)	
ODDS RATIO		
ESTIMATE	5.14	
EXACT 95% CI	(0.63, 61.76)	
P-VALUE [1]	0.0754	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS ATTACK SEVERITY AT BASELINE PGI-S = NONE OR MILD		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	30/33 (90.9)	24/34 (70.6)
RISK DIFFERENCE		
ESTIMATE	20.32	
EXACT 95% CI	(-3.04, 43.07)	
RELATIVE RISK		
ESTIMATE	1.29	
EXACT 95% CI	(1.01, 1.74)	
ODDS RATIO		
ESTIMATE	4.17	
EXACT 95% CI	(0.91, 25.65)	
P-VALUE [1]	0.0369†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS ATTACK SEVERITY AT BASELINE PGI-S = MODERATE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	27/33 (81.8)	19/28 (67.9)
RISK DIFFERENCE		
ESTIMATE	13.96	
EXACT 95% CI	(-11.38, 37.79)	
RELATIVE RISK		
ESTIMATE	1.21	
EXACT 95% CI	(0.89, 1.74)	
ODDS RATIO		
ESTIMATE	2.13	
EXACT 95% CI	(0.56, 8.51)	
P-VALUE [1]	0.2108	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS ATTACK SEVERITY AT BASELINE PGI-S = SEVERE OR VERY SEVERE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	12/14 (85.7)	7/13 (53.8)
RISK DIFFERENCE		
ESTIMATE	31.87	
EXACT 95% CI	(-8.03, 63.37)	
RELATIVE RISK		
ESTIMATE	1.59	
EXACT 95% CI	(0.94, 3.41)	
ODDS RATIO		
ESTIMATE	5.14	
EXACT 95% CI	(0.63, 61.76)	
P-VALUE [1]	0.0754	

1.2 Anzahl und Anteil der Attacken mit einem Beginn der Symptomverbesserung definiert als mindestens „besser“ im PGI-C

1.2.1 Geschlecht

- PGI-C=Patient Global Impression of Change; CI=Confidence Interval
- Attack with beginning of symptom relief is defined as at least “better” (2 time points in a row with or without missing values in between) within 2, 4, 6, 8, 10, 12, 24, and 48 hours of the first IMP administration. Time to beginning of symptom relief is calculated as Date/time of first rating of “better” or higher (i.e. much better) which is immediately followed by another rating of “better” or higher (with or without possible missing values in between) – Date/time of first IMP administration.
- Attacks that did not have at least 2 post-baseline assessments within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- †: p-value < 0.05.
- [1] P-value from Cochran-Mantel-Haenszel test.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS SEX = MALE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	8/31 (25.8)	2/26 (7.7)
RISK DIFFERENCE		
ESTIMATE	18.11	
EXACT 95% CI	(-8.15, 42.29)	
RELATIVE RISK		
ESTIMATE	3.35	
EXACT 95% CI	(0.85, 27.85)	
ODDS RATIO		
ESTIMATE	4.17	
EXACT 95% CI	(0.71, 43.42)	
P-VALUE [1]	0.0759	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS SEX = FEMALE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	11/48 (22.9)	3/51 (5.9)
RISK DIFFERENCE		
ESTIMATE	17.03	
EXACT 95% CI	(-3.13, 36.09)	
RELATIVE RISK		
ESTIMATE	3.90	
EXACT 95% CI	(1.11, 21.42)	
ODDS RATIO		
ESTIMATE	4.76	
EXACT 95% CI	(1.13, 28.03)	
P-VALUE [1]	0.0156†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS SEX = MALE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	14/32 (43.8)	4/27 (14.8)
RISK DIFFERENCE		
ESTIMATE	28.94	
EXACT 95% CI	(3.27, 51.78)	
RELATIVE RISK		
ESTIMATE	2.95	
EXACT 95% CI	(1.08, 12.52)	
ODDS RATIO		
ESTIMATE	4.47	
EXACT 95% CI	(1.11, 21.39)	
P-VALUE [1]	0.0171†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS SEX = FEMALE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	21/49 (42.9)	12/52 (23.1)
RISK DIFFERENCE		
ESTIMATE	19.78	
EXACT 95% CI	(0.14, 38.31)	
RELATIVE RISK		
ESTIMATE	1.86	
EXACT 95% CI	(1.02, 3.59)	
ODDS RATIO		
ESTIMATE	2.50	
EXACT 95% CI	(0.98, 6.51)	
P-VALUE [1]	0.0351†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS SEX = MALE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	17/32 (53.1)	5/27 (18.5)
RISK DIFFERENCE		
ESTIMATE	34.61	
EXACT 95% CI	(9.04, 56.61)	
RELATIVE RISK		
ESTIMATE	2.87	
EXACT 95% CI	(1.16, 12.44)	
ODDS RATIO		
ESTIMATE	4.99	
EXACT 95% CI	(1.34, 20.62)	
P-VALUE [1]	0.0066†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS SEX = FEMALE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	21/49 (42.9)	12/52 (23.1)
RISK DIFFERENCE		
ESTIMATE	19.78	
EXACT 95% CI	(0.14, 38.31)	
RELATIVE RISK		
ESTIMATE	1.86	
EXACT 95% CI	(1.02, 3.59)	
ODDS RATIO		
ESTIMATE	2.50	
EXACT 95% CI	(0.98, 6.51)	
P-VALUE [1]	0.0351†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS SEX = MALE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	18/32 (56.3)	5/27 (18.5)
RISK DIFFERENCE		
ESTIMATE	37.73	
EXACT 95% CI	(12.31, 59.25)	
RELATIVE RISK		
ESTIMATE	3.04	
EXACT 95% CI	(1.24, 12.44)	
ODDS RATIO		
ESTIMATE	5.66	
EXACT 95% CI	(1.52, 23.41)	
P-VALUE [1]	0.0033†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS SEX = FEMALE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	26/49 (53.1)	14/52 (26.9)
RISK DIFFERENCE		
ESTIMATE	26.14	
EXACT 95% CI	(6.32, 44.01)	
RELATIVE RISK		
ESTIMATE	1.97	
EXACT 95% CI	(1.10, 3.59)	
ODDS RATIO		
ESTIMATE	3.07	
EXACT 95% CI	(1.24, 7.69)	
P-VALUE [1]	0.0076†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS SEX = MALE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	19/32 (59.4)	5/27 (18.5)
RISK DIFFERENCE		
ESTIMATE	40.86	
EXACT 95% CI	(15.64, 61.99)	
RELATIVE RISK		
ESTIMATE	3.21	
EXACT 95% CI	(1.40, 12.44)	
ODDS RATIO		
ESTIMATE	6.43	
EXACT 95% CI	(1.71, 26.67)	
P-VALUE [1]	0.0016†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS SEX = FEMALE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	29/49 (59.2)	16/53 (30.2)
RISK DIFFERENCE		
ESTIMATE	28.99	
EXACT 95% CI	(9.38, 46.78)	
RELATIVE RISK		
ESTIMATE	1.96	
EXACT 95% CI	(1.18, 3.49)	
ODDS RATIO		
ESTIMATE	3.35	
EXACT 95% CI	(1.37, 8.25)	
P-VALUE [1]	0.0034†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS SEX = MALE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	22/32 (68.8)	5/27 (18.5)
RISK DIFFERENCE		
ESTIMATE	50.23	
EXACT 95% CI	(25.81, 69.97)	
RELATIVE RISK		
ESTIMATE	3.71	
EXACT 95% CI	(1.74, 12.52)	
ODDS RATIO		
ESTIMATE	9.68	
EXACT 95% CI	(2.50, 40.94)	
P-VALUE [1]	0.0001†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS SEX = FEMALE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	31/51 (60.8)	16/53 (30.2)
RISK DIFFERENCE		
ESTIMATE	30.60	
EXACT 95% CI	(11.03, 48.19)	
RELATIVE RISK		
ESTIMATE	2.01	
EXACT 95% CI	(1.22, 3.48)	
ODDS RATIO		
ESTIMATE	3.58	
EXACT 95% CI	(1.48, 8.77)	
P-VALUE [1]	0.0018†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS SEX = MALE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	27/32 (84.4)	10/27 (37.0)
RISK DIFFERENCE		
ESTIMATE	47.34	
EXACT 95% CI	(22.51, 67.62)	
RELATIVE RISK		
ESTIMATE	2.28	
EXACT 95% CI	(1.40, 4.61)	
ODDS RATIO		
ESTIMATE	9.18	
EXACT 95% CI	(2.34, 39.16)	
P-VALUE [1]	0.0002†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS SEX = FEMALE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	33/51 (64.7)	24/53 (45.3)
RISK DIFFERENCE		
ESTIMATE	19.42	
EXACT 95% CI	(-0.00, 38.10)	
RELATIVE RISK		
ESTIMATE	1.43	
EXACT 95% CI	(1.00, 2.12)	
ODDS RATIO		
ESTIMATE	2.22	
EXACT 95% CI	(0.94, 5.27)	
P-VALUE [1]	0.0477†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS SEX = MALE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	28/32 (87.5)	12/27 (44.4)
RISK DIFFERENCE		
ESTIMATE	43.06	
EXACT 95% CI	(18.37, 63.99)	
RELATIVE RISK		
ESTIMATE	1.97	
EXACT 95% CI	(1.29, 3.52)	
ODDS RATIO		
ESTIMATE	8.75	
EXACT 95% CI	(2.11, 42.23)	
P-VALUE [1]	0.0005†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS SEX = FEMALE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	33/51 (64.7)	27/53 (50.9)
RISK DIFFERENCE		
ESTIMATE	13.76	
EXACT 95% CI	(-5.49, 32.78)	
RELATIVE RISK		
ESTIMATE	1.27	
EXACT 95% CI	(0.90, 1.84)	
ODDS RATIO		
ESTIMATE	1.77	
EXACT 95% CI	(0.75, 4.19)	
P-VALUE [1]	0.1576	

1.2.2 Alter

- Attacks that did not have at least 2 post-baseline assessments within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- †: p-value < 0.05.
- [1] P-value from Cochran-Mantel-Haenszel test.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS | AGE GROUP = <18 YEARS

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	1/9 (11.1)	2/9 (22.2)
RISK DIFFERENCE		
ESTIMATE	-11.11	
EXACT 95% CI	(-56.94, 38.49)	
RELATIVE RISK		
ESTIMATE	0.50	
EXACT 95% CI	(0.02, 5.18)	
ODDS RATIO		
ESTIMATE	0.44	
EXACT 95% CI	(0.01, 10.63)	
P-VALUE [1]	0.5388	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS | AGE GROUP = >=18 YEARS

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	18/70 (25.7)	3/68 (4.4)
RISK DIFFERENCE		
ESTIMATE	21.30	
EXACT 95% CI	(4.35, 36.81)	
RELATIVE RISK		
ESTIMATE	5.83	
EXACT 95% CI	(1.86, 32.44)	
ODDS RATIO		
ESTIMATE	7.50	
EXACT 95% CI	(2.00, 41.34)	
P-VALUE [1]	0.0005†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | AGE GROUP = <18 YEARS

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/9 (44.4)	2/9 (22.2)
RISK DIFFERENCE		
ESTIMATE	22.22	
EXACT 95% CI	(-28.51, 65.40)	
RELATIVE RISK		
ESTIMATE	2.00	
EXACT 95% CI	(0.48, 14.22)	
ODDS RATIO		
ESTIMATE	2.80	
EXACT 95% CI	(0.25, 40.51)	
P-VALUE [1]	0.3311	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | AGE GROUP = >=18 YEARS

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	31/72 (43.1)	14/70 (20.0)
RISK DIFFERENCE		
ESTIMATE	23.06	
EXACT 95% CI	(6.85, 38.69)	
RELATIVE RISK		
ESTIMATE	2.15	
EXACT 95% CI	(1.21, 4.01)	
ODDS RATIO		
ESTIMATE	3.02	
EXACT 95% CI	(1.35, 6.93)	
P-VALUE [1]	0.0033†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS | AGE GROUP = <18 YEARS

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/9 (44.4)	2/9 (22.2)
RISK DIFFERENCE		
ESTIMATE	22.22	
EXACT 95% CI	(-28.51, 65.40)	
RELATIVE RISK		
ESTIMATE	2.00	
EXACT 95% CI	(0.48, 14.22)	
ODDS RATIO		
ESTIMATE	2.80	
EXACT 95% CI	(0.25, 40.51)	
P-VALUE [1]	0.3311	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS | AGE GROUP = >=18 YEARS

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	34/72 (47.2)	15/70 (21.4)
RISK DIFFERENCE		
ESTIMATE	25.79	
EXACT 95% CI	(9.72, 41.34)	
RELATIVE RISK		
ESTIMATE	2.20	
EXACT 95% CI	(1.28, 3.98)	
ODDS RATIO		
ESTIMATE	3.28	
EXACT 95% CI	(1.49, 7.38)	
P-VALUE [1]	0.0013†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | AGE GROUP = <18 YEARS

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/9 (44.4)	2/9 (22.2)
RISK DIFFERENCE		
ESTIMATE	22.22	
EXACT 95% CI	(-28.51, 65.40)	
RELATIVE RISK		
ESTIMATE	2.00	
EXACT 95% CI	(0.48, 14.22)	
ODDS RATIO		
ESTIMATE	2.80	
EXACT 95% CI	(0.25, 40.51)	
P-VALUE [1]	0.3311	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | AGE GROUP = >=18 YEARS

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	40/72 (55.6)	17/70 (24.3)
RISK DIFFERENCE		
ESTIMATE	31.27	
EXACT 95% CI	(15.36, 46.55)	
RELATIVE RISK		
ESTIMATE	2.29	
EXACT 95% CI	(1.42, 3.96)	
ODDS RATIO		
ESTIMATE	3.90	
EXACT 95% CI	(1.80, 8.55)	
P-VALUE [1]	0.0002†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS | AGE GROUP = <18 YEARS

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/9 (55.6)	3/9 (33.3)
RISK DIFFERENCE		
ESTIMATE	22.22	
EXACT 95% CI	(-28.51, 65.40)	
RELATIVE RISK		
ESTIMATE	1.67	
EXACT 95% CI	(0.54, 10.22)	
ODDS RATIO		
ESTIMATE	2.50	
EXACT 95% CI	(0.27, 25.52)	
P-VALUE [1]	0.3566	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS | AGE GROUP = >=18 YEARS

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	43/72 (59.7)	18/71 (25.4)
RISK DIFFERENCE		
ESTIMATE	34.37	
EXACT 95% CI	(18.38, 49.48)	
RELATIVE RISK		
ESTIMATE	2.36	
EXACT 95% CI	(1.50, 4.01)	
ODDS RATIO		
ESTIMATE	4.37	
EXACT 95% CI	(2.03, 9.51)	
P-VALUE [1]	< 0.0001†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | AGE GROUP = <18 YEARS

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/10 (50.0)	3/9 (33.3)
RISK DIFFERENCE		
ESTIMATE	16.67	
EXACT 95% CI	(-29.55, 58.91)	
RELATIVE RISK		
ESTIMATE	1.50	
EXACT 95% CI	(0.48, 9.67)	
ODDS RATIO		
ESTIMATE	2.00	
EXACT 95% CI	(0.23, 19.39)	
P-VALUE [1]	0.4745	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | AGE GROUP = >=18 YEARS

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	48/73 (65.8)	18/71 (25.4)
RISK DIFFERENCE		
ESTIMATE	40.40	
EXACT 95% CI	(24.58, 54.86)	
RELATIVE RISK		
ESTIMATE	2.59	
EXACT 95% CI	(1.70, 4.25)	
ODDS RATIO		
ESTIMATE	5.65	
EXACT 95% CI	(2.60, 12.43)	
P-VALUE [1]	< 0.0001†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | AGE GROUP = <18 YEARS

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	6/10 (60.0)	4/9 (44.4)
RISK DIFFERENCE		
ESTIMATE	15.56	
EXACT 95% CI	(-31.52, 57.78)	
RELATIVE RISK		
ESTIMATE	1.35	
EXACT 95% CI	(0.53, 4.71)	
ODDS RATIO		
ESTIMATE	1.88	
EXACT 95% CI	(0.22, 16.65)	
P-VALUE [1]	0.5093	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | AGE GROUP = >=18 YEARS

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	54/73 (74.0)	30/71 (42.3)
RISK DIFFERENCE		
ESTIMATE	31.72	
EXACT 95% CI	(15.24, 46.52)	
RELATIVE RISK		
ESTIMATE	1.75	
EXACT 95% CI	(1.28, 2.56)	
ODDS RATIO		
ESTIMATE	3.88	
EXACT 95% CI	(1.82, 8.37)	
P-VALUE [1]	0.0001†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | AGE GROUP = <18 YEARS

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	7/10 (70.0)	5/9 (55.6)
RISK DIFFERENCE		
ESTIMATE	14.44	
EXACT 95% CI	(-32.68, 56.08)	
RELATIVE RISK		
ESTIMATE	1.26	
EXACT 95% CI	(0.55, 3.34)	
ODDS RATIO		
ESTIMATE	1.87	
EXACT 95% CI	(0.20, 18.60)	
P-VALUE [1]	0.5259	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS AGE GROUP = >=18 YEARS		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	54/73 (74.0)	34/71 (47.9)
RISK DIFFERENCE		
ESTIMATE	26.09	
EXACT 95% CI	(9.49, 41.08)	
RELATIVE RISK		
ESTIMATE	1.54	
EXACT 95% CI	(1.14, 2.12)	
ODDS RATIO		
ESTIMATE	3.09	
EXACT 95% CI	(1.45, 6.64)	
P-VALUE [1]	0.0014†	

1.2.3 Region (Variante 1)

- PGI-C=Patient Global Impression of Change; CI=Confidence Interval
- Attack with beginning of symptom relief is defined as at least “better” (2 time points in a row with or without missing values in between) within 2, 4, 6, 8, 10, 12, 24, and 48 hours of the first IMP administration. Time to beginning of symptom relief is calculated as Date/time of first rating of “better” or higher (i.e. much better) which is immediately followed by another rating of “better” or higher (with or without possible missing values in between) – Date/time of first IMP administration.
- Attacks that did not have at least 2 post-baseline assessments within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- †: p-value < 0.05.
- [1] P-value from Cochran-Mantel-Haenszel test.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS REGION 1 = US		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	7/24 (29.2)	1/21 (4.8)
RISK DIFFERENCE		
ESTIMATE	24.40	
EXACT 95% CI	(-5.67, 51.39)	
RELATIVE RISK		
ESTIMATE	6.13	
EXACT 95% CI	(1.02, 159.66)	
ODDS RATIO		
ESTIMATE	8.24	
EXACT 95% CI	(0.87, 389.28)	
P-VALUE [1]	0.0347†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS REGION 1 = ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	12/55 (21.8)	4/56 (7.1)
RISK DIFFERENCE		
ESTIMATE	14.68	
EXACT 95% CI	(-4.19, 32.28)	
RELATIVE RISK		
ESTIMATE	3.05	
EXACT 95% CI	(1.05, 15.12)	
ODDS RATIO		
ESTIMATE	3.63	
EXACT 95% CI	(0.99, 16.38)	
P-VALUE [1]	0.0285†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS REGION 1 = US		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	14/24 (58.3)	4/21 (19.0)
RISK DIFFERENCE		
ESTIMATE	39.29	
EXACT 95% CI	(10.63, 63.76)	
RELATIVE RISK		
ESTIMATE	3.06	
EXACT 95% CI	(1.16, 12.91)	
ODDS RATIO		
ESTIMATE	5.95	
EXACT 95% CI	(1.31, 30.70)	
P-VALUE [1]	0.0080†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS REGION 1 = ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	21/57 (36.8)	12/58 (20.7)
RISK DIFFERENCE		
ESTIMATE	16.15	
EXACT 95% CI	(-2.62, 33.15)	
RELATIVE RISK		
ESTIMATE	1.78	
EXACT 95% CI	(0.97, 3.51)	
ODDS RATIO		
ESTIMATE	2.24	
EXACT 95% CI	(0.90, 5.66)	
P-VALUE [1]	0.0566	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS REGION 1 = US		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	14/24 (58.3)	4/21 (19.0)
RISK DIFFERENCE		
ESTIMATE	39.29	
EXACT 95% CI	(10.63, 63.76)	
RELATIVE RISK		
ESTIMATE	3.06	
EXACT 95% CI	(1.16, 12.91)	
ODDS RATIO		
ESTIMATE	5.95	
EXACT 95% CI	(1.31, 30.70)	
P-VALUE [1]	0.0080†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS REGION 1 = ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	24/57 (42.1)	13/58 (22.4)
RISK DIFFERENCE		
ESTIMATE	19.69	
EXACT 95% CI	(0.88, 36.43)	
RELATIVE RISK		
ESTIMATE	1.88	
EXACT 95% CI	(1.05, 3.58)	
ODDS RATIO		
ESTIMATE	2.52	
EXACT 95% CI	(1.04, 6.20)	
P-VALUE [1]	0.0244†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS REGION 1 = US		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	16/24 (66.7)	6/21 (28.6)
RISK DIFFERENCE		
ESTIMATE	38.10	
EXACT 95% CI	(8.49, 63.01)	
RELATIVE RISK		
ESTIMATE	2.33	
EXACT 95% CI	(1.11, 7.33)	
ODDS RATIO		
ESTIMATE	5.00	
EXACT 95% CI	(1.20, 21.80)	
P-VALUE [1]	0.0117†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS REGION 1 = ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	28/57 (49.1)	13/58 (22.4)
RISK DIFFERENCE		
ESTIMATE	26.71	
EXACT 95% CI	(7.95, 43.13)	
RELATIVE RISK		
ESTIMATE	2.19	
EXACT 95% CI	(1.22, 4.14)	
ODDS RATIO		
ESTIMATE	3.34	
EXACT 95% CI	(1.39, 8.18)	
P-VALUE [1]	0.0029†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS REGION 1 = US		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	17/24 (70.8)	6/21 (28.6)
RISK DIFFERENCE		
ESTIMATE	42.26	
EXACT 95% CI	(12.76, 66.42)	
RELATIVE RISK		
ESTIMATE	2.48	
EXACT 95% CI	(1.17, 8.22)	
ODDS RATIO		
ESTIMATE	6.07	
EXACT 95% CI	(1.42, 27.15)	
P-VALUE [1]	0.0051†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS REGION 1 = ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	31/57 (54.4)	15/59 (25.4)
RISK DIFFERENCE		
ESTIMATE	28.96	
EXACT 95% CI	(10.45, 45.48)	
RELATIVE RISK		
ESTIMATE	2.14	
EXACT 95% CI	(1.26, 3.72)	
ODDS RATIO		
ESTIMATE	3.50	
EXACT 95% CI	(1.49, 8.30)	
P-VALUE [1]	0.0015†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS REGION 1 = US		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	18/24 (75.0)	6/21 (28.6)
RISK DIFFERENCE		
ESTIMATE	46.43	
EXACT 95% CI	(17.12, 69.76)	
RELATIVE RISK		
ESTIMATE	2.63	
EXACT 95% CI	(1.28, 9.20)	
ODDS RATIO		
ESTIMATE	7.50	
EXACT 95% CI	(1.70, 34.87)	
P-VALUE [1]	0.0021†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS REGION 1 = ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	35/59 (59.3)	15/59 (25.4)
RISK DIFFERENCE		
ESTIMATE	33.90	
EXACT 95% CI	(15.38, 50.67)	
RELATIVE RISK		
ESTIMATE	2.33	
EXACT 95% CI	(1.42, 4.16)	
ODDS RATIO		
ESTIMATE	4.28	
EXACT 95% CI	(1.83, 10.13)	
P-VALUE [1]	0.0002†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS REGION 1 = US		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	19/24 (79.2)	11/21 (52.4)
RISK DIFFERENCE		
ESTIMATE	26.79	
EXACT 95% CI	(-2.91, 52.89)	
RELATIVE RISK		
ESTIMATE	1.51	
EXACT 95% CI	(0.97, 2.72)	
ODDS RATIO		
ESTIMATE	3.45	
EXACT 95% CI	(0.79, 16.08)	
P-VALUE [1]	0.0601	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS REGION 1 = ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	41/59 (69.5)	23/59 (39.0)
RISK DIFFERENCE		
ESTIMATE	30.51	
EXACT 95% CI	(11.88, 47.57)	
RELATIVE RISK		
ESTIMATE	1.78	
EXACT 95% CI	(1.22, 2.75)	
ODDS RATIO		
ESTIMATE	3.57	
EXACT 95% CI	(1.56, 8.22)	
P-VALUE [1]	0.0009†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS REGION 1 = US		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	19/24 (79.2)	12/21 (57.1)
RISK DIFFERENCE		
ESTIMATE	22.02	
EXACT 95% CI	(-7.49, 48.93)	
RELATIVE RISK		
ESTIMATE	1.39	
EXACT 95% CI	(0.91, 2.49)	
ODDS RATIO		
ESTIMATE	2.85	
EXACT 95% CI	(0.65, 13.36)	
P-VALUE [1]	0.1154	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS REGION 1 = ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	42/59 (71.2)	27/59 (45.8)
RISK DIFFERENCE		
ESTIMATE	25.42	
EXACT 95% CI	(6.66, 42.88)	
RELATIVE RISK		
ESTIMATE	1.56	
EXACT 95% CI	(1.09, 2.26)	
ODDS RATIO		
ESTIMATE	2.93	
EXACT 95% CI	(1.28, 6.75)	
P-VALUE [1]	0.0053†	

1.2.4 Region (Variante 2)

- PGI-C=Patient Global Impression of Change; CI=Confidence Interval
- Attack with beginning of symptom relief is defined as at least “better” (2 time points in a row with or without missing values in between) within 2, 4, 6, 8, 10, 12, 24, and 48 hours of the first IMP administration. Time to beginning of symptom relief is calculated as Date/time of first rating of “better” or higher (i.e. much better) which is immediately followed by another rating of “better” or higher (with or without possible missing values in between) – Date/time of first IMP administration.
- Attacks that did not have at least 2 post-baseline assessments within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- †: p-value < 0.05.
- [1] P-value from Cochran-Mantel-Haenszel test.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS | REGION 2 = NORTH AMERICA

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	7/24 (29.2)	1/21 (4.8)
RISK DIFFERENCE		
ESTIMATE	24.40	
EXACT 95% CI	(-5.67, 51.39)	
RELATIVE RISK		
ESTIMATE	6.13	
EXACT 95% CI	(1.02, 159.66)	
ODDS RATIO		
ESTIMATE	8.24	
EXACT 95% CI	(0.87, 389.28)	
P-VALUE [1]	0.0347†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS | REGION 2 = EUROPE

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	7/40 (17.5)	2/43 (4.7)
RISK DIFFERENCE		
ESTIMATE	12.85	
EXACT 95% CI	(-9.09, 33.63)	
RELATIVE RISK		
ESTIMATE	3.76	
EXACT 95% CI	(0.91, 35.78)	
ODDS RATIO		
ESTIMATE	4.35	
EXACT 95% CI	(0.75, 44.89)	
P-VALUE [1]	0.0615	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS | REGION 2 = ROW

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/15 (33.3)	2/13 (15.4)
RISK DIFFERENCE		
ESTIMATE	17.95	
EXACT 95% CI	(-19.34, 51.59)	
RELATIVE RISK		
ESTIMATE	2.17	
EXACT 95% CI	(0.49, 13.97)	
ODDS RATIO		
ESTIMATE	2.75	
EXACT 95% CI	(0.34, 33.89)	
P-VALUE [1]	0.2827	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | REGION 2 = NORTH AMERICA

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	14/24 (58.3)	4/21 (19.0)
RISK DIFFERENCE		
ESTIMATE	39.29	
EXACT 95% CI	(10.63, 63.76)	
RELATIVE RISK		
ESTIMATE	3.06	
EXACT 95% CI	(1.16, 12.91)	
ODDS RATIO		
ESTIMATE	5.95	
EXACT 95% CI	(1.31, 30.70)	
P-VALUE [1]	0.0080†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | REGION 2 = EUROPE

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	14/41 (34.1)	10/45 (22.2)
RISK DIFFERENCE		
ESTIMATE	11.92	
EXACT 95% CI	(-9.23, 32.61)	
RELATIVE RISK		
ESTIMATE	1.54	
EXACT 95% CI	(0.75, 3.52)	
ODDS RATIO		
ESTIMATE	1.81	
EXACT 95% CI	(0.63, 5.31)	
P-VALUE [1]	0.2209	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | REGION 2 = ROW

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	7/16 (43.8)	2/13 (15.4)
RISK DIFFERENCE		
ESTIMATE	28.37	
EXACT 95% CI	(-8.86, 59.44)	
RELATIVE RISK		
ESTIMATE	2.84	
EXACT 95% CI	(0.80, 26.73)	
ODDS RATIO		
ESTIMATE	4.28	
EXACT 95% CI	(0.57, 49.76)	
P-VALUE [1]	0.1066	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS | REGION 2 = NORTH AMERICA

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	14/24 (58.3)	4/21 (19.0)
RISK DIFFERENCE		
ESTIMATE	39.29	
EXACT 95% CI	(10.63, 63.76)	
RELATIVE RISK		
ESTIMATE	3.06	
EXACT 95% CI	(1.16, 12.91)	
ODDS RATIO		
ESTIMATE	5.95	
EXACT 95% CI	(1.31, 30.70)	
P-VALUE [1]	0.0080†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS | REGION 2 = EUROPE

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	16/41 (39.0)	11/45 (24.4)
RISK DIFFERENCE		
ESTIMATE	14.58	
EXACT 95% CI	(-6.44, 35.09)	
RELATIVE RISK		
ESTIMATE	1.60	
EXACT 95% CI	(0.83, 3.51)	
ODDS RATIO		
ESTIMATE	1.98	
EXACT 95% CI	(0.71, 5.57)	
P-VALUE [1]	0.1480	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS | REGION 2 = ROW

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	8/16 (50.0)	2/13 (15.4)
RISK DIFFERENCE		
ESTIMATE	34.62	
EXACT 95% CI	(-2.36, 64.70)	
RELATIVE RISK		
ESTIMATE	3.25	
EXACT 95% CI	(0.95, 26.73)	
ODDS RATIO		
ESTIMATE	5.50	
EXACT 95% CI	(0.74, 63.07)	
P-VALUE [1]	0.0553	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | REGION 2 = NORTH AMERICA

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	16/24 (66.7)	6/21 (28.6)
RISK DIFFERENCE		
ESTIMATE	38.10	
EXACT 95% CI	(8.49, 63.01)	
RELATIVE RISK		
ESTIMATE	2.33	
EXACT 95% CI	(1.11, 7.33)	
ODDS RATIO		
ESTIMATE	5.00	
EXACT 95% CI	(1.20, 21.80)	
P-VALUE [1]	0.0117†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | REGION 2 = EUROPE

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	19/41 (46.3)	11/45 (24.4)
RISK DIFFERENCE		
ESTIMATE	21.90	
EXACT 95% CI	(0.66, 41.80)	
RELATIVE RISK		
ESTIMATE	1.90	
EXACT 95% CI	(1.03, 3.83)	
ODDS RATIO		
ESTIMATE	2.67	
EXACT 95% CI	(0.98, 7.44)	
P-VALUE [1]	0.0344†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | REGION 2 = ROW

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/16 (56.3)	2/13 (15.4)
RISK DIFFERENCE		
ESTIMATE	40.87	
EXACT 95% CI	(4.37, 69.77)	
RELATIVE RISK		
ESTIMATE	3.66	
EXACT 95% CI	(1.06, 28.04)	
ODDS RATIO		
ESTIMATE	7.07	
EXACT 95% CI	(0.95, 80.44)	
P-VALUE [1]	0.0267†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS | REGION 2 = NORTH AMERICA

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	17/24 (70.8)	6/21 (28.6)
RISK DIFFERENCE		
ESTIMATE	42.26	
EXACT 95% CI	(12.76, 66.42)	
RELATIVE RISK		
ESTIMATE	2.48	
EXACT 95% CI	(1.17, 8.22)	
ODDS RATIO		
ESTIMATE	6.07	
EXACT 95% CI	(1.42, 27.15)	
P-VALUE [1]	0.0051†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS | REGION 2 = EUROPE

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	20/41 (48.8)	13/46 (28.3)
RISK DIFFERENCE		
ESTIMATE	20.52	
EXACT 95% CI	(-0.63, 40.37)	
RELATIVE RISK		
ESTIMATE	1.73	
EXACT 95% CI	(0.98, 3.48)	
ODDS RATIO		
ESTIMATE	2.42	
EXACT 95% CI	(0.91, 6.48)	
P-VALUE [1]	0.0503	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS | REGION 2 = ROW

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	11/16 (68.8)	2/13 (15.4)
RISK DIFFERENCE		
ESTIMATE	53.37	
EXACT 95% CI	(17.35, 79.24)	
RELATIVE RISK		
ESTIMATE	4.47	
EXACT 95% CI	(1.34, 43.94)	
ODDS RATIO		
ESTIMATE	12.10	
EXACT 95% CI	(1.55, 138.12)	
P-VALUE [1]	0.0047†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | REGION 2 = NORTH AMERICA

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	18/24 (75.0)	6/21 (28.6)
RISK DIFFERENCE		
ESTIMATE	46.43	
EXACT 95% CI	(17.12, 69.76)	
RELATIVE RISK		
ESTIMATE	2.63	
EXACT 95% CI	(1.28, 9.20)	
ODDS RATIO		
ESTIMATE	7.50	
EXACT 95% CI	(1.70, 34.87)	
P-VALUE [1]	0.0021†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | REGION 2 = EUROPE

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	23/43 (53.5)	13/46 (28.3)
RISK DIFFERENCE		
ESTIMATE	25.23	
EXACT 95% CI	(4.03, 44.36)	
RELATIVE RISK		
ESTIMATE	1.89	
EXACT 95% CI	(1.08, 3.53)	
ODDS RATIO		
ESTIMATE	2.92	
EXACT 95% CI	(1.12, 7.74)	
P-VALUE [1]	0.0160†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | REGION 2 = ROW

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	12/16 (75.0)	2/13 (15.4)
RISK DIFFERENCE		
ESTIMATE	59.62	
EXACT 95% CI	(23.98, 83.63)	
RELATIVE RISK		
ESTIMATE	4.88	
EXACT 95% CI	(1.46, 43.94)	
ODDS RATIO		
ESTIMATE	16.50	
EXACT 95% CI	(2.00, 191.54)	
P-VALUE [1]	0.0017†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | REGION 2 = NORTH AMERICA

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	19/24 (79.2)	11/21 (52.4)
RISK DIFFERENCE		
ESTIMATE	26.79	
EXACT 95% CI	(-2.91, 52.89)	
RELATIVE RISK		
ESTIMATE	1.51	
EXACT 95% CI	(0.97, 2.72)	
ODDS RATIO		
ESTIMATE	3.45	
EXACT 95% CI	(0.79, 16.08)	
P-VALUE [1]	0.0601	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | REGION 2 = EUROPE

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	29/43 (67.4)	19/46 (41.3)
RISK DIFFERENCE		
ESTIMATE	26.14	
EXACT 95% CI	(5.23, 45.62)	
RELATIVE RISK		
ESTIMATE	1.63	
EXACT 95% CI	(1.08, 2.66)	
ODDS RATIO		
ESTIMATE	2.94	
EXACT 95% CI	(1.14, 7.69)	
P-VALUE [1]	0.0140†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | REGION 2 = ROW

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	12/16 (75.0)	4/13 (30.8)
RISK DIFFERENCE		
ESTIMATE	44.23	
EXACT 95% CI	(6.71, 73.00)	
RELATIVE RISK		
ESTIMATE	2.44	
EXACT 95% CI	(1.13, 11.78)	
ODDS RATIO		
ESTIMATE	6.75	
EXACT 95% CI	(1.04, 47.33)	
P-VALUE [1]	0.0193†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | REGION 2 = NORTH AMERICA

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	19/24 (79.2)	12/21 (57.1)
RISK DIFFERENCE		
ESTIMATE	22.02	
EXACT 95% CI	(-7.49, 48.93)	
RELATIVE RISK		
ESTIMATE	1.39	
EXACT 95% CI	(0.91, 2.49)	
ODDS RATIO		
ESTIMATE	2.85	
EXACT 95% CI	(0.65, 13.36)	
P-VALUE [1]	0.1154	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | REGION 2 = EUROPE

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	30/43 (69.8)	21/46 (45.7)
RISK DIFFERENCE		
ESTIMATE	24.12	
EXACT 95% CI	(3.40, 43.75)	
RELATIVE RISK		
ESTIMATE	1.53	
EXACT 95% CI	(1.05, 2.34)	
ODDS RATIO		
ESTIMATE	2.75	
EXACT 95% CI	(1.06, 7.24)	
P-VALUE [1]	0.0223†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS REGION 2 = ROW		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	12/16 (75.0)	6/13 (46.2)
RISK DIFFERENCE		
ESTIMATE	28.85	
EXACT 95% CI	(-8.78, 60.87)	
RELATIVE RISK		
ESTIMATE	1.63	
EXACT 95% CI	(0.86, 4.12)	
ODDS RATIO		
ESTIMATE	3.50	
EXACT 95% CI	(0.57, 22.74)	
P-VALUE [1]	0.1177	

1.2.5 Prophylaxe-Status (Variante 1)

- PGI-C=Patient Global Impression of Change; CI=Confidence Interval
- Attack with beginning of symptom relief is defined as at least “better” (2 time points in a row with or without missing values in between) within 2, 4, 6, 8, 10, 12, 24, and 48 hours of the first IMP administration. Time to beginning of symptom relief is calculated as Date/time of first rating of “better” or higher (i.e. much better) which is immediately followed by another rating of “better” or higher (with or without possible missing values in between) – Date/time of first IMP administration.
- Attacks that did not have at least 2 post-baseline assessments within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- †: p-value < 0.05.
- [1] P-value from Cochran-Mantel-Haenszel test.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	3/18 (16.7)	2/18 (11.1)
RISK DIFFERENCE		
ESTIMATE	5.56	
EXACT 95% CI	(-29.03, 39.19)	
RELATIVE RISK		
ESTIMATE	1.50	
EXACT 95% CI	(0.26, 14.64)	
ODDS RATIO		
ESTIMATE	1.60	
EXACT 95% CI	(0.16, 21.40)	
P-VALUE [1]	0.6347	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
DEMAND

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	16/61 (26.2)	3/59 (5.1)
RISK DIFFERENCE		
ESTIMATE	21.14	
EXACT 95% CI	(2.94, 37.74)	
RELATIVE RISK		
ESTIMATE	5.16	
EXACT 95% CI	(1.60, 32.28)	
ODDS RATIO		
ESTIMATE	6.64	
EXACT 95% CI	(1.72, 37.20)	
P-VALUE [1]	0.0016†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/18 (27.8)	6/18 (33.3)
RISK DIFFERENCE		
ESTIMATE	-5.56	
EXACT 95% CI	(-39.19, 29.03)	
RELATIVE RISK		
ESTIMATE	0.83	
EXACT 95% CI	(0.27, 2.57)	
ODDS RATIO		
ESTIMATE	0.77	
EXACT 95% CI	(0.14, 3.99)	
P-VALUE [1]	0.7213	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
DEMAND

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	30/63 (47.6)	10/61 (16.4)
RISK DIFFERENCE		
ESTIMATE	31.23	
EXACT 95% CI	(14.10, 47.35)	
RELATIVE RISK		
ESTIMATE	2.90	
EXACT 95% CI	(1.57, 6.82)	
ODDS RATIO		
ESTIMATE	4.64	
EXACT 95% CI	(1.88, 11.97)	
P-VALUE [1]	0.0002†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	6/18 (33.3)	6/18 (33.3)
RISK DIFFERENCE		
ESTIMATE	0.00	
EXACT 95% CI	(-34.16, 34.16)	
RELATIVE RISK		
ESTIMATE	1.00	
EXACT 95% CI	(0.33, 3.05)	
ODDS RATIO		
ESTIMATE	1.00	
EXACT 95% CI	(0.20, 4.99)	
P-VALUE [1]	1.0000	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
DEMAND

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	32/63 (50.8)	11/61 (18.0)
RISK DIFFERENCE		
ESTIMATE	32.76	
EXACT 95% CI	(15.77, 48.83)	
RELATIVE RISK		
ESTIMATE	2.82	
EXACT 95% CI	(1.57, 6.04)	
ODDS RATIO		
ESTIMATE	4.69	
EXACT 95% CI	(1.94, 11.75)	
P-VALUE [1]	0.0001†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/18 (50.0)	8/18 (44.4)
RISK DIFFERENCE		
ESTIMATE	5.56	
EXACT 95% CI	(-29.03, 39.19)	
RELATIVE RISK		
ESTIMATE	1.13	
EXACT 95% CI	(0.52, 2.62)	
ODDS RATIO		
ESTIMATE	1.25	
EXACT 95% CI	(0.28, 5.62)	
P-VALUE [1]	0.7420	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
DEMAND

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	35/63 (55.6)	11/61 (18.0)
RISK DIFFERENCE		
ESTIMATE	37.52	
EXACT 95% CI	(20.81, 53.23)	
RELATIVE RISK		
ESTIMATE	3.08	
EXACT 95% CI	(1.74, 6.88)	
ODDS RATIO		
ESTIMATE	5.68	
EXACT 95% CI	(2.34, 14.24)	
P-VALUE [1]	< 0.0001†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	11/18 (61.1)	8/18 (44.4)
RISK DIFFERENCE		
ESTIMATE	16.67	
EXACT 95% CI	(-18.49, 48.97)	
RELATIVE RISK		
ESTIMATE	1.38	
EXACT 95% CI	(0.70, 3.05)	
ODDS RATIO		
ESTIMATE	1.96	
EXACT 95% CI	(0.43, 9.08)	
P-VALUE [1]	0.3234	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
DEMAND

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	37/63 (58.7)	13/62 (21.0)
RISK DIFFERENCE		
ESTIMATE	37.76	
EXACT 95% CI	(21.03, 53.57)	
RELATIVE RISK		
ESTIMATE	2.80	
EXACT 95% CI	(1.67, 5.43)	
ODDS RATIO		
ESTIMATE	5.36	
EXACT 95% CI	(2.28, 12.89)	
P-VALUE [1]	< 0.0001†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	12/18 (66.7)	8/18 (44.4)
RISK DIFFERENCE		
ESTIMATE	22.22	
EXACT 95% CI	(-13.07, 53.72)	
RELATIVE RISK		
ESTIMATE	1.50	
EXACT 95% CI	(0.81, 3.17)	
ODDS RATIO		
ESTIMATE	2.50	
EXACT 95% CI	(0.54, 11.99)	
P-VALUE [1]	0.1859	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
DEMAND

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	41/65 (63.1)	13/62 (21.0)
RISK DIFFERENCE		
ESTIMATE	42.11	
EXACT 95% CI	(25.61, 57.19)	
RELATIVE RISK		
ESTIMATE	3.01	
EXACT 95% CI	(1.81, 5.95)	
ODDS RATIO		
ESTIMATE	6.44	
EXACT 95% CI	(2.73, 15.48)	
P-VALUE [1]	< 0.0001†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	14/18 (77.8)	13/18 (72.2)
RISK DIFFERENCE		
ESTIMATE	5.56	
EXACT 95% CI	(-29.03, 39.19)	
RELATIVE RISK		
ESTIMATE	1.08	
EXACT 95% CI	(0.70, 1.74)	
ODDS RATIO		
ESTIMATE	1.35	
EXACT 95% CI	(0.23, 8.33)	
P-VALUE [1]	0.7043	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
DEMAND

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	46/65 (70.8)	21/62 (33.9)
RISK DIFFERENCE		
ESTIMATE	36.90	
EXACT 95% CI	(19.61, 52.41)	
RELATIVE RISK		
ESTIMATE	2.09	
EXACT 95% CI	(1.42, 3.25)	
ODDS RATIO		
ESTIMATE	4.73	
EXACT 95% CI	(2.10, 10.73)	
P-VALUE [1]	< 0.0001†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	14/18 (77.8)	14/18 (77.8)
RISK DIFFERENCE		
ESTIMATE	0.00	
EXACT 95% CI	(-34.16, 34.16)	
RELATIVE RISK		
ESTIMATE	1.00	
EXACT 95% CI	(0.65, 1.53)	
ODDS RATIO		
ESTIMATE	1.00	
EXACT 95% CI	(0.15, 6.55)	
P-VALUE [1]	1.0000	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS PROPHYLACTIC TREATMENT STATUS 1 = ON DEMAND		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	47/65 (72.3)	25/62 (40.3)
RISK DIFFERENCE		
ESTIMATE	31.99	
EXACT 95% CI	(14.48, 47.76)	
RELATIVE RISK		
ESTIMATE	1.79	
EXACT 95% CI	(1.26, 2.72)	
ODDS RATIO		
ESTIMATE	3.86	
EXACT 95% CI	(1.73, 8.72)	
P-VALUE [1]	0.0003†	

1.2.6 Prophylaxe-Status (Variante 2)

- PGI-C=Patient Global Impression of Change; CI=Confidence Interval; NE=Not Evaluable
- Attack with beginning of symptom relief is defined as at least “better” (2 time points in a row with or without missing values in between) within 2, 4, 6, 8, 10, 12, 24, and 48 hours of the first IMP administration. Time to beginning of symptom relief is calculated as Date/time of first rating of “better” or higher (i.e. much better) which is immediately followed by another rating of “better” or higher (with or without possible missing values in between) – Date/time of first IMP administration.
- Attacks that did not have at least 2 post-baseline assessments within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- †: p-value < 0.05.
- [1] P-value from Cochran-Mantel-Haenszel test.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	3/13 (23.1)	2/14 (14.3)
RISK DIFFERENCE		
ESTIMATE	8.79	
EXACT 95% CI	(-29.51, 42.83)	
RELATIVE RISK		
ESTIMATE	1.62	
EXACT 95% CI	(0.29, 15.59)	
ODDS RATIO		
ESTIMATE	1.80	
EXACT 95% CI	(0.17, 25.07)	
P-VALUE [1]	0.5642	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	0/5 (0)	0/4 (0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
DEMAND

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	16/61 (26.2)	3/59 (5.1)
RISK DIFFERENCE		
ESTIMATE	21.14	
EXACT 95% CI	(2.94, 37.74)	
RELATIVE RISK		
ESTIMATE	5.16	
EXACT 95% CI	(1.60, 32.28)	
ODDS RATIO		
ESTIMATE	6.64	
EXACT 95% CI	(1.72, 37.20)	
P-VALUE [1]	0.0016†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/13 (30.8)	6/14 (42.9)
RISK DIFFERENCE		
ESTIMATE	-12.09	
EXACT 95% CI	(-48.89, 25.52)	
RELATIVE RISK		
ESTIMATE	0.72	
EXACT 95% CI	(0.20, 2.05)	
ODDS RATIO		
ESTIMATE	0.59	
EXACT 95% CI	(0.09, 3.71)	
P-VALUE [1]	0.5236	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	1/5 (20.0)	0/4 (0)
RISK DIFFERENCE		
ESTIMATE	20.00	
EXACT 95% CI	(-41.85, 73.22)	
RELATIVE RISK		
ESTIMATE	NE	
EXACT 95% CI	NE	
ODDS RATIO		
ESTIMATE	NE	
EXACT 95% CI	NE	
P-VALUE [1]	0.3711	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
DEMAND

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	30/63 (47.6)	10/61 (16.4)
RISK DIFFERENCE		
ESTIMATE	31.23	
EXACT 95% CI	(14.10, 47.35)	
RELATIVE RISK		
ESTIMATE	2.90	
EXACT 95% CI	(1.57, 6.82)	
ODDS RATIO		
ESTIMATE	4.64	
EXACT 95% CI	(1.88, 11.97)	
P-VALUE [1]	0.0002†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/13 (38.5)	6/14 (42.9)
RISK DIFFERENCE		
ESTIMATE	-4.40	
EXACT 95% CI	(-42.28, 33.27)	
RELATIVE RISK		
ESTIMATE	0.90	
EXACT 95% CI	(0.32, 2.56)	
ODDS RATIO		
ESTIMATE	0.83	
EXACT 95% CI	(0.14, 4.98)	
P-VALUE [1]	0.8197	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	1/5 (20.0)	0/4 (0)
RISK DIFFERENCE		
ESTIMATE	20.00	
EXACT 95% CI	(-41.85, 73.22)	
RELATIVE RISK		
ESTIMATE	NE	
EXACT 95% CI	NE	
ODDS RATIO		
ESTIMATE	NE	
EXACT 95% CI	NE	
P-VALUE [1]	0.3711	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
DEMAND

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	32/63 (50.8)	11/61 (18.0)
RISK DIFFERENCE		
ESTIMATE	32.76	
EXACT 95% CI	(15.77, 48.83)	
RELATIVE RISK		
ESTIMATE	2.82	
EXACT 95% CI	(1.57, 6.04)	
ODDS RATIO		
ESTIMATE	4.69	
EXACT 95% CI	(1.94, 11.75)	
P-VALUE [1]	0.0001†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	7/13 (53.8)	8/14 (57.1)
RISK DIFFERENCE		
ESTIMATE	-3.30	
EXACT 95% CI	(-40.64, 35.38)	
RELATIVE RISK		
ESTIMATE	0.94	
EXACT 95% CI	(0.39, 2.03)	
ODDS RATIO		
ESTIMATE	0.88	
EXACT 95% CI	(0.15, 5.13)	
P-VALUE [1]	0.8658	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	2/5 (40.0)	0/4 (0)
RISK DIFFERENCE		
ESTIMATE	40.00	
EXACT 95% CI	(-26.16, 85.52)	
RELATIVE RISK		
ESTIMATE	NE	
EXACT 95% CI	NE	
ODDS RATIO		
ESTIMATE	NE	
EXACT 95% CI	NE	
P-VALUE [1]	0.1763	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
DEMAND

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	35/63 (55.6)	11/61 (18.0)
RISK DIFFERENCE		
ESTIMATE	37.52	
EXACT 95% CI	(20.81, 53.23)	
RELATIVE RISK		
ESTIMATE	3.08	
EXACT 95% CI	(1.74, 6.88)	
ODDS RATIO		
ESTIMATE	5.68	
EXACT 95% CI	(2.34, 14.24)	
P-VALUE [1]	< 0.0001†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/13 (69.2)	8/14 (57.1)
RISK DIFFERENCE		
ESTIMATE	12.09	
EXACT 95% CI	(-25.52, 48.89)	
RELATIVE RISK		
ESTIMATE	1.21	
EXACT 95% CI	(0.61, 2.57)	
ODDS RATIO		
ESTIMATE	1.69	
EXACT 95% CI	(0.27, 11.23)	
P-VALUE [1]	0.5236	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	2/5 (40.0)	0/4 (0)
RISK DIFFERENCE		
ESTIMATE	40.00	
EXACT 95% CI	(-26.16, 85.52)	
RELATIVE RISK		
ESTIMATE	NE	
EXACT 95% CI	NE	
ODDS RATIO		
ESTIMATE	NE	
EXACT 95% CI	NE	
P-VALUE [1]	0.1763	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
DEMAND

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	37/63 (58.7)	13/62 (21.0)
RISK DIFFERENCE		
ESTIMATE	37.76	
EXACT 95% CI	(21.03, 53.57)	
RELATIVE RISK		
ESTIMATE	2.80	
EXACT 95% CI	(1.67, 5.43)	
ODDS RATIO		
ESTIMATE	5.36	
EXACT 95% CI	(2.28, 12.89)	
P-VALUE [1]	< 0.0001†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	10/13 (76.9)	8/14 (57.1)
RISK DIFFERENCE		
ESTIMATE	19.78	
EXACT 95% CI	(-17.32, 55.22)	
RELATIVE RISK		
ESTIMATE	1.35	
EXACT 95% CI	(0.74, 2.79)	
ODDS RATIO		
ESTIMATE	2.50	
EXACT 95% CI	(0.37, 19.87)	
P-VALUE [1]	0.2850	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	2/5 (40.0)	0/4 (0)
RISK DIFFERENCE		
ESTIMATE	40.00	
EXACT 95% CI	(-26.16, 85.52)	
RELATIVE RISK		
ESTIMATE	NE	
EXACT 95% CI	NE	
ODDS RATIO		
ESTIMATE	NE	
EXACT 95% CI	NE	
P-VALUE [1]	0.1763	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
DEMAND

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	41/65 (63.1)	13/62 (21.0)
RISK DIFFERENCE		
ESTIMATE	42.11	
EXACT 95% CI	(25.61, 57.19)	
RELATIVE RISK		
ESTIMATE	3.01	
EXACT 95% CI	(1.81, 5.95)	
ODDS RATIO		
ESTIMATE	6.44	
EXACT 95% CI	(2.73, 15.48)	
P-VALUE [1]	< 0.0001†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	11/13 (84.6)	11/14 (78.6)
RISK DIFFERENCE		
ESTIMATE	6.04	
EXACT 95% CI	(-29.52, 42.82)	
RELATIVE RISK		
ESTIMATE	1.08	
EXACT 95% CI	(0.67, 1.76)	
ODDS RATIO		
ESTIMATE	1.50	
EXACT 95% CI	(0.14, 21.00)	
P-VALUE [1]	0.6918	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	3/5 (60.0)	2/4 (50.0)
RISK DIFFERENCE		
ESTIMATE	10.00	
EXACT 95% CI	(-56.06, 70.06)	
RELATIVE RISK		
ESTIMATE	1.20	
EXACT 95% CI	(0.28, 10.85)	
ODDS RATIO		
ESTIMATE	1.50	
EXACT 95% CI	(0.05, 39.79)	
P-VALUE [1]	0.7773	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
DEMAND

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	46/65 (70.8)	21/62 (33.9)
RISK DIFFERENCE		
ESTIMATE	36.90	
EXACT 95% CI	(19.61, 52.41)	
RELATIVE RISK		
ESTIMATE	2.09	
EXACT 95% CI	(1.42, 3.25)	
ODDS RATIO		
ESTIMATE	4.73	
EXACT 95% CI	(2.10, 10.73)	
P-VALUE [1]	< 0.0001†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	11/13 (84.6)	12/14 (85.7)
RISK DIFFERENCE		
ESTIMATE	-1.10	
EXACT 95% CI	(-36.27, 36.27)	
RELATIVE RISK		
ESTIMATE	0.99	
EXACT 95% CI	(0.61, 1.51)	
ODDS RATIO		
ESTIMATE	0.92	
EXACT 95% CI	(0.06, 14.75)	
P-VALUE [1]	0.9372	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	3/5 (60.0)	2/4 (50.0)
RISK DIFFERENCE		
ESTIMATE	10.00	
EXACT 95% CI	(-56.06, 70.06)	
RELATIVE RISK		
ESTIMATE	1.20	
EXACT 95% CI	(0.28, 10.85)	
ODDS RATIO		
ESTIMATE	1.50	
EXACT 95% CI	(0.05, 39.79)	
P-VALUE [1]	0.7773	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	47/65 (72.3)	25/62 (40.3)
RISK DIFFERENCE		
ESTIMATE	31.99	
EXACT 95% CI	(14.48, 47.76)	
RELATIVE RISK		
ESTIMATE	1.79	
EXACT 95% CI	(1.26, 2.72)	
ODDS RATIO		
ESTIMATE	3.86	
EXACT 95% CI	(1.73, 8.72)	
P-VALUE [1]	0.0003†	

1.2.7 Attacken-Schwere (PGI-S) zu Baseline

- PGI-C=Patient Global Impression of Change; CI=Confidence Interval; NE=Not Evaluable
- Attack with beginning of symptom relief is defined as at least “better” (2 time points in a row with or without missing values in between) within 2, 4, 6, 8, 10, 12, 24, and 48 hours of the first IMP administration. Time to beginning of symptom relief is calculated as Date/time of first rating of “better” or higher (i.e. much better) which is immediately followed by another rating of “better” or higher (with or without possible missing values in between) – Date/time of first IMP administration.
- Attacks that did not have at least 2 post-baseline assessments within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- †: p-value < 0.05.
- [1] P-value from Cochran-Mantel-Haenszel test.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
NONE OR MILD

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	10/34 (29.4)	4/36 (11.1)
RISK DIFFERENCE		
ESTIMATE	18.30	
EXACT 95% CI	(-4.99, 40.61)	
RELATIVE RISK		
ESTIMATE	2.65	
EXACT 95% CI	(0.95, 15.63)	
ODDS RATIO		
ESTIMATE	3.33	
EXACT 95% CI	(0.82, 16.09)	
P-VALUE [1]	0.0575	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
MODERATE

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	6/31 (19.4)	1/28 (3.6)
RISK DIFFERENCE		
ESTIMATE	15.78	
EXACT 95% CI	(-9.91, 40.23)	
RELATIVE RISK		
ESTIMATE	5.42	
EXACT 95% CI	(0.88, 138.63)	
ODDS RATIO		
ESTIMATE	6.48	
EXACT 95% CI	(0.69, 308.86)	
P-VALUE [1]	0.0634	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
SEVERE OR VERY SEVERE

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	3/14 (21.4)	0/13 (0)
RISK DIFFERENCE		
ESTIMATE	21.43	
EXACT 95% CI	(-15.44, 55.37)	
RELATIVE RISK		
ESTIMATE	NE	
EXACT 95% CI	NE	
ODDS RATIO		
ESTIMATE	NE	
EXACT 95% CI	NE	
P-VALUE [1]	0.0824	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
NONE OR MILD

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	17/35 (48.6)	8/36 (22.2)
RISK DIFFERENCE		
ESTIMATE	26.35	
EXACT 95% CI	(2.18, 47.12)	
RELATIVE RISK		
ESTIMATE	2.19	
EXACT 95% CI	(1.08, 5.20)	
ODDS RATIO		
ESTIMATE	3.31	
EXACT 95% CI	(1.06, 10.68)	
P-VALUE [1]	0.0210†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
MODERATE

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	13/32 (40.6)	7/30 (23.3)
RISK DIFFERENCE		
ESTIMATE	17.29	
EXACT 95% CI	(-7.31, 41.13)	
RELATIVE RISK		
ESTIMATE	1.74	
EXACT 95% CI	(0.81, 4.24)	
ODDS RATIO		
ESTIMATE	2.25	
EXACT 95% CI	(0.66, 8.01)	
P-VALUE [1]	0.1488	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
SEVERE OR VERY SEVERE

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/14 (35.7)	1/13 (7.7)
RISK DIFFERENCE		
ESTIMATE	28.02	
EXACT 95% CI	(-8.10, 61.34)	
RELATIVE RISK		
ESTIMATE	4.64	
EXACT 95% CI	(0.81, 120.49)	
ODDS RATIO		
ESTIMATE	6.67	
EXACT 95% CI	(0.56, 340.99)	
P-VALUE [1]	0.0859	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
NONE OR MILD

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	17/35 (48.6)	8/36 (22.2)
RISK DIFFERENCE		
ESTIMATE	26.35	
EXACT 95% CI	(2.18, 47.12)	
RELATIVE RISK		
ESTIMATE	2.19	
EXACT 95% CI	(1.08, 5.20)	
ODDS RATIO		
ESTIMATE	3.31	
EXACT 95% CI	(1.06, 10.68)	
P-VALUE [1]	0.0210†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
MODERATE

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	14/32 (43.8)	7/30 (23.3)
RISK DIFFERENCE		
ESTIMATE	20.42	
EXACT 95% CI	(-4.08, 44.03)	
RELATIVE RISK		
ESTIMATE	1.88	
EXACT 95% CI	(0.89, 4.85)	
ODDS RATIO		
ESTIMATE	2.56	
EXACT 95% CI	(0.76, 9.05)	
P-VALUE [1]	0.0922	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
SEVERE OR VERY SEVERE

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	7/14 (50.0)	2/13 (15.4)
RISK DIFFERENCE		
ESTIMATE	34.62	
EXACT 95% CI	(-2.12, 66.99)	
RELATIVE RISK		
ESTIMATE	3.25	
EXACT 95% CI	(0.93, 30.47)	
ODDS RATIO		
ESTIMATE	5.50	
EXACT 95% CI	(0.70, 64.91)	
P-VALUE [1]	0.0614	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
NONE OR MILD

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	18/35 (51.4)	9/36 (25.0)
RISK DIFFERENCE		
ESTIMATE	26.43	
EXACT 95% CI	(2.22, 47.48)	
RELATIVE RISK		
ESTIMATE	2.06	
EXACT 95% CI	(1.07, 4.35)	
ODDS RATIO		
ESTIMATE	3.18	
EXACT 95% CI	(1.05, 9.89)	
P-VALUE [1]	0.0228†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
MODERATE

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	17/32 (53.1)	8/30 (26.7)
RISK DIFFERENCE		
ESTIMATE	26.46	
EXACT 95% CI	(1.74, 49.64)	
RELATIVE RISK		
ESTIMATE	1.99	
EXACT 95% CI	(1.03, 4.60)	
ODDS RATIO		
ESTIMATE	3.12	
EXACT 95% CI	(0.96, 10.50)	
P-VALUE [1]	0.0353†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
SEVERE OR VERY SEVERE

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/14 (64.3)	2/13 (15.4)
RISK DIFFERENCE		
ESTIMATE	48.90	
EXACT 95% CI	(11.49, 77.62)	
RELATIVE RISK		
ESTIMATE	4.18	
EXACT 95% CI	(1.22, 30.59)	
ODDS RATIO		
ESTIMATE	9.90	
EXACT 95% CI	(1.23, 115.79)	
P-VALUE [1]	0.0112†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
NONE OR MILD

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	21/35 (60.0)	9/36 (25.0)
RISK DIFFERENCE		
ESTIMATE	35.00	
EXACT 95% CI	(11.03, 55.48)	
RELATIVE RISK		
ESTIMATE	2.40	
EXACT 95% CI	(1.23, 5.37)	
ODDS RATIO		
ESTIMATE	4.50	
EXACT 95% CI	(1.47, 14.14)	
P-VALUE [1]	0.0030†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
MODERATE

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	18/32 (56.3)	10/31 (32.3)
RISK DIFFERENCE		
ESTIMATE	23.99	
EXACT 95% CI	(-1.12, 47.50)	
RELATIVE RISK		
ESTIMATE	1.74	
EXACT 95% CI	(0.97, 3.41)	
ODDS RATIO		
ESTIMATE	2.70	
EXACT 95% CI	(0.86, 8.59)	
P-VALUE [1]	0.0573	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
SEVERE OR VERY SEVERE

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/14 (64.3)	2/13 (15.4)
RISK DIFFERENCE		
ESTIMATE	48.90	
EXACT 95% CI	(11.49, 77.62)	
RELATIVE RISK		
ESTIMATE	4.18	
EXACT 95% CI	(1.22, 30.59)	
ODDS RATIO		
ESTIMATE	9.90	
EXACT 95% CI	(1.23, 115.79)	
P-VALUE [1]	0.0112†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
NONE OR MILD

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	23/36 (63.9)	9/36 (25.0)
RISK DIFFERENCE		
ESTIMATE	38.89	
EXACT 95% CI	(14.94, 59.52)	
RELATIVE RISK		
ESTIMATE	2.56	
EXACT 95% CI	(1.34, 5.82)	
ODDS RATIO		
ESTIMATE	5.31	
EXACT 95% CI	(1.73, 16.72)	
P-VALUE [1]	0.0010†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
MODERATE

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	20/33 (60.6)	10/31 (32.3)
RISK DIFFERENCE		
ESTIMATE	28.35	
EXACT 95% CI	(3.45, 51.00)	
RELATIVE RISK		
ESTIMATE	1.88	
EXACT 95% CI	(1.06, 3.80)	
ODDS RATIO		
ESTIMATE	3.23	
EXACT 95% CI	(1.03, 10.27)	
P-VALUE [1]	0.0242†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
SEVERE OR VERY SEVERE

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	10/14 (71.4)	2/13 (15.4)
RISK DIFFERENCE		
ESTIMATE	56.04	
EXACT 95% CI	(18.66, 82.50)	
RELATIVE RISK		
ESTIMATE	4.64	
EXACT 95% CI	(1.33, 50.18)	
ODDS RATIO		
ESTIMATE	13.75	
EXACT 95% CI	(1.62, 162.89)	
P-VALUE [1]	0.0041†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
NONE OR MILD

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	26/36 (72.2)	12/36 (33.3)
RISK DIFFERENCE		
ESTIMATE	38.89	
EXACT 95% CI	(14.94, 59.52)	
RELATIVE RISK		
ESTIMATE	2.17	
EXACT 95% CI	(1.30, 3.99)	
ODDS RATIO		
ESTIMATE	5.20	
EXACT 95% CI	(1.71, 16.13)	
P-VALUE [1]	0.0010†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
MODERATE

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	23/33 (69.7)	16/31 (51.6)
RISK DIFFERENCE		
ESTIMATE	18.08	
EXACT 95% CI	(-7.25, 41.06)	
RELATIVE RISK		
ESTIMATE	1.35	
EXACT 95% CI	(0.90, 2.23)	
ODDS RATIO		
ESTIMATE	2.16	
EXACT 95% CI	(0.69, 6.83)	
P-VALUE [1]	0.1415	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
SEVERE OR VERY SEVERE

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	11/14 (78.6)	6/13 (46.2)
RISK DIFFERENCE		
ESTIMATE	32.42	
EXACT 95% CI	(-7.75, 64.56)	
RELATIVE RISK		
ESTIMATE	1.70	
EXACT 95% CI	(0.91, 3.98)	
ODDS RATIO		
ESTIMATE	4.28	
EXACT 95% CI	(0.63, 33.80)	
P-VALUE [1]	0.0872	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
NONE OR MILD

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	26/36 (72.2)	15/36 (41.7)
RISK DIFFERENCE		
ESTIMATE	30.56	
EXACT 95% CI	(6.27, 52.24)	
RELATIVE RISK		
ESTIMATE	1.73	
EXACT 95% CI	(1.11, 3.11)	
ODDS RATIO		
ESTIMATE	3.64	
EXACT 95% CI	(1.23, 11.02)	
P-VALUE [1]	0.0093†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
MODERATE

TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	23/33 (69.7)	17/31 (54.8)
RISK DIFFERENCE		
ESTIMATE	14.86	
EXACT 95% CI	(-10.42, 37.93)	
RELATIVE RISK		
ESTIMATE	1.27	
EXACT 95% CI	(0.86, 2.00)	
ODDS RATIO		
ESTIMATE	1.89	
EXACT 95% CI	(0.60, 6.01)	
P-VALUE [1]	0.2234	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS ATTACK SEVERITY AT BASELINE PGI-S = SEVERE OR VERY SEVERE		
TIME TO BEGINNING OF SYMPTOM RELIEF ON PGI-C	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	12/14 (85.7)	7/13 (53.8)
RISK DIFFERENCE		
ESTIMATE	31.87	
EXACT 95% CI	(-8.03, 63.37)	
RELATIVE RISK		
ESTIMATE	1.59	
EXACT 95% CI	(0.94, 3.41)	
ODDS RATIO		
ESTIMATE	5.14	
EXACT 95% CI	(0.63, 61.76)	
P-VALUE [1]	0.0754	

1.3 Anzahl und Anteil der Attacken mit Auflösung der Attacke definiert als „keine“ im PGI-S

1.3.1 Geschlecht

- PGI-S=Patient Global Impression of Severity; CI=Confidence Interval
- Attack resolution is defined as 'none' within 4, 8, 12, 24, and 48 hours of the first IMP administration.
- Time to HAE attack resolution (hours) = Date/time of first rating of "None"– Date/time of first IMP administration.
- Attacks that did not have at least 1 post-baseline assessment within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline PGI-S category (none or mild, moderate, and severe or very severe).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline PGI-S category (none or mild, moderate, and severe or very severe).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | SEX = MALE

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/32 (12.5)	2/27 (7.4)
RISK DIFFERENCE [1]		
ESTIMATE	5.17	
95% CI	(-9.83, 20.18)	
RELATIVE RISK [2]		
ESTIMATE	1.48	
95% CI	(0.33, 6.54)	
ODDS RATIO [2]		
ESTIMATE	1.59*	
95% CI	(0.30, 8.48)*	
P-VALUE [3]	0.5203	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | SEX = FEMALE

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/49 (18.4)	4/52 (7.7)
RISK DIFFERENCE [1]		
ESTIMATE	11.11	
95% CI	(-1.72, 23.94)	
RELATIVE RISK [2]		
ESTIMATE	2.30	
95% CI	(0.81, 6.49)	
ODDS RATIO [2]		
ESTIMATE	2.69*	
95% CI	(0.80, 9.08)*	
P-VALUE [3]	0.0940	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | SEX = MALE

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	7/32 (21.9)	3/27 (11.1)
RISK DIFFERENCE [1]		
ESTIMATE	10.80	
95% CI	(-8.16, 29.75)	
RELATIVE RISK [2]		
ESTIMATE	1.54	
95% CI	(0.41, 5.82)	
ODDS RATIO [2]		
ESTIMATE	1.85*	
95% CI	(0.39, 8.79)*	
P-VALUE [3]	0.2822	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | SEX = FEMALE

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	13/49 (26.5)	9/52 (17.3)
RISK DIFFERENCE [1]		
ESTIMATE	9.66	
95% CI	(-6.27, 25.59)	
RELATIVE RISK [2]		
ESTIMATE	1.45	
95% CI	(0.70, 3.04)	
ODDS RATIO [2]		
ESTIMATE	1.68*	
95% CI	(0.64, 4.43)*	
P-VALUE [3]	0.2411	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | SEX = MALE

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/32 (28.1)	3/27 (11.1)
RISK DIFFERENCE [1]		
ESTIMATE	17.02	
95% CI	(-3.18, 37.22)	
RELATIVE RISK [2]		
ESTIMATE	1.87	
95% CI	(0.50, 6.91)	
ODDS RATIO [2]		
ESTIMATE	2.44*	
95% CI	(0.52, 11.35)*	
P-VALUE [3]	0.1149	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | SEX = FEMALE

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	19/51 (37.3)	11/53 (20.8)
RISK DIFFERENCE [1]		
ESTIMATE	17.07	
95% CI	(0.46, 33.69)	
RELATIVE RISK [2]		
ESTIMATE	1.79	
95% CI	(0.98, 3.28)	
ODDS RATIO [2]		
ESTIMATE	2.36*	
95% CI	(0.94, 5.91)*	
P-VALUE [3]	0.0478†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | SEX = MALE

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	13/32 (40.6)	5/27 (18.5)
RISK DIFFERENCE [1]		
ESTIMATE	22.12	
95% CI	(-0.18, 44.41)	
RELATIVE RISK [2]		
ESTIMATE	1.65	
95% CI	(0.67, 4.04)	
ODDS RATIO [2]		
ESTIMATE	2.91	
95% CI	(0.77, 10.96)	
P-VALUE [3]	0.0684	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | SEX = FEMALE

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	24/51 (47.1)	18/53 (34.0)
RISK DIFFERENCE [1]		
ESTIMATE	13.47	
95% CI	(-4.85, 31.79)	
RELATIVE RISK [2]		
ESTIMATE	1.39	
95% CI	(0.88, 2.21)	
ODDS RATIO [2]		
ESTIMATE	1.80	
95% CI	(0.80, 4.05)	
P-VALUE [3]	0.1589	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | SEX = MALE

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	16/32 (50.0)	10/27 (37.0)
RISK DIFFERENCE [1]		
ESTIMATE	12.87	
95% CI	(-11.20, 36.95)	
RELATIVE RISK [2]		
ESTIMATE	1.30	
95% CI	(0.74, 2.29)	
ODDS RATIO [2]		
ESTIMATE	1.75	
95% CI	(0.55, 5.56)	
P-VALUE [3]	0.3046	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS SEX = FEMALE		
TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	25/51 (49.0)	24/53 (45.3)
RISK DIFFERENCE [1]		
ESTIMATE	3.93	
95% CI	(-14.96, 22.83)	
RELATIVE RISK [2]		
ESTIMATE	1.08	
95% CI	(0.72, 1.60)	
ODDS RATIO [2]		
ESTIMATE	1.17	
95% CI	(0.53, 2.60)	
P-VALUE [3]	0.6858	

1.3.2 Alter

- PGI-S=Patient Global Impression of Severity; CI=Confidence Interval
- Attack resolution is defined as 'none' within 4, 8, 12, 24, and 48 hours of the first IMP administration.
- Time to HAE attack resolution (hours) = Date/time of first rating of "None"– Date/time of first IMP administration.
- Attacks that did not have at least 1 post-baseline assessment within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline PGI-S category (none or mild, moderate, and severe or very severe).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline PGI-S category (none or mild, moderate, and severe or very severe).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | <18 YEARS

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	2/9 (22.2)	1/9 (11.1)
RISK DIFFERENCE [1]		
ESTIMATE	5.22	
95% CI	(-31.18, 41.62)	
RELATIVE RISK [2]		
ESTIMATE	1.33	
95% CI	(0.17, 10.25)	
ODDS RATIO [2]		
ESTIMATE	1.50*	
95% CI	(0.09, 25.39)*	
P-VALUE [3]	0.7893	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | >=18 YEARS

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	11/72 (15.3)	5/70 (7.1)
RISK DIFFERENCE [1]		
ESTIMATE	8.60	
95% CI	(-1.64, 18.84)	
RELATIVE RISK [2]		
ESTIMATE	2.22	
95% CI	(0.82, 6.04)	
ODDS RATIO [2]		
ESTIMATE	2.48	
95% CI	(0.81, 7.65)	
P-VALUE [3]	0.1078	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | <18 YEARS

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	2/9 (22.2)	1/9 (11.1)
RISK DIFFERENCE [1]		
ESTIMATE	5.22	
95% CI	(-31.18, 41.62)	
RELATIVE RISK [2]		
ESTIMATE	1.33	
95% CI	(0.17, 10.25)	
ODDS RATIO [2]		
ESTIMATE	1.50*	
95% CI	(0.09, 25.39)*	
P-VALUE [3]	0.7893	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | >=18 YEARS

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	18/72 (25.0)	11/70 (15.7)
RISK DIFFERENCE [1]		
ESTIMATE	9.59	
95% CI	(-3.53, 22.71)	
RELATIVE RISK [2]		
ESTIMATE	1.60	
95% CI	(0.81, 3.16)	
ODDS RATIO [2]		
ESTIMATE	1.82	
95% CI	(0.78, 4.24)	
P-VALUE [3]	0.1611	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | <18 YEARS

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/10 (40.0)	1/9 (11.1)
RISK DIFFERENCE [1]		
ESTIMATE	23.39	
95% CI	(-13.09, 59.87)	
RELATIVE RISK [2]		
ESTIMATE	2.67	
95% CI	(0.45, 15.96)	
ODDS RATIO [2]		
ESTIMATE	6.00*	
95% CI	(0.35, 101.57)*	
P-VALUE [3]	0.2207	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | >=18 YEARS

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	24/73 (32.9)	13/71 (18.3)
RISK DIFFERENCE [1]		
ESTIMATE	15.02	
95% CI	(1.08, 28.96)	
RELATIVE RISK [2]		
ESTIMATE	1.84	
95% CI	(1.02, 3.30)	
ODDS RATIO [2]		
ESTIMATE	2.27	
95% CI	(1.04, 4.97)	
P-VALUE [3]	0.0397†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | <18 YEARS

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/10 (40.0)	3/9 (33.3)
RISK DIFFERENCE [1]		
ESTIMATE	5.85	
95% CI	(-41.68, 53.38)	
RELATIVE RISK [2]		
ESTIMATE	1.40	
95% CI	(0.31, 6.27)	
ODDS RATIO [2]		
ESTIMATE	1.48*	
95% CI	(0.17, 12.92)*	
P-VALUE [3]	0.8089	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | >=18 YEARS

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	33/73 (45.2)	20/71 (28.2)
RISK DIFFERENCE [1]		
ESTIMATE	17.19	
95% CI	(1.69, 32.69)	
RELATIVE RISK [2]		
ESTIMATE	1.59	
95% CI	(1.01, 2.51)	
ODDS RATIO [2]		
ESTIMATE	2.11	
95% CI	(1.05, 4.24)	
P-VALUE [3]	0.0344†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | <18 YEARS

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/10 (50.0)	5/9 (55.6)
RISK DIFFERENCE [1]		
ESTIMATE	-16.96	
95% CI	(-64.57, 30.65)	
RELATIVE RISK [2]		
ESTIMATE	1.01	
95% CI	(0.36, 2.87)	
ODDS RATIO [2]		
ESTIMATE	0.66*	
95% CI	(0.08, 5.19)*	
P-VALUE [3]	0.4975	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS >=18 YEARS		
TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	36/73 (49.3)	29/71 (40.8)
RISK DIFFERENCE [1]		
ESTIMATE	7.98	
95% CI	(-8.24, 24.21)	
RELATIVE RISK [2]		
ESTIMATE	1.16	
95% CI	(0.81, 1.66)	
ODDS RATIO [2]		
ESTIMATE	1.38	
95% CI	(0.71, 2.69)	
P-VALUE [3]	0.3386	

1.3.3 Region (Variante 1)

- PGI-S=Patient Global Impression of Severity; CI=Confidence Interval
- Attack resolution is defined as 'none' within 4, 8, 12, 24, and 48 hours of the first IMP administration.
- Time to HAE attack resolution (hours) = Date/time of first rating of "None" – Date/time of first IMP administration.
- Attacks that did not have at least 1 post-baseline assessment within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline PGI-S category (none or mild, moderate, and severe or very severe).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline PGI-S category (none or mild, moderate, and severe or very severe).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | REGION 1 = US

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/24 (16.7)	1/21 (4.8)
RISK DIFFERENCE [1]		
ESTIMATE	16.13	
95% CI	(-1.67, 33.93)	
RELATIVE RISK [2]		
ESTIMATE	3.16	
95% CI	(0.56, 17.87)	
ODDS RATIO [2]		
ESTIMATE	3.84*	
95% CI	(0.53, 27.96)*	
P-VALUE [3]	0.0979	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | REGION 1 = ROW

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/57 (15.8)	5/58 (8.6)
RISK DIFFERENCE [1]		
ESTIMATE	6.61	
95% CI	(-5.25, 18.47)	
RELATIVE RISK [2]		
ESTIMATE	1.72	
95% CI	(0.62, 4.79)	
ODDS RATIO [2]		
ESTIMATE	1.89	
95% CI	(0.59, 6.12)	
P-VALUE [3]	0.2819	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | REGION 1 = US

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/24 (20.8)	4/21 (19.0)
RISK DIFFERENCE [1]		
ESTIMATE	5.19	
95% CI	(-18.49, 28.86)	
RELATIVE RISK [2]		
ESTIMATE	1.30	
95% CI	(0.41, 4.13)	
ODDS RATIO [2]		
ESTIMATE	1.40*	
95% CI	(0.30, 6.51)*	
P-VALUE [3]	0.6751	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | REGION 1 = ROW

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	15/57 (26.3)	8/58 (13.8)
RISK DIFFERENCE [1]		
ESTIMATE	12.17	
95% CI	(-2.37, 26.70)	
RELATIVE RISK [2]		
ESTIMATE	1.82	
95% CI	(0.84, 3.95)	
ODDS RATIO [2]		
ESTIMATE	2.16	
95% CI	(0.83, 5.64)	
P-VALUE [3]	0.1073	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | REGION 1 = US

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/24 (37.5)	5/21 (23.8)
RISK DIFFERENCE [1]		
ESTIMATE	21.32	
95% CI	(-3.83, 46.47)	
RELATIVE RISK [2]		
ESTIMATE	2.03	
95% CI	(0.87, 4.76)	
ODDS RATIO [2]		
ESTIMATE	3.20*	
95% CI	(0.73, 13.96)*	
P-VALUE [3]	0.1229	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | REGION 1 = ROW

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	19/59 (32.2)	9/59 (15.3)
RISK DIFFERENCE [1]		
ESTIMATE	16.19	
95% CI	(1.16, 31.21)	
RELATIVE RISK [2]		
ESTIMATE	2.04	
95% CI	(1.00, 4.15)	
ODDS RATIO [2]		
ESTIMATE	2.54	
95% CI	(1.03, 6.29)	
P-VALUE [3]	0.0401†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | REGION 1 = US

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	12/24 (50.0)	8/21 (38.1)
RISK DIFFERENCE [1]		
ESTIMATE	14.89	
95% CI	(-15.07, 44.86)	
RELATIVE RISK [2]		
ESTIMATE	1.49	
95% CI	(0.76, 2.92)	
ODDS RATIO [2]		
ESTIMATE	1.87*	
95% CI	(0.53, 6.61)*	
P-VALUE [3]	0.3384	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | REGION 1 = ROW

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	25/59 (42.4)	15/59 (25.4)
RISK DIFFERENCE [1]		
ESTIMATE	16.67	
95% CI	(-0.18, 33.51)	
RELATIVE RISK [2]		
ESTIMATE	1.65	
95% CI	(0.97, 2.81)	
ODDS RATIO [2]		
ESTIMATE	2.13	
95% CI	(0.97, 4.67)	
P-VALUE [3]	0.0594	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | REGION 1 = US

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	12/24 (50.0)	11/21 (52.4)
RISK DIFFERENCE [1]		
ESTIMATE	-1.67	
95% CI	(-32.08, 28.73)	
RELATIVE RISK [2]		
ESTIMATE	1.01	
95% CI	(0.59, 1.73)	
ODDS RATIO [2]		
ESTIMATE	0.95*	
95% CI	(0.27, 3.33)*	
P-VALUE [3]	0.9143	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS REGION 1 = ROW		
TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	29/59 (49.2)	23/59 (39.0)
RISK DIFFERENCE [1]		
ESTIMATE	10.90	
95% CI	(-7.17, 28.97)	
RELATIVE RISK [2]		
ESTIMATE	1.23	
95% CI	(0.80, 1.90)	
ODDS RATIO [2]		
ESTIMATE	1.52	
95% CI	(0.71, 3.23)	
P-VALUE [3]	0.2380	

1.3.4 Region (Variante 2)

- PGI-S=Patient Global Impression of Severity; CI=Confidence Interval
- Attack resolution is defined as 'none' within 4, 8, 12, 24, and 48 hours of the first IMP administration.
- Time to HAE attack resolution (hours) = Date/time of first rating of "None" – Date/time of first IMP administration.
- Attacks that did not have at least 1 post-baseline assessment within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline PGI-S category (none or mild, moderate, and severe or very severe).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline PGI-S category (none or mild, moderate, and severe or very severe).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | REGION 2 = NORTH AMERICA

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/24 (16.7)	1/21 (4.8)
RISK DIFFERENCE [1]		
ESTIMATE	16.13	
95% CI	(-1.67, 33.93)	
RELATIVE RISK [2]		
ESTIMATE	3.16	
95% CI	(0.56, 17.87)	
ODDS RATIO [2]		
ESTIMATE	3.84*	
95% CI	(0.53, 27.96)*	
P-VALUE [3]	0.0979	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | REGION 2 = EUROPE

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/41 (12.2)	3/45 (6.7)
RISK DIFFERENCE [1]		
ESTIMATE	5.29	
95% CI	(-7.10, 17.67)	
RELATIVE RISK [2]		
ESTIMATE	1.77	
95% CI	(0.45, 7.02)	
ODDS RATIO [2]		
ESTIMATE	1.88	
95% CI	(0.41, 8.61)	
P-VALUE [3]	0.4066	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | REGION 2 = ROW

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/16 (25.0)	2/13 (15.4)
RISK DIFFERENCE [1]		
ESTIMATE	5.88	
95% CI	(-22.60, 34.36)	
RELATIVE RISK [2]		
ESTIMATE	1.33	
95% CI	(0.32, 5.64)	
ODDS RATIO [2]		
ESTIMATE	1.50*	
95% CI	(0.20, 11.09)*	
P-VALUE [3]	0.6978	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | REGION 2 = NORTH AMERICA

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/24 (20.8)	4/21 (19.0)
RISK DIFFERENCE [1]		
ESTIMATE	5.19	
95% CI	(-18.49, 28.86)	
RELATIVE RISK [2]		
ESTIMATE	1.30	
95% CI	(0.41, 4.13)	
ODDS RATIO [2]		
ESTIMATE	1.40*	
95% CI	(0.30, 6.51)*	
P-VALUE [3]	0.6751	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | REGION 2 = EUROPE

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/41 (22.0)	6/45 (13.3)
RISK DIFFERENCE [1]		
ESTIMATE	8.17	
95% CI	(-7.92, 24.25)	
RELATIVE RISK [2]		
ESTIMATE	1.59	
95% CI	(0.62, 4.06)	
ODDS RATIO [2]		
ESTIMATE	1.78	
95% CI	(0.57, 5.56)	
P-VALUE [3]	0.3264	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | REGION 2 = ROW

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	6/16 (37.5)	2/13 (15.4)
RISK DIFFERENCE [1]		
ESTIMATE	20.59	
95% CI	(-12.46, 53.64)	
RELATIVE RISK [2]		
ESTIMATE	1.77	
95% CI	(0.49, 6.35)	
ODDS RATIO [2]		
ESTIMATE	2.37*	
95% CI	(0.42, 13.33)*	
P-VALUE [3]	0.2514	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | REGION 2 = NORTH AMERICA

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/24 (37.5)	5/21 (23.8)
RISK DIFFERENCE [1]		
ESTIMATE	21.32	
95% CI	(-3.83, 46.47)	
RELATIVE RISK [2]		
ESTIMATE	2.03	
95% CI	(0.87, 4.76)	
ODDS RATIO [2]		
ESTIMATE	3.20*	
95% CI	(0.73, 13.96)*	
P-VALUE [3]	0.1229	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | REGION 2 = EUROPE

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	10/43 (23.3)	7/46 (15.2)
RISK DIFFERENCE [1]		
ESTIMATE	7.67	
95% CI	(-8.67, 24.01)	
RELATIVE RISK [2]		
ESTIMATE	1.49	
95% CI	(0.62, 3.59)	
ODDS RATIO [2]		
ESTIMATE	1.64	
95% CI	(0.56, 4.86)	
P-VALUE [3]	0.3659	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | REGION 2 = ROW

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/16 (56.3)	2/13 (15.4)
RISK DIFFERENCE [1]		
ESTIMATE	38.24	
95% CI	(5.72, 70.75)	
RELATIVE RISK [2]		
ESTIMATE	2.67	
95% CI	(0.83, 8.62)	
ODDS RATIO [2]		
ESTIMATE	5.08*	
95% CI	(0.92, 27.96)*	
P-VALUE [3]	0.0448†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | REGION 2 = NORTH AMERICA

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	12/24 (50.0)	8/21 (38.1)
RISK DIFFERENCE [1]		
ESTIMATE	14.89	
95% CI	(-15.07, 44.86)	
RELATIVE RISK [2]		
ESTIMATE	1.49	
95% CI	(0.76, 2.92)	
ODDS RATIO [2]		
ESTIMATE	1.87*	
95% CI	(0.53, 6.61)*	
P-VALUE [3]	0.3384	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | REGION 2 = EUROPE

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	16/43 (37.2)	12/46 (26.1)
RISK DIFFERENCE [1]		
ESTIMATE	11.03	
95% CI	(-8.16, 30.22)	
RELATIVE RISK [2]		
ESTIMATE	1.42	
95% CI	(0.76, 2.65)	
ODDS RATIO [2]		
ESTIMATE	1.68	
95% CI	(0.67, 4.17)	
P-VALUE [3]	0.2701	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | REGION 2 = ROW

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/16 (56.3)	3/13 (23.1)
RISK DIFFERENCE [1]		
ESTIMATE	29.41	
95% CI	(-5.30, 64.12)	
RELATIVE RISK [2]		
ESTIMATE	1.79	
95% CI	(0.69, 4.63)	
ODDS RATIO [2]		
ESTIMATE	3.16*	
95% CI	(0.63, 15.90)*	
P-VALUE [3]	0.1241	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | REGION 2 = NORTH AMERICA

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	12/24 (50.0)	11/21 (52.4)
RISK DIFFERENCE [1]		
ESTIMATE	-1.67	
95% CI	(-32.08, 28.73)	
RELATIVE RISK [2]		
ESTIMATE	1.01	
95% CI	(0.59, 1.73)	
ODDS RATIO [2]		
ESTIMATE	0.95*	
95% CI	(0.27, 3.33)*	
P-VALUE [3]	0.9143	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | REGION 2 = EUROPE

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	20/43 (46.5)	17/46 (37.0)
RISK DIFFERENCE [1]		
ESTIMATE	9.87	
95% CI	(-10.53, 30.28)	
RELATIVE RISK [2]		
ESTIMATE	1.21	
95% CI	(0.72, 2.04)	
ODDS RATIO [2]		
ESTIMATE	1.48	
95% CI	(0.60, 3.64)	
P-VALUE [3]	0.3422	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS REGION 2 = ROW		
TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/16 (56.3)	6/13 (46.2)
RISK DIFFERENCE [1]		
ESTIMATE	5.88	
95% CI	(-31.59, 43.36)	
RELATIVE RISK [2]		
ESTIMATE	1.12	
95% CI	(0.55, 2.30)	
ODDS RATIO [2]		
ESTIMATE	1.27	
95% CI	(0.28, 5.73)	
P-VALUE [3]	0.7670	

1.3.5 Prophylaxe-Status (Variante 1)

- PGI-S=Patient Global Impression of Severity; CI=Confidence Interval
- Attack resolution is defined as 'none' within 4, 8, 12, 24, and 48 hours of the first IMP administration.
- Time to HAE attack resolution (hours) = Date/time of first rating of "None" – Date/time of first IMP administration.
- Attacks that did not have at least 1 post-baseline assessment within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline PGI-S category (none or mild, moderate, and severe or very severe).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline PGI-S category (none or mild, moderate, and severe or very severe).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	2/18 (11.1)	2/18 (11.1)
RISK DIFFERENCE [1]		
ESTIMATE	2.21	
95% CI	(-17.81, 22.23)	
RELATIVE RISK [2]		
ESTIMATE	1.07	
95% CI	(0.18, 6.37)	
ODDS RATIO [2]		
ESTIMATE	1.11*	
95% CI	(0.14, 8.83)*	
P-VALUE [3]	0.8368	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

PROPHYLACTIC TREATMENT STATUS 1 = ON DEMAND

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	11/63 (17.5)	4/61 (6.6)
RISK DIFFERENCE [1]		
ESTIMATE	10.76	
95% CI	(-0.41, 21.92)	
RELATIVE RISK [2]		
ESTIMATE	2.61	
95% CI	(0.87, 7.77)	
ODDS RATIO [2]		
ESTIMATE	2.99	
95% CI	(0.88, 10.13)	
P-VALUE [3]	0.0667	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	2/18 (11.1)	6/18 (33.3)
RISK DIFFERENCE [1]		
ESTIMATE	-18.45	
95% CI	(-44.38, 7.49)	
RELATIVE RISK [2]		
ESTIMATE	0.40	
95% CI	(0.09, 1.88)	
ODDS RATIO [2]		
ESTIMATE	0.30*	
95% CI	(0.04, 1.99)*	
P-VALUE [3]	0.1805	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
DEMAND

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	18/63 (28.6)	6/61 (9.8)
RISK DIFFERENCE [1]		
ESTIMATE	18.71	
95% CI	(5.28, 32.14)	
RELATIVE RISK [2]		
ESTIMATE	2.75	
95% CI	(1.16, 6.54)	
ODDS RATIO [2]		
ESTIMATE	3.56	
95% CI	(1.28, 9.93)	
P-VALUE [3]	0.0091†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	6/18 (33.3)	7/18 (38.9)
RISK DIFFERENCE [1]		
ESTIMATE	3.75	
95% CI	(-22.27, 29.77)	
RELATIVE RISK [2]		
ESTIMATE	1.15	
95% CI	(0.59, 2.25)	
ODDS RATIO [2]		
ESTIMATE	1.27*	
95% CI	(0.23, 6.97)*	
P-VALUE [3]	0.7856	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
DEMAND

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	22/65 (33.8)	7/62 (11.3)
RISK DIFFERENCE [1]		
ESTIMATE	22.45	
95% CI	(8.43, 36.47)	
RELATIVE RISK [2]		
ESTIMATE	2.74	
95% CI	(1.23, 6.08)	
ODDS RATIO [2]		
ESTIMATE	3.72	
95% CI	(1.42, 9.77)	
P-VALUE [3]	0.0029†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	12/18 (66.7)	11/18 (61.1)
RISK DIFFERENCE [1]		
ESTIMATE	9.68	
95% CI	(-21.49, 40.86)	
RELATIVE RISK [2]		
ESTIMATE	1.04	
95% CI	(0.64, 1.69)	
ODDS RATIO [2]		
ESTIMATE	1.54	
95% CI	(0.36, 6.57)	
P-VALUE [3]	0.5561	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
DEMAND

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	25/65 (38.5)	12/62 (19.4)
RISK DIFFERENCE [1]		
ESTIMATE	19.12	
95% CI	(3.60, 34.64)	
RELATIVE RISK [2]		
ESTIMATE	1.83	
95% CI	(0.99, 3.39)	
ODDS RATIO [2]		
ESTIMATE	2.46	
95% CI	(1.07, 5.64)	
P-VALUE [3]	0.0192†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	12/18 (66.7)	13/18 (72.2)
RISK DIFFERENCE [1]		
ESTIMATE	-3.38	
95% CI	(-33.85, 27.09)	
RELATIVE RISK [2]		
ESTIMATE	0.93	
95% CI	(0.60, 1.45)	
ODDS RATIO [2]		
ESTIMATE	0.85	
95% CI	(0.20, 3.63)	
P-VALUE [3]	0.8341	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS PROPHYLACTIC TREATMENT STATUS 1 = ON DEMAND		
TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	29/65 (44.6)	21/62 (33.9)
RISK DIFFERENCE [1]		
ESTIMATE	11.07	
95% CI	(-5.95, 28.09)	
RELATIVE RISK [2]		
ESTIMATE	1.22	
95% CI	(0.77, 1.92)	
ODDS RATIO [2]		
ESTIMATE	1.57	
95% CI	(0.74, 3.32)	
P-VALUE [3]	0.2041	

1.3.6 Prophylaxe-Status (Variante 2)

- PGI-S=Patient Global Impression of Severity; CI=Confidence Interval
- Attack resolution is defined as 'none' within 4, 8, 12, 24, and 48 hours of the first IMP administration.
- Time to HAE attack resolution (hours) = Date/time of first rating of "None" – Date/time of first IMP administration.
- Attacks that did not have at least 1 post-baseline assessment within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline PGI-S category (none or mild, moderate, and severe or very severe).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline PGI-S category (none or mild, moderate, and severe or very severe).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	2/13 (15.4)	2/14 (14.3)
RISK DIFFERENCE [1]		
ESTIMATE	2.39	
95% CI	(-23.85, 28.63)	
RELATIVE RISK [2]		
ESTIMATE	1.05	
95% CI	(0.18, 6.01)	
ODDS RATIO [2]		
ESTIMATE	1.10*	
95% CI	(0.13, 9.11)*	
P-VALUE [3]	0.8648	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	0/5 (0)	0/4 (0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
DEMAND

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	11/63 (17.5)	4/61 (6.6)
RISK DIFFERENCE [1]		
ESTIMATE	10.76	
95% CI	(-0.41, 21.92)	
RELATIVE RISK [2]		
ESTIMATE	2.61	
95% CI	(0.87, 7.77)	
ODDS RATIO [2]		
ESTIMATE	2.99	
95% CI	(0.88, 10.13)	
P-VALUE [3]	0.0667	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	2/13 (15.4)	6/14 (42.9)
RISK DIFFERENCE [1]		
ESTIMATE	-25.30	
95% CI	(-57.32, 6.72)	
RELATIVE RISK [2]		
ESTIMATE	0.40	
95% CI	(0.09, 1.76)	
ODDS RATIO [2]		
ESTIMATE	0.25*	
95% CI	(0.03, 1.84)*	
P-VALUE [3]	0.1455	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	0/5 (0)	0/4 (0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
DEMAND

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	18/63 (28.6)	6/61 (9.8)
RISK DIFFERENCE [1]		
ESTIMATE	18.71	
95% CI	(5.28, 32.14)	
RELATIVE RISK [2]		
ESTIMATE	2.75	
95% CI	(1.16, 6.54)	
ODDS RATIO [2]		
ESTIMATE	3.56	
95% CI	(1.28, 9.93)	
P-VALUE [3]	0.0091†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	6/13 (46.2)	7/14 (50.0)
RISK DIFFERENCE [1]		
ESTIMATE	2.63	
95% CI	(-26.14, 31.39)	
RELATIVE RISK [2]		
ESTIMATE	1.09	
95% CI	(0.65, 1.85)	
ODDS RATIO [2]		
ESTIMATE	1.19*	
95% CI	(0.15, 9.17)*	
P-VALUE [3]	0.8649	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	0/5 (0)	0/4 (0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
DEMAND

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	22/65 (33.8)	7/62 (11.3)
RISK DIFFERENCE [1]		
ESTIMATE	22.45	
95% CI	(8.43, 36.47)	
RELATIVE RISK [2]		
ESTIMATE	2.74	
95% CI	(1.23, 6.08)	
ODDS RATIO [2]		
ESTIMATE	3.72	
95% CI	(1.42, 9.77)	
P-VALUE [3]	0.0029†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/13 (69.2)	10/14 (71.4)
RISK DIFFERENCE [1]		
ESTIMATE	1.19	
95% CI	(-31.51, 33.90)	
RELATIVE RISK [2]		
ESTIMATE	0.98	
95% CI	(0.65, 1.47)	
ODDS RATIO [2]		
ESTIMATE	1.07	
95% CI	(0.18, 6.27)	
P-VALUE [3]	0.9466	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	3/5 (60.0)	1/4 (25.0)
RISK DIFFERENCE [1]		
ESTIMATE	25.00	
95% CI	(-50.15, 100.00)	
RELATIVE RISK [2]		
ESTIMATE	1.38	
95% CI	(0.21, 8.95)	
ODDS RATIO [2]		
ESTIMATE	1.87*	
95% CI	(0.13, 27.03)*	
P-VALUE [3]	0.5408	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
DEMAND

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	25/65 (38.5)	12/62 (19.4)
RISK DIFFERENCE [1]		
ESTIMATE	19.12	
95% CI	(3.60, 34.64)	
RELATIVE RISK [2]		
ESTIMATE	1.83	
95% CI	(0.99, 3.39)	
ODDS RATIO [2]		
ESTIMATE	2.46	
95% CI	(1.07, 5.64)	
P-VALUE [3]	0.0192†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/13 (69.2)	11/14 (78.6)
RISK DIFFERENCE [1]		
ESTIMATE	-7.16	
95% CI	(-39.05, 24.73)	
RELATIVE RISK [2]		
ESTIMATE	0.92	
95% CI	(0.63, 1.37)	
ODDS RATIO [2]		
ESTIMATE	0.67	
95% CI	(0.11, 4.18)	
P-VALUE [3]	0.6809	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	3/5 (60.0)	2/4 (50.0)
RISK DIFFERENCE [1]		
ESTIMATE	-7.14	
95% CI	(-78.09, 63.80)	
RELATIVE RISK [2]		
ESTIMATE	1.03	
95% CI	(0.26, 4.04)	
ODDS RATIO [2]		
ESTIMATE	0.87*	
95% CI	(0.06, 12.61)*	
P-VALUE [3]	0.8613	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	29/65 (44.6)	21/62 (33.9)
RISK DIFFERENCE [1]		
ESTIMATE	11.07	
95% CI	(-5.95, 28.09)	
RELATIVE RISK [2]		
ESTIMATE	1.22	
95% CI	(0.77, 1.92)	
ODDS RATIO [2]		
ESTIMATE	1.57	
95% CI	(0.74, 3.32)	
P-VALUE [3]	0.2041	

1.3.7 Attacken-Schwere (PGI-S) zu Baseline

- PGI-S=Patient Global Impression of Severity; CI=Confidence Interval
- Attack resolution is defined as 'none' within 4, 8, 12, 24, and 48 hours of the first IMP administration.
- Time to HAE attack resolution (hours) = Date/time of first rating of "None" – Date/time of first IMP administration.
- Attacks that did not have at least 1 post-baseline assessment within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test.
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test.
- [3] P-value from Cochran-Mantel-Haenszel test.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
NONE OR MILD

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	8/35 (22.9)	4/36 (11.1)
RISK DIFFERENCE [1]		
ESTIMATE	11.75	
95% CI	(-5.54, 29.04)	
RELATIVE RISK [2]		
ESTIMATE	2.06	
95% CI	(0.68, 6.22)	
ODDS RATIO [2]		
ESTIMATE	2.37	
95% CI	(0.64, 8.74)	
P-VALUE [3]	0.1899	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
MODERATE

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	3/32 (9.4)	1/30 (3.3)
RISK DIFFERENCE [1]		
ESTIMATE	6.04	
95% CI	(-5.93, 18.01)	
RELATIVE RISK [2]		
ESTIMATE	2.81	
95% CI	(0.31, 25.58)	
ODDS RATIO [2]		
ESTIMATE	3.00	
95% CI	(0.29, 30.56)	
P-VALUE [3]	0.3371	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
SEVERE OR VERY SEVERE

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	2/14 (14.3)	1/13 (7.7)
RISK DIFFERENCE [1]		
ESTIMATE	6.59	
95% CI	(-16.77, 29.96)	
RELATIVE RISK [2]		
ESTIMATE	1.86	
95% CI	(0.19, 18.13)	
ODDS RATIO [2]		
ESTIMATE	2.00	
95% CI	(0.16, 25.11)	
P-VALUE [3]	0.5930	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
NONE OR MILD

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	10/35 (28.6)	7/36 (19.4)
RISK DIFFERENCE [1]		
ESTIMATE	9.13	
95% CI	(-10.65, 28.90)	
RELATIVE RISK [2]		
ESTIMATE	1.47	
95% CI	(0.63, 3.43)	
ODDS RATIO [2]		
ESTIMATE	1.66	
95% CI	(0.55, 5.00)	
P-VALUE [3]	0.3710	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
MODERATE

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	7/32 (21.9)	3/30 (10.0)
RISK DIFFERENCE [1]		
ESTIMATE	11.88	
95% CI	(-6.02, 29.77)	
RELATIVE RISK [2]		
ESTIMATE	2.19	
95% CI	(0.62, 7.69)	
ODDS RATIO [2]		
ESTIMATE	2.52	
95% CI	(0.59, 10.83)	
P-VALUE [3]	0.2076	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
SEVERE OR VERY SEVERE

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	3/14 (21.4)	2/13 (15.4)
RISK DIFFERENCE [1]		
ESTIMATE	6.04	
95% CI	(-23.05, 35.14)	
RELATIVE RISK [2]		
ESTIMATE	1.39	
95% CI	(0.28, 7.05)	
ODDS RATIO [2]		
ESTIMATE	1.50	
95% CI	(0.21, 10.81)	
P-VALUE [3]	0.6918	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
NONE OR MILD

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	17/36 (47.2)	8/36 (22.2)
RISK DIFFERENCE [1]		
ESTIMATE	25.00	
95% CI	(3.78, 46.22)	
RELATIVE RISK [2]		
ESTIMATE	2.13	
95% CI	(1.05, 4.29)	
ODDS RATIO [2]		
ESTIMATE	3.13	
95% CI	(1.13, 8.71)	
P-VALUE [3]	0.0269†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
MODERATE

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	8/33 (24.2)	4/31 (12.9)
RISK DIFFERENCE [1]		
ESTIMATE	11.34	
95% CI	(-7.45, 30.13)	
RELATIVE RISK [2]		
ESTIMATE	1.88	
95% CI	(0.63, 5.62)	
ODDS RATIO [2]		
ESTIMATE	2.16	
95% CI	(0.58, 8.07)	
P-VALUE [3]	0.2492	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
SEVERE OR VERY SEVERE

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	3/14 (21.4)	2/13 (15.4)
RISK DIFFERENCE [1]		
ESTIMATE	6.04	
95% CI	(-23.05, 35.14)	
RELATIVE RISK [2]		
ESTIMATE	1.39	
95% CI	(0.28, 7.05)	
ODDS RATIO [2]		
ESTIMATE	1.50	
95% CI	(0.21, 10.81)	
P-VALUE [3]	0.6918	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
NONE OR MILD

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	18/36 (50.0)	11/36 (30.6)
RISK DIFFERENCE [1]		
ESTIMATE	19.44	
95% CI	(-2.76, 41.65)	
RELATIVE RISK [2]		
ESTIMATE	1.64	
95% CI	(0.91, 2.95)	
ODDS RATIO [2]		
ESTIMATE	2.27	
95% CI	(0.87, 5.96)	
P-VALUE [3]	0.0949	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
MODERATE

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	14/33 (42.4)	8/31 (25.8)
RISK DIFFERENCE [1]		
ESTIMATE	16.62	
95% CI	(-6.22, 39.46)	
RELATIVE RISK [2]		
ESTIMATE	1.64	
95% CI	(0.80, 3.37)	
ODDS RATIO [2]		
ESTIMATE	2.12	
95% CI	(0.73, 6.12)	
P-VALUE [3]	0.1652	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
SEVERE OR VERY SEVERE

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/14 (35.7)	4/13 (30.8)
RISK DIFFERENCE [1]		
ESTIMATE	4.95	
95% CI	(-30.54, 40.43)	
RELATIVE RISK [2]		
ESTIMATE	1.16	
95% CI	(0.40, 3.41)	
ODDS RATIO [2]		
ESTIMATE	1.25	
95% CI	(0.25, 6.23)	
P-VALUE [3]	0.7893	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
NONE OR MILD

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	18/36 (50.0)	13/36 (36.1)
RISK DIFFERENCE [1]		
ESTIMATE	13.89	
95% CI	(-8.76, 36.54)	
RELATIVE RISK [2]		
ESTIMATE	1.38	
95% CI	(0.80, 2.38)	
ODDS RATIO [2]		
ESTIMATE	1.77	
95% CI	(0.69, 4.54)	
P-VALUE [3]	0.2373	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
MODERATE

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	15/33 (45.5)	17/31 (54.8)
RISK DIFFERENCE [1]		
ESTIMATE	-9.38	
95% CI	(-33.79, 15.02)	
RELATIVE RISK [2]		
ESTIMATE	0.83	
95% CI	(0.51, 1.36)	
ODDS RATIO [2]		
ESTIMATE	0.69	
95% CI	(0.26, 1.84)	
P-VALUE [3]	0.4566	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
SEVERE OR VERY SEVERE

TIME TO HAE ATTACK RESOLUTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	8/14 (57.1)	4/13 (30.8)
RISK DIFFERENCE [1]		
ESTIMATE	26.37	
95% CI	(-9.70, 62.45)	
RELATIVE RISK [2]		
ESTIMATE	1.86	
95% CI	(0.73, 4.72)	
ODDS RATIO [2]		
ESTIMATE	3.00	
95% CI	(0.62, 14.62)	
P-VALUE [3]	0.1763	

1.4 Anzahl und Anteil der Attacken mit einer ersten Verringerung der Attacken-Schwere von mindestens einem Punkt oder mehr im PGI-S

1.4.1 Geschlecht

- PGI-S=Patient Global Impression of Severity; CI=Confidence Interval
- First incidence of decrease in attack severity at two time points in a row (with possible missing values in between) within 4, 8, 12, 24, and 48 hours of the first IMP administration.
- Time to first incidence of symptom decrease from baseline at two consecutive time points (hours) = Date/time of first incidence of decrease from baseline for two time points in a row (with possible missing values in between) – Date/time of first IMP administration.
- Attacks that did not have at least 1 post-baseline assessment within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline PGI-S category (none or mild, moderate, and severe or very severe).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline PGI-S category (none or mild, moderate, and severe or very severe).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | SEX = MALE

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	14/30 (46.7)	7/25 (28.0)
RISK DIFFERENCE [1]		
ESTIMATE	16.10	
95% CI	(-5.64, 37.85)	
RELATIVE RISK [2]		
ESTIMATE	1.51	
95% CI	(0.83, 2.75)	
ODDS RATIO [2]		
ESTIMATE	2.62	
95% CI	(0.69, 9.99)	
P-VALUE [3]	0.1626	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | SEX = FEMALE

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	17/49 (34.7)	9/49 (18.4)
RISK DIFFERENCE [1]		
ESTIMATE	15.87	
95% CI	(-0.59, 32.34)	
RELATIVE RISK [2]		
ESTIMATE	1.88	
95% CI	(0.96, 3.70)	
ODDS RATIO [2]		
ESTIMATE	2.50	
95% CI	(0.93, 6.69)	
P-VALUE [3]	0.0649	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | SEX = MALE

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	17/31 (54.8)	7/25 (28.0)
RISK DIFFERENCE [1]		
ESTIMATE	23.94	
95% CI	(1.95, 45.94)	
RELATIVE RISK [2]		
ESTIMATE	1.68	
95% CI	(0.94, 3.00)	
ODDS RATIO [2]		
ESTIMATE	3.96	
95% CI	(1.05, 15.02)	
P-VALUE [3]	0.0430†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | SEX = FEMALE

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	21/49 (42.9)	14/49 (28.6)
RISK DIFFERENCE [1]		
ESTIMATE	13.87	
95% CI	(-4.01, 31.76)	
RELATIVE RISK [2]		
ESTIMATE	1.45	
95% CI	(0.87, 2.40)	
ODDS RATIO [2]		
ESTIMATE	1.96	
95% CI	(0.81, 4.77)	
P-VALUE [3]	0.1376	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | SEX = MALE

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	18/31 (58.1)	8/25 (32.0)
RISK DIFFERENCE [1]		
ESTIMATE	22.80	
95% CI	(1.16, 44.44)	
RELATIVE RISK [2]		
ESTIMATE	1.59	
95% CI	(0.94, 2.68)	
ODDS RATIO [2]		
ESTIMATE	3.96	
95% CI	(1.01, 15.54)	
P-VALUE [3]	0.0480†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | SEX = FEMALE

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	26/49 (53.1)	18/50 (36.0)
RISK DIFFERENCE [1]		
ESTIMATE	16.15	
95% CI	(-2.26, 34.56)	
RELATIVE RISK [2]		
ESTIMATE	1.42	
95% CI	(0.93, 2.16)	
ODDS RATIO [2]		
ESTIMATE	2.08	
95% CI	(0.89, 4.87)	
P-VALUE [3]	0.0939	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | SEX = MALE

TIME TO FIRST INCIDENT IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	20/31 (64.5)	11/26 (42.3)
RISK DIFFERENCE [1]		
ESTIMATE	19.67	
95% CI	(0.93, 38.42)	
RELATIVE RISK [2]		
ESTIMATE	1.29	
95% CI	(0.95, 1.74)	
ODDS RATIO [2]		
ESTIMATE	4.34*	
95% CI	(0.92, 20.39)*	
P-VALUE [3]	0.0461†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | SEX = FEMALE

TIME TO FIRST INCIDENT IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	33/50 (66.0)	25/50 (50.0)
RISK DIFFERENCE [1]		
ESTIMATE	14.90	
95% CI	(-3.70, 33.49)	
RELATIVE RISK [2]		
ESTIMATE	1.19	
95% CI	(0.87, 1.63)	
ODDS RATIO [2]		
ESTIMATE	1.93	
95% CI	(0.83, 4.48)	
P-VALUE [3]	0.1230	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | SEX = MALE

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	20/31 (64.5)	12/26 (46.2)
RISK DIFFERENCE [1]		
ESTIMATE	15.57	
95% CI	(-2.46, 33.60)	
RELATIVE RISK [2]		
ESTIMATE	1.22	
95% CI	(0.93, 1.61)	
ODDS RATIO [2]		
ESTIMATE	3.47*	
95% CI	(0.72, 16.68)*	
P-VALUE [3]	0.0991	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS SEX = FEMALE		
TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	34/50 (68.0)	26/50 (52.0)
RISK DIFFERENCE [1]		
ESTIMATE	14.89	
95% CI	(-3.49, 33.27)	
RELATIVE RISK [2]		
ESTIMATE	1.21	
95% CI	(0.90, 1.64)	
ODDS RATIO [2]		
ESTIMATE	1.96	
95% CI	(0.84, 4.56)	
P-VALUE [3]	0.1204	

1.4.2 Alter

- PGI-S=Patient Global Impression of Severity; CI=Confidence Interval
- First incidence of decrease in attack severity at two time points in a row (with possible missing values in between) within 4, 8, 12, 24, and 48 hours of the first IMP administration.
- Time to first incidence of symptom decrease from baseline at two consecutive time points (hours) = Date/time of first incidence of decrease from baseline for two time points in a row (with possible missing values in between) – Date/time of first IMP administration.
- Attacks that did not have at least 1 post-baseline assessment within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline PGI-S category (none or mild, moderate, and severe or very severe).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline PGI-S category (none or mild, moderate, and severe or very severe).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | AGE GROUP = <18 YEARS

TIME TO FIRST INCIDENT IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	2/9 (22.2)	3/8 (37.5)
RISK DIFFERENCE [1]		
ESTIMATE	-5.56	
95% CI	(-55.01, 43.90)	
RELATIVE RISK [2]		
ESTIMATE	0.91	
95% CI	(0.22, 3.74)	
ODDS RATIO [2]		
ESTIMATE	0.76	
95% CI	(0.08, 7.64)	
P-VALUE [3]	0.8311	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | AGE GROUP = >=18 YEARS

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	29/70 (41.4)	13/66 (19.7)
RISK DIFFERENCE [1]		
ESTIMATE	19.77	
95% CI	(5.98, 33.57)	
RELATIVE RISK [2]		
ESTIMATE	1.97	
95% CI	(1.20, 3.25)	
ODDS RATIO [2]		
ESTIMATE	3.25	
95% CI	(1.36, 7.78)	
P-VALUE [3]	0.0062†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | AGE GROUP = <18 YEARS

TIME TO FIRST INCIDENT IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	3/9 (33.3)	3/8 (37.5)
RISK DIFFERENCE [1]		
ESTIMATE	4.17	
95% CI	(-46.81, 55.15)	
RELATIVE RISK [2]		
ESTIMATE	1.13	
95% CI	(0.31, 4.18)	
ODDS RATIO [2]		
ESTIMATE	1.20	
95% CI	(0.13, 10.74)	
P-VALUE [3]	0.8808	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | AGE GROUP = >=18 YEARS

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	35/71 (49.3)	18/66 (27.3)
RISK DIFFERENCE [1]		
ESTIMATE	19.85	
95% CI	(5.28, 34.43)	
RELATIVE RISK [2]		
ESTIMATE	1.63	
95% CI	(1.10, 2.42)	
ODDS RATIO [2]		
ESTIMATE	2.85	
95% CI	(1.28, 6.36)	
P-VALUE [3]	0.0093†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | AGE GROUP = <18 YEARS

TIME TO FIRST INCIDENT IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/9 (44.4)	4/9 (44.4)
RISK DIFFERENCE [1]		
ESTIMATE	20.15	
95% CI	(-21.15, 61.45)	
RELATIVE RISK [2]		
ESTIMATE	1.63	
95% CI	(0.83, 3.20)	
ODDS RATIO [2]		
ESTIMATE	2.13*	
95% CI	(0.24, 18.93)*	
P-VALUE [3]	0.4162	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12HOURS | AGE GROUP = >=18 YEARS

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	40/71 (56.3)	22/66 (33.3)
RISK DIFFERENCE [1]		
ESTIMATE	20.38	
95% CI	(5.35, 35.41)	
RELATIVE RISK [2]		
ESTIMATE	1.56	
95% CI	(1.10, 2.21)	
ODDS RATIO [2]		
ESTIMATE	2.75	
95% CI	(1.27, 5.94)	
P-VALUE [3]	0.0094†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | AGE GROUP = <18 YEARS

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	6/10 (60.0)	5/9 (55.6)
RISK DIFFERENCE [1]		
ESTIMATE	13.45	
95% CI	(-22.36, 49.26)	
RELATIVE RISK [2]		
ESTIMATE	1.25	
95% CI	(0.82, 1.92)	
ODDS RATIO [2]		
ESTIMATE	1.79*	
95% CI	(0.20, 16.10)*	
P-VALUE [3]	0.5188	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | AGE GROUP = >=18 YEARS

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	47/71 (66.2)	31/67 (46.3)
RISK DIFFERENCE [1]		
ESTIMATE	17.53	
95% CI	(2.37, 32.69)	
RELATIVE RISK [2]		
ESTIMATE	1.27	
95% CI	(0.98, 1.65)	
ODDS RATIO [2]		
ESTIMATE	2.34	
95% CI	(1.10, 4.98)	
P-VALUE [3]	0.0258†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | AGE GROUP = <18 YEARS

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	6/10 (60.0)	5/9 (55.6)
RISK DIFFERENCE [1]		
ESTIMATE	13.45	
95% CI	(-22.36, 49.26)	
RELATIVE RISK [2]		
ESTIMATE	1.25	
95% CI	(0.82, 1.92)	
ODDS RATIO [2]		
ESTIMATE	1.79*	
95% CI	(0.20, 16.10)*	
P-VALUE [3]	0.5188	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS AGE GROUP = >=18 YEARS		
TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	48/71 (67.6)	33/67 (49.3)
RISK DIFFERENCE [1]		
ESTIMATE	15.75	
95% CI	(0.72, 30.79)	
RELATIVE RISK [2]		
ESTIMATE	1.23	
95% CI	(0.97, 1.58)	
ODDS RATIO [2]		
ESTIMATE	2.19	
95% CI	(1.02, 4.67)	
P-VALUE [3]	0.0428†	

1.4.3 Region (Variante 1)

- PGI-S=Patient Global Impression of Severity; CI=Confidence Interval
- First incidence of decrease in attack severity at two time points in a row (with possible missing values in between) within 4, 8, 12, 24, and 48 hours of the first IMP administration.
- Time to first incidence of symptom decrease from baseline at two consecutive time points (hours) = Date/time of first incidence of decrease from baseline for two time points in a row (with possible missing values in between) – Date/time of first IMP administration.
- Attacks that did not have at least 1 post-baseline assessment within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline PGI-S category (none or mild, moderate, and severe or very severe).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline PGI-S category (none or mild, moderate, and severe or very severe).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | REGION 1 = US

TIME TO FIRST INCIDENT IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	11/24 (45.8)	2/21 (9.5)
RISK DIFFERENCE [1]		
ESTIMATE	31.43	
95% CI	(6.28, 56.58)	
RELATIVE RISK [2]		
ESTIMATE	3.39	
95% CI	(0.97, 11.90)	
ODDS RATIO [2]		
ESTIMATE	5.73*	
95% CI	(1.12, 29.26)*	
P-VALUE [3]	0.0201†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | REGION 1 = ROW

TIME TO FIRST INCIDENT IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	20/55 (36.4)	14/53 (26.4)
RISK DIFFERENCE [1]		
ESTIMATE	11.39	
95% CI	(-4.44, 27.22)	
RELATIVE RISK [2]		
ESTIMATE	1.45	
95% CI	(0.88, 2.40)	
ODDS RATIO [2]		
ESTIMATE	1.91	
95% CI	(0.77, 4.75)	
P-VALUE [3]	0.1677	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | REGION 1 = US

TIME TO FIRST INCIDENT IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	11/24 (45.8)	6/21 (28.6)
RISK DIFFERENCE [1]		
ESTIMATE	11.61	
95% CI	(-15.94, 39.16)	
RELATIVE RISK [2]		
ESTIMATE	1.47	
95% CI	(0.66, 3.29)	
ODDS RATIO [2]		
ESTIMATE	1.70*	
95% CI	(0.44, 6.52)*	
P-VALUE [3]	0.4170	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | REGION 1 = ROW

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	27/56 (48.2)	15/53 (28.3)
RISK DIFFERENCE [1]		
ESTIMATE	21.36	
95% CI	(5.10, 37.63)	
RELATIVE RISK [2]		
ESTIMATE	1.60	
95% CI	(1.03, 2.49)	
ODDS RATIO [2]		
ESTIMATE	3.04	
95% CI	(1.24, 7.45)	
P-VALUE [3]	0.0141†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | REGION 1 = US

TIME TO FIRST INCIDENT IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	12/24 (50.0)	7/21 (33.3)
RISK DIFFERENCE [1]		
ESTIMATE	10.89	
95% CI	(-17.76, 39.54)	
RELATIVE RISK [2]		
ESTIMATE	1.42	
95% CI	(0.65, 3.10)	
ODDS RATIO [2]		
ESTIMATE	1.61*	
95% CI	(0.43, 6.05)*	
P-VALUE [3]	0.4600	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | REGION 1 = ROW

TIME TO FIRST INCIDENT IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	32/56 (57.1)	19/54 (35.2)
RISK DIFFERENCE [1]		
ESTIMATE	23.67	
95% CI	(7.62, 39.73)	
RELATIVE RISK [2]		
ESTIMATE	1.53	
95% CI	(1.06, 2.20)	
ODDS RATIO [2]		
ESTIMATE	3.42	
95% CI	(1.36, 8.60)	
P-VALUE [3]	0.0065†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | REGION 1 = US

TIME TO FIRST INCIDENT IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	17/24 (70.8)	10/21 (47.6)
RISK DIFFERENCE [1]		
ESTIMATE	19.97	
95% CI	(-9.28, 49.21)	
RELATIVE RISK [2]		
ESTIMATE	1.33	
95% CI	(0.81, 2.19)	
ODDS RATIO [2]		
ESTIMATE	2.27*	
95% CI	(0.64, 8.09)*	
P-VALUE [3]	0.1906	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | REGION 1 = ROW

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	36/57 (63.2)	26/55 (47.3)
RISK DIFFERENCE [1]		
ESTIMATE	17.89	
95% CI	(2.53, 33.26)	
RELATIVE RISK [2]		
ESTIMATE	1.26	
95% CI	(0.97, 1.64)	
ODDS RATIO [2]		
ESTIMATE	2.77	
95% CI	(1.09, 7.06)	
P-VALUE [3]	0.0290†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | REGION 1 = US

TIME TO FIRST INCIDENT IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	17/24 (70.8)	10/21 (47.6)
RISK DIFFERENCE [1]		
ESTIMATE	19.97	
95% CI	(-9.28, 49.21)	
RELATIVE RISK [2]		
ESTIMATE	1.33	
95% CI	(0.81, 2.19)	
ODDS RATIO [2]		
ESTIMATE	2.27*	
95% CI	(0.64, 8.09)*	
P-VALUE [3]	0.1906	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS REGION 1 = ROW		
TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	37/57 (64.9)	28/55 (50.9)
RISK DIFFERENCE [1]		
ESTIMATE	16.07	
95% CI	(0.91, 31.24)	
RELATIVE RISK [2]		
ESTIMATE	1.24	
95% CI	(0.98, 1.58)	
ODDS RATIO [2]		
ESTIMATE	2.57	
95% CI	(1.00, 6.60)	
P-VALUE [3]	0.0460†	

1.4.4 Region (Variante 2)

- PGI-S=Patient Global Impression of Severity; CI=Confidence Interval
- First incidence of decrease in attack severity at two time points in a row (with possible missing values in between) within 4, 8, 12, 24, and 48 hours of the first IMP administration.
- Time to first incidence of symptom decrease from baseline at two consecutive time points (hours) = Date/time of first incidence of decrease from baseline for two time points in a row (with possible missing values in between) – Date/time of first IMP administration.
- Attacks that did not have at least 1 post-baseline assessment within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline PGI-S category (none or mild, moderate, and severe or very severe).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline PGI-S category (none or mild, moderate, and severe or very severe).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | REGION 2 = NORTH AMERICA

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	11/24 (45.8)	2/21 (9.5)
RISK DIFFERENCE [1]		
ESTIMATE	31.43	
95% CI	(6.28, 56.58)	
RELATIVE RISK [2]		
ESTIMATE	3.39	
95% CI	(0.97, 11.90)	
ODDS RATIO [2]		
ESTIMATE	5.73*	
95% CI	(1.12, 29.26)*	
P-VALUE [3]	0.0201†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | REGION 2 = EUROPE

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	15/41 (36.6)	9/42 (21.4)
RISK DIFFERENCE [1]		
ESTIMATE	13.32	
95% CI	(-3.51, 30.16)	
RELATIVE RISK [2]		
ESTIMATE	1.61	
95% CI	(0.87, 2.97)	
ODDS RATIO [2]		
ESTIMATE	2.43*	
95% CI	(0.78, 7.56)*	
P-VALUE [3]	0.1264	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | REGION 2 = ROW

TIME TO FIRST INCIDENT IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/14 (35.7)	5/11 (45.5)
RISK DIFFERENCE [1]		
ESTIMATE	0.90	
95% CI	(-38.25, 40.05)	
RELATIVE RISK [2]		
ESTIMATE	1.09	
95% CI	(0.41, 2.85)	
ODDS RATIO [2]		
ESTIMATE	1.03	
95% CI	(0.18, 6.06)	
P-VALUE [3]	0.9653	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | REGION 2 = NORTH AMERICA

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	11/24 (45.8)	6/21 (28.6)
RISK DIFFERENCE [1]		
ESTIMATE	11.61	
95% CI	(-15.94, 39.16)	
RELATIVE RISK [2]		
ESTIMATE	1.47	
95% CI	(0.66, 3.29)	
ODDS RATIO [2]		
ESTIMATE	1.70*	
95% CI	(0.44, 6.52)*	
P-VALUE [3]	0.4170	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | REGION 2 = EUROPE

TIME TO FIRST INCIDENT IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	20/41 (48.8)	10/42 (23.8)
RISK DIFFERENCE [1]		
ESTIMATE	23.36	
95% CI	(5.54, 41.17)	
RELATIVE RISK [2]		
ESTIMATE	1.69	
95% CI	(1.00, 2.85)	
ODDS RATIO [2]		
ESTIMATE	3.58*	
95% CI	(1.22, 10.46)*	
P-VALUE [3]	0.0135†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | REGION 2 = ROW

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	7/15 (46.7)	5/11 (45.5)
RISK DIFFERENCE [1]		
ESTIMATE	10.50	
95% CI	(-27.95, 48.95)	
RELATIVE RISK [2]		
ESTIMATE	1.32	
95% CI	(0.55, 3.16)	
ODDS RATIO [2]		
ESTIMATE	1.57	
95% CI	(0.28, 8.74)	
P-VALUE [3]	0.6114	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | REGION 2 = NORTH AMERICA

TIME TO FIRST INCIDENT IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	12/24 (50.0)	7/21 (33.3)
RISK DIFFERENCE [1]		
ESTIMATE	10.89	
95% CI	(-17.76, 39.54)	
RELATIVE RISK [2]		
ESTIMATE	1.42	
95% CI	(0.65, 3.10)	
ODDS RATIO [2]		
ESTIMATE	1.61*	
95% CI	(0.43, 6.05)*	
P-VALUE [3]	0.4600	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | REGION 2 = EUROPE

TIME TO FIRST INCIDENT IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	22/41 (53.7)	14/42 (33.3)
RISK DIFFERENCE [1]		
ESTIMATE	19.37	
95% CI	(1.76, 36.97)	
RELATIVE RISK [2]		
ESTIMATE	1.46	
95% CI	(0.96, 2.23)	
ODDS RATIO [2]		
ESTIMATE	2.92*	
95% CI	(0.99, 8.60)*	
P-VALUE [3]	0.0382†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | REGION 2 = ROW

TIME TO FIRST INCIDENT IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	10/15 (66.7)	5/12 (41.7)
RISK DIFFERENCE [1]		
ESTIMATE	33.63	
95% CI	(-0.99, 68.24)	
RELATIVE RISK [2]		
ESTIMATE	1.97	
95% CI	(0.90, 4.29)	
ODDS RATIO [2]		
ESTIMATE	4.00*	
95% CI	(0.70, 22.77)*	
P-VALUE [3]	0.0896	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | REGION 2 = NORTH AMERICA

TIME TO FIRST INCIDENT IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	17/24 (70.8)	10/21 (47.6)
RISK DIFFERENCE [1]		
ESTIMATE	19.97	
95% CI	(-9.28, 49.21)	
RELATIVE RISK [2]		
ESTIMATE	1.33	
95% CI	(0.81, 2.19)	
ODDS RATIO [2]		
ESTIMATE	2.27*	
95% CI	(0.64, 8.09)*	
P-VALUE [3]	0.1906	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | REGION 2 = EUROPE

TIME TO FIRST INCIDENT IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	26/42 (61.9)	19/43 (44.2)
RISK DIFFERENCE [1]		
ESTIMATE	16.69	
95% CI	(0.20, 33.18)	
RELATIVE RISK [2]		
ESTIMATE	1.23	
95% CI	(0.91, 1.68)	
ODDS RATIO [2]		
ESTIMATE	2.68*	
95% CI	(0.84, 8.55)*	
P-VALUE [3]	0.0552	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | REGION 2 = ROW

TIME TO FIRST INCIDENT IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	10/15 (66.7)	7/12 (58.3)
RISK DIFFERENCE [1]		
ESTIMATE	15.93	
95% CI	(-19.00, 50.86)	
RELATIVE RISK [2]		
ESTIMATE	1.32	
95% CI	(0.80, 2.16)	
ODDS RATIO [2]		
ESTIMATE	1.96*	
95% CI	(0.37, 10.47)*	
P-VALUE [3]	0.3950	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | REGION 2 = NORTH AMERICA

TIME TO FIRST INCIDENT IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	17/24 (70.8)	10/21 (47.6)
RISK DIFFERENCE [1]		
ESTIMATE	19.97	
95% CI	(-9.28, 49.21)	
RELATIVE RISK [2]		
ESTIMATE	1.33	
95% CI	(0.81, 2.19)	
ODDS RATIO [2]		
ESTIMATE	2.27*	
95% CI	(0.64, 8.09)*	
P-VALUE [3]	0.1906	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | REGION 2 = EUROPE

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	27/42 (64.3)	21/43 (48.8)
RISK DIFFERENCE [1]		
ESTIMATE	14.55	
95% CI	(-1.76, 30.86)	
RELATIVE RISK [2]		
ESTIMATE	1.22	
95% CI	(0.93, 1.61)	
ODDS RATIO [2]		
ESTIMATE	2.70	
95% CI	(0.83, 8.76)	
P-VALUE [3]	0.0906	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS REGION 2 = ROW		
TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	10/15 (66.7)	7/12 (58.3)
RISK DIFFERENCE [1]		
ESTIMATE	15.93	
95% CI	(-19.00, 50.86)	
RELATIVE RISK [2]		
ESTIMATE	1.32	
95% CI	(0.80, 2.16)	
ODDS RATIO [2]		
ESTIMATE	1.96*	
95% CI	(0.37, 10.47)*	
P-VALUE [3]	0.3950	

1.4.5 Prophylaxe-Status (Variante 1)

- PGI-S=Patient Global Impression of Severity; CI=Confidence Interval
- First incidence of decrease in attack severity at two time points in a row (with possible missing values in between) within 4, 8, 12, 24, and 48 hours of the first IMP administration.
- Time to first incidence of symptom decrease from baseline at two consecutive time points (hours) = Date/time of first incidence of decrease from baseline for two time points in a row (with possible missing values in between) – Date/time of first IMP administration.
- Attacks that did not have at least 1 post-baseline assessment within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline PGI-S category (none or mild, moderate, and severe or very severe).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline PGI-S category (none or mild, moderate, and severe or very severe).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	8/18 (44.4)	3/18 (16.7)
RISK DIFFERENCE [1]		
ESTIMATE	24.10	
95% CI	(-6.21, 54.41)	
RELATIVE RISK [2]		
ESTIMATE	2.15	
95% CI	(0.61, 7.55)	
ODDS RATIO [2]		
ESTIMATE	2.97*	
95% CI	(0.55, 15.94)*	
P-VALUE [3]	0.1206	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
DEMAND

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	23/61 (37.7)	13/56 (23.2)
RISK DIFFERENCE [1]		
ESTIMATE	14.88	
95% CI	(0.11, 29.65)	
RELATIVE RISK [2]		
ESTIMATE	1.55	
95% CI	(0.94, 2.57)	
ODDS RATIO [2]		
ESTIMATE	2.39	
95% CI	(0.95, 6.01)	
P-VALUE [3]	0.0569	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	8/18 (44.4)	7/18 (38.9)
RISK DIFFERENCE [1]		
ESTIMATE	1.29	
95% CI	(-30.73, 33.30)	
RELATIVE RISK [2]		
ESTIMATE	1.27	
95% CI	(0.54, 3.01)	
ODDS RATIO [2]		
ESTIMATE	1.14*	
95% CI	(0.25, 5.09)*	
P-VALUE [3]	0.9374	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
DEMAND

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	30/62 (48.4)	14/56 (25.0)
RISK DIFFERENCE [1]		
ESTIMATE	23.63	
95% CI	(8.41, 38.85)	
RELATIVE RISK [2]		
ESTIMATE	1.62	
95% CI	(1.03, 2.53)	
ODDS RATIO [2]		
ESTIMATE	3.46	
95% CI	(1.38, 8.69)	
P-VALUE [3]	0.0041†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	11/18 (61.1)	8/18 (44.4)
RISK DIFFERENCE [1]		
ESTIMATE	14.93	
95% CI	(-18.09, 47.96)	
RELATIVE RISK [2]		
ESTIMATE	1.35	
95% CI	(0.67, 2.72)	
ODDS RATIO [2]		
ESTIMATE	1.77*	
95% CI	(0.45, 6.91)*	
P-VALUE [3]	0.3843	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
DEMAND

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	33/62 (53.2)	18/57 (31.6)
RISK DIFFERENCE [1]		
ESTIMATE	21.49	
95% CI	(6.49, 36.49)	
RELATIVE RISK [2]		
ESTIMATE	1.46	
95% CI	(1.01, 2.12)	
ODDS RATIO [2]		
ESTIMATE	3.16	
95% CI	(1.25, 8.03)	
P-VALUE [3]	0.0074†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	13/18 (72.2)	12/18 (66.7)
RISK DIFFERENCE [1]		
ESTIMATE	5.90	
95% CI	(-25.17, 36.97)	
RELATIVE RISK [2]		
ESTIMATE	1.07	
95% CI	(0.67, 1.69)	
ODDS RATIO [2]		
ESTIMATE	1.27*	
95% CI	(0.31, 5.25)*	
P-VALUE [3]	0.7150	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
DEMAND

TIME TO FIRST INCIDENT IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	40/63 (63.5)	24/58 (41.4)
RISK DIFFERENCE [1]		
ESTIMATE	22.00	
95% CI	(7.58, 36.42)	
RELATIVE RISK [2]		
ESTIMATE	1.24	
95% CI	(0.95, 1.62)	
ODDS RATIO [2]		
ESTIMATE	3.30	
95% CI	(1.20, 9.08)	
P-VALUE [3]	0.0041†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	13/18 (72.2)	12/18 (66.7)
RISK DIFFERENCE [1]		
ESTIMATE	5.90	
95% CI	(-25.17, 36.97)	
RELATIVE RISK [2]		
ESTIMATE	1.07	
95% CI	(0.67, 1.69)	
ODDS RATIO [2]		
ESTIMATE	1.27*	
95% CI	(0.31, 5.25)*	
P-VALUE [3]	0.7150	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS PROPHYLACTIC TREATMENT STATUS 1 = ON DEMAND		
TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	41/63 (65.1)	26/58 (44.8)
RISK DIFFERENCE [1]		
ESTIMATE	20.07	
95% CI	(5.78, 34.35)	
RELATIVE RISK [2]		
ESTIMATE	1.23	
95% CI	(0.97, 1.57)	
ODDS RATIO [2]		
ESTIMATE	3.38	
95% CI	(1.27, 9.00)	
P-VALUE [3]	0.0080†	

1.4.6 Prophylaxe-Status (Variante 2)

- PGI-S=Patient Global Impression of Severity; CI=Confidence Interval
- First incidence of decrease in attack severity at two time points in a row (with possible missing values in between) within 4, 8, 12, 24, and 48 hours of the first IMP administration.
- Time to first incidence of symptom decrease from baseline at two consecutive time points (hours) = Date/time of first incidence of decrease from baseline for two time points in a row (with possible missing values in between) – Date/time of first IMP administration.
- Attacks that did not have at least 1 post-baseline assessment within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline PGI-S category (none or mild, moderate, and severe or very severe).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline PGI-S category (none or mild, moderate, and severe or very severe).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

TIME TO FIRST INCIDENT IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/13 (38.5)	3/14 (21.4)
RISK DIFFERENCE [1]		
ESTIMATE	15.75	
95% CI	(-20.40, 51.90)	
RELATIVE RISK [2]		
ESTIMATE	1.56	
95% CI	(0.43, 5.57)	
ODDS RATIO [2]		
ESTIMATE	1.81*	
95% CI	(0.30, 10.80)*	
P-VALUE [3]	0.3940	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	3/5 (60.0)	0/4 (0)
RISK DIFFERENCE [1]		
ESTIMATE	42.86	
95% CI	(-10.58, 96.30)	
RELATIVE RISK [2]		
ESTIMATE	3.75	
95% CI	(0.27, 52.64)	
ODDS RATIO [2]		
ESTIMATE	8.33*	
95% CI	(0.22, 320.38)*	
P-VALUE [3]	0.1824	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
DEMAND

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	23/61 (37.7)	13/56 (23.2)
RISK DIFFERENCE [1]		
ESTIMATE	14.88	
95% CI	(0.11, 29.65)	
RELATIVE RISK [2]		
ESTIMATE	1.55	
95% CI	(0.94, 2.57)	
ODDS RATIO [2]		
ESTIMATE	2.39	
95% CI	(0.95, 6.01)	
P-VALUE [3]	0.0569	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/13 (38.5)	7/14 (50.0)
RISK DIFFERENCE [1]		
ESTIMATE	-13.01	
95% CI	(-50.25, 24.24)	
RELATIVE RISK [2]		
ESTIMATE	0.97	
95% CI	(0.40, 2.35)	
ODDS RATIO [2]		
ESTIMATE	0.59*	
95% CI	(0.11, 3.10)*	
P-VALUE [3]	0.5089	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

TIME TO FIRST INCIDENT IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	3/5 (60.0)	0/4 (0)
RISK DIFFERENCE [1]		
ESTIMATE	42.86	
95% CI	(-10.58, 96.30)	
RELATIVE RISK [2]		
ESTIMATE	3.75	
95% CI	(0.27, 52.64)	
ODDS RATIO [2]		
ESTIMATE	8.33*	
95% CI	(0.22, 320.38)*	
P-VALUE [3]	0.1824	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
DEMAND

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	30/62 (48.4)	14/56 (25.0)
RISK DIFFERENCE [1]		
ESTIMATE	23.63	
95% CI	(8.41, 38.85)	
RELATIVE RISK [2]		
ESTIMATE	1.62	
95% CI	(1.03, 2.53)	
ODDS RATIO [2]		
ESTIMATE	3.46	
95% CI	(1.38, 8.69)	
P-VALUE [3]	0.0041†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	8/13 (61.5)	8/14 (57.1)
RISK DIFFERENCE [1]		
ESTIMATE	4.42	
95% CI	(-33.50, 42.33)	
RELATIVE RISK [2]		
ESTIMATE	1.11	
95% CI	(0.57, 2.16)	
ODDS RATIO [2]		
ESTIMATE	1.15*	
95% CI	(0.25, 5.29)*	
P-VALUE [3]	0.8254	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	3/5 (60.0)	0/4 (0)
RISK DIFFERENCE [1]		
ESTIMATE	42.86	
95% CI	(-10.58, 96.30)	
RELATIVE RISK [2]		
ESTIMATE	3.75	
95% CI	(0.27, 52.64)	
ODDS RATIO [2]		
ESTIMATE	8.33*	
95% CI	(0.22, 320.38)*	
P-VALUE [3]	0.1824	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
DEMAND

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	33/62 (53.2)	18/57 (31.6)
RISK DIFFERENCE [1]		
ESTIMATE	21.49	
95% CI	(6.49, 36.49)	
RELATIVE RISK [2]		
ESTIMATE	1.46	
95% CI	(1.01, 2.12)	
ODDS RATIO [2]		
ESTIMATE	3.16	
95% CI	(1.25, 8.03)	
P-VALUE [3]	0.0074†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	10/13 (76.9)	10/14 (71.4)
RISK DIFFERENCE [1]		
ESTIMATE	6.80	
95% CI	(-26.79, 40.39)	
RELATIVE RISK [2]		
ESTIMATE	1.09	
95% CI	(0.70, 1.69)	
ODDS RATIO [2]		
ESTIMATE	1.36*	
95% CI	(0.24, 7.74)*	
P-VALUE [3]	0.7049	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	3/5 (60.0)	2/4 (50.0)
RISK DIFFERENCE [1]		
ESTIMATE	-7.14	
95% CI	(-78.09, 63.80)	
RELATIVE RISK [2]		
ESTIMATE	1.03	
95% CI	(0.26, 4.04)	
ODDS RATIO [2]		
ESTIMATE	0.87*	
95% CI	(0.06, 12.61)*	
P-VALUE [3]	0.8613	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
DEMAND

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	40/63 (63.5)	24/58 (41.4)
RISK DIFFERENCE [1]		
ESTIMATE	22.00	
95% CI	(7.58, 36.42)	
RELATIVE RISK [2]		
ESTIMATE	1.24	
95% CI	(0.95, 1.62)	
ODDS RATIO [2]		
ESTIMATE	3.30	
95% CI	(1.20, 9.08)	
P-VALUE [3]	0.0041†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	10/13 (76.9)	10/14 (71.4)
RISK DIFFERENCE [1]		
ESTIMATE	6.80	
95% CI	(-26.79, 40.39)	
RELATIVE RISK [2]		
ESTIMATE	1.09	
95% CI	(0.70, 1.69)	
ODDS RATIO [2]		
ESTIMATE	1.36*	
95% CI	(0.24, 7.74)*	
P-VALUE [3]	0.7049	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	3/5 (60.0)	2/4 (50.0)
RISK DIFFERENCE [1]		
ESTIMATE	-7.14	
95% CI	(-78.09, 63.80)	
RELATIVE RISK [2]		
ESTIMATE	1.03	
95% CI	(0.26, 4.04)	
ODDS RATIO [2]		
ESTIMATE	0.87*	
95% CI	(0.06, 12.61)*	
P-VALUE [3]	0.8613	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	41/63 (65.1)	26/58 (44.8)
RISK DIFFERENCE [1]		
ESTIMATE	20.07	
95% CI	(5.78, 34.35)	
RELATIVE RISK [2]		
ESTIMATE	1.23	
95% CI	(0.97, 1.57)	
ODDS RATIO [2]		
ESTIMATE	3.38	
95% CI	(1.27, 9.00)	
P-VALUE [3]	0.0080†	

1.4.7 Attacken-Schwere (PGI-S) zu Baseline

- PGI-S=Patient Global Impression of Severity; CI=Confidence Interval
- First incidence of decrease in attack severity at two time points in a row (with possible missing values in between) within 4, 8, 12, 24, and 48 hours of the first IMP administration.
- Time to first incidence of symptom decrease from baseline at two consecutive time points (hours) = Date/time of first incidence of decrease from baseline for two time points in a row (with possible missing values in between) – Date/time of first IMP administration.
- Attacks that did not have at least 1 post-baseline assessment within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test.
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test.
- [3] P-value from Cochran-Mantel-Haenszel test.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
NONE OR MILD

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/34 (14.7)	3/34 (8.8)
RISK DIFFERENCE [1]		
ESTIMATE	5.88	
95% CI	(-9.37, 21.13)	
RELATIVE RISK [2]		
ESTIMATE	1.67	
95% CI	(0.43, 6.43)	
ODDS RATIO [2]		
ESTIMATE	1.78	
95% CI	(0.39, 8.13)	
P-VALUE [3]	0.4549	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
MODERATE

TIME TO FIRST INCIDENT IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	15/31 (48.4)	8/28 (28.6)
RISK DIFFERENCE [1]		
ESTIMATE	19.82	
95% CI	(-4.46, 44.09)	
RELATIVE RISK [2]		
ESTIMATE	1.69	
95% CI	(0.85, 3.37)	
ODDS RATIO [2]		
ESTIMATE	2.34	
95% CI	(0.80, 6.91)	
P-VALUE [3]	0.1223	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
SEVERE OR VERY SEVERE

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	11/14 (78.6)	5/12 (41.7)
RISK DIFFERENCE [1]		
ESTIMATE	36.90	
95% CI	(1.69, 72.12)	
RELATIVE RISK [2]		
ESTIMATE	1.89	
95% CI	(0.91, 3.89)	
ODDS RATIO [2]		
ESTIMATE	5.13	
95% CI	(0.92, 28.57)	
P-VALUE [3]	0.0587	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
NONE OR MILD

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	8/34 (23.5)	5/34 (14.7)
RISK DIFFERENCE [1]		
ESTIMATE	8.82	
95% CI	(-9.75, 27.40)	
RELATIVE RISK [2]		
ESTIMATE	1.60	
95% CI	(0.58, 4.40)	
ODDS RATIO [2]		
ESTIMATE	1.78	
95% CI	(0.52, 6.14)	
P-VALUE [3]	0.3584	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
MODERATE

TIME TO FIRST INCIDENT IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	19/32 (59.4)	9/28 (32.1)
RISK DIFFERENCE [1]		
ESTIMATE	27.23	
95% CI	(2.97, 51.50)	
RELATIVE RISK [2]		
ESTIMATE	1.85	
95% CI	(1.00, 3.40)	
ODDS RATIO [2]		
ESTIMATE	3.09	
95% CI	(1.07, 8.92)	
P-VALUE [3]	0.0365†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
SEVERE OR VERY SEVERE

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	11/14 (78.6)	7/12 (58.3)
RISK DIFFERENCE [1]		
ESTIMATE	20.24	
95% CI	(-14.98, 55.45)	
RELATIVE RISK [2]		
ESTIMATE	1.35	
95% CI	(0.78, 2.34)	
ODDS RATIO [2]		
ESTIMATE	2.62	
95% CI	(0.47, 14.58)	
P-VALUE [3]	0.2744	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
NONE OR MILD

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	10/34 (29.4)	6/35 (17.1)
RISK DIFFERENCE [1]		
ESTIMATE	12.27	
95% CI	(-7.49, 32.03)	
RELATIVE RISK [2]		
ESTIMATE	1.72	
95% CI	(0.70, 4.20)	
ODDS RATIO [2]		
ESTIMATE	2.01	
95% CI	(0.64, 6.34)	
P-VALUE [3]	0.2307	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
MODERATE

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	23/32 (71.9)	13/28 (46.4)
RISK DIFFERENCE [1]		
ESTIMATE	25.45	
95% CI	(1.28, 49.61)	
RELATIVE RISK [2]		
ESTIMATE	1.55	
95% CI	(0.98, 2.44)	
ODDS RATIO [2]		
ESTIMATE	2.95	
95% CI	(1.01, 8.60)	
P-VALUE [3]	0.0465†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
SEVERE OR VERY SEVERE

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	11/14 (78.6)	7/12 (58.3)
RISK DIFFERENCE [1]		
ESTIMATE	20.24	
95% CI	(-14.98, 55.45)	
RELATIVE RISK [2]		
ESTIMATE	1.35	
95% CI	(0.78, 2.34)	
ODDS RATIO [2]		
ESTIMATE	2.62	
95% CI	(0.47, 14.58)	
P-VALUE [3]	0.2744	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
NONE OR MILD

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	15/34 (44.1)	8/35 (22.9)
RISK DIFFERENCE [1]		
ESTIMATE	21.26	
95% CI	(-0.47, 42.99)	
RELATIVE RISK [2]		
ESTIMATE	1.93	
95% CI	(0.94, 3.95)	
ODDS RATIO [2]		
ESTIMATE	2.66	
95% CI	(0.94, 7.54)	
P-VALUE [3]	0.0630	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
MODERATE

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	26/33 (78.8)	19/28 (67.9)
RISK DIFFERENCE [1]		
ESTIMATE	10.93	
95% CI	(-11.29, 33.15)	
RELATIVE RISK [2]		
ESTIMATE	1.16	
95% CI	(0.85, 1.58)	
ODDS RATIO [2]		
ESTIMATE	1.76	
95% CI	(0.56, 5.56)	
P-VALUE [3]	0.3375	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
SEVERE OR VERY SEVERE

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	12/14 (85.7)	9/13 (69.2)
RISK DIFFERENCE [1]		
ESTIMATE	16.48	
95% CI	(-14.59, 47.56)	
RELATIVE RISK [2]		
ESTIMATE	1.24	
95% CI	(0.81, 1.89)	
ODDS RATIO [2]		
ESTIMATE	2.67	
95% CI	(0.40, 17.91)	
P-VALUE [3]	0.3124	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
NONE OR MILD

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	15/34 (44.1)	9/35 (25.7)
RISK DIFFERENCE [1]		
ESTIMATE	18.40	
95% CI	(-3.69, 40.50)	
RELATIVE RISK [2]		
ESTIMATE	1.72	
95% CI	(0.87, 3.38)	
ODDS RATIO [2]		
ESTIMATE	2.28	
95% CI	(0.83, 6.30)	
P-VALUE [3]	0.1112	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
MODERATE

TIME TO FIRST INCIDENT IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	27/33 (81.8)	20/28 (71.4)
RISK DIFFERENCE [1]		
ESTIMATE	10.39	
95% CI	(-10.90, 31.68)	
RELATIVE RISK [2]		
ESTIMATE	1.15	
95% CI	(0.86, 1.52)	
ODDS RATIO [2]		
ESTIMATE	1.80	
95% CI	(0.54, 6.01)	
P-VALUE [3]	0.3403	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
SEVERE OR VERY SEVERE

TIME TO FIRST INCIDENCE IN ATTACK SEVERITY	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	12/14 (85.7)	9/13 (69.2)
RISK DIFFERENCE [1]		
ESTIMATE	16.48	
95% CI	(-14.59, 47.56)	
RELATIVE RISK [2]		
ESTIMATE	1.24	
95% CI	(0.81, 1.89)	
ODDS RATIO [2]		
ESTIMATE	2.67	
95% CI	(0.40, 17.91)	
P-VALUE [3]	0.3124	

1.5 Anzahl und Anteil der Attacken mit einer Verringerung des GA-NRS um ≥ 2 Punkte

1.5.1 Geschlecht

- GA-NRS=General Anxiety Numeric Rating Scale; CI=Confidence Interval
- Time to first incidence of GA-NRS reduction of ≥ 2 points within 4, 8, 12, 24, and 48 hours of the first IMP administration = Date/time of first ≥ 2 points reduction in GA-NRS score for 2 consecutive time points in a row – Date/time of first IMP administration.
- Attacks that had a baseline GA-NRS score below a cutoff point were excluded from the corresponding analysis.
- Attacks that did not have at least 1 post-baseline assessment within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | SEX = MALE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	13/20 (65.0)	6/14 (42.9)
RISK DIFFERENCE [1]		
ESTIMATE	23.37	
95% CI	(-10.85, 57.59)	
RELATIVE RISK [2]		
ESTIMATE	1.39	
95% CI	(0.70, 2.78)	
ODDS RATIO [2]		
ESTIMATE	2.53	
95% CI	(0.57, 11.30)	
P-VALUE [3]	0.2060	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | SEX = FEMALE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	22/34 (64.7)	18/37 (48.6)
RISK DIFFERENCE [1]		
ESTIMATE	15.79	
95% CI	(-8.02, 39.60)	
RELATIVE RISK [2]		
ESTIMATE	1.24	
95% CI	(0.80, 1.91)	
ODDS RATIO [2]		
ESTIMATE	1.84	
95% CI	(0.67, 5.08)	
P-VALUE [3]	0.1895	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | SEX = MALE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	15/20 (75.0)	6/14 (42.9)
RISK DIFFERENCE [1]		
ESTIMATE	32.53	
95% CI	(-0.42, 65.48)	
RELATIVE RISK [2]		
ESTIMATE	1.55	
95% CI	(0.81, 2.97)	
ODDS RATIO [2]		
ESTIMATE	3.93	
95% CI	(0.84, 18.34)	
P-VALUE [3]	0.0713	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | SEX = FEMALE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	23/34 (67.6)	22/37 (59.5)
RISK DIFFERENCE [1]		
ESTIMATE	7.69	
95% CI	(-15.06, 30.44)	
RELATIVE RISK [2]		
ESTIMATE	1.10	
95% CI	(0.77, 1.58)	
ODDS RATIO [2]		
ESTIMATE	1.35	
95% CI	(0.49, 3.72)	
P-VALUE [3]	0.5098	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | SEX = MALE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	16/20 (80.0)	6/14 (42.9)
RISK DIFFERENCE [1]		
ESTIMATE	36.42	
95% CI	(3.52, 69.33)	
RELATIVE RISK [2]		
ESTIMATE	1.58	
95% CI	(0.83, 3.03)	
ODDS RATIO [2]		
ESTIMATE	4.60	
95% CI	(0.94, 22.54)	
P-VALUE [3]	0.0398†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | SEX = FEMALE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	24/34 (70.6)	24/38 (63.2)
RISK DIFFERENCE [1]		
ESTIMATE	7.14	
95% CI	(-14.74, 29.02)	
RELATIVE RISK [2]		
ESTIMATE	1.11	
95% CI	(0.80, 1.53)	
ODDS RATIO [2]		
ESTIMATE	1.36	
95% CI	(0.49, 3.75)	
P-VALUE [3]	0.5308	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | SEX = MALE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	17/20 (85.0)	7/14 (50.0)
RISK DIFFERENCE [1]		
ESTIMATE	36.07	
95% CI	(4.49, 67.65)	
RELATIVE RISK [2]		
ESTIMATE	1.50	
95% CI	(0.86, 2.62)	
ODDS RATIO [2]		
ESTIMATE	5.39	
95% CI	(1.01, 28.81)	
P-VALUE [3]	0.0331†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | SEX = FEMALE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	24/34 (70.6)	29/38 (76.3)
RISK DIFFERENCE [1]		
ESTIMATE	-5.36	
95% CI	(-25.86, 15.15)	
RELATIVE RISK [2]		
ESTIMATE	0.94	
95% CI	(0.71, 1.24)	
ODDS RATIO [2]		
ESTIMATE	0.76	
95% CI	(0.26, 2.21)	
P-VALUE [3]	0.6150	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | SEX = MALE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	17/20 (85.0)	8/14 (57.1)
RISK DIFFERENCE [1]		
ESTIMATE	28.69	
95% CI	(-2.73, 60.12)	
RELATIVE RISK [2]		
ESTIMATE	1.20	
95% CI	(0.77, 1.88)	
ODDS RATIO [2]		
ESTIMATE	4.01	
95% CI	(0.71, 22.64)	
P-VALUE [3]	0.0761	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS SEX = FEMALE		
TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	24/34 (70.6)	31/38 (81.6)
RISK DIFFERENCE [1]		
ESTIMATE	-9.95	
95% CI	(-29.64, 9.74)	
RELATIVE RISK [2]		
ESTIMATE	0.87	
95% CI	(0.67, 1.13)	
ODDS RATIO [2]		
ESTIMATE	0.57	
95% CI	(0.19, 1.77)	
P-VALUE [3]	0.3277	

1.5.2 Alter

- GA-NRS=General Anxiety Numeric Rating Scale; CI=Confidence Interval
- Time to first incidence of GA-NRS reduction of ≥ 2 points within 4, 8, 12, 24, and 48 hours of the first IMP administration = Date/time of first ≥ 2 points reduction in GA-NRS score for 2 consecutive time points in a row – Date/time of first IMP administration.
- Attacks that had a baseline GA-NRS score below a cutoff point were excluded from the corresponding analysis.
- Attacks that did not have at least 1 post-baseline assessment within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | AGE GROUP = <18 YEARS

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	1/4 (25.0)	5/8 (62.5)
RISK DIFFERENCE [1]		
ESTIMATE	-40.00	
95% CI	(-98.14, 18.14)	
RELATIVE RISK [2]		
ESTIMATE	1.20	
95% CI	(0.57, 2.50)	
ODDS RATIO [2]		
ESTIMATE	0.41*	
95% CI	(0.04, 3.94)*	
P-VALUE [3]	0.2348	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | AGE GROUP = >=18 YEARS

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	34/50 (68.0)	19/43 (44.2)
RISK DIFFERENCE [1]		
ESTIMATE	23.68	
95% CI	(3.78, 43.58)	
RELATIVE RISK [2]		
ESTIMATE	1.46	
95% CI	(1.00, 2.14)	
ODDS RATIO [2]		
ESTIMATE	2.62	
95% CI	(1.11, 6.21)	
P-VALUE [3]	0.0236†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | AGE GROUP = <18 YEARS

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	2/4 (50.0)	5/8 (62.5)
RISK DIFFERENCE [1]		
ESTIMATE	-20.00	
95% CI	(-72.59, 32.59)	
RELATIVE RISK [2]		
ESTIMATE	1.10	
95% CI	(0.56, 2.16)	
ODDS RATIO [2]		
ESTIMATE	0.58*	
95% CI	(0.07, 5.21)*	
P-VALUE [3]	0.5271	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | AGE GROUP = >=18 YEARS

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	36/50 (72.0)	23/43 (53.5)
RISK DIFFERENCE [1]		
ESTIMATE	18.66	
95% CI	(-0.82, 38.14)	
RELATIVE RISK [2]		
ESTIMATE	1.35	
95% CI	(0.97, 1.87)	
ODDS RATIO [2]		
ESTIMATE	2.23	
95% CI	(0.93, 5.33)	
P-VALUE [3]	0.0670	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | AGE GROUP = <18 YEARS

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	2/4 (50.0)	6/8 (75.0)
RISK DIFFERENCE [1]		
ESTIMATE	-30.00	
95% CI	(-87.14, 27.14)	
RELATIVE RISK [2]		
ESTIMATE	1.06	
95% CI	(0.54, 2.07)	
ODDS RATIO [2]		
ESTIMATE	0.42*	
95% CI	(0.05, 3.70)*	
P-VALUE [3]	0.3657	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | AGE GROUP = >=18 YEARS

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	38/50 (76.0)	24/44 (54.5)
RISK DIFFERENCE [1]		
ESTIMATE	21.42	
95% CI	(2.51, 40.34)	
RELATIVE RISK [2]		
ESTIMATE	1.39	
95% CI	(1.02, 1.90)	
ODDS RATIO [2]		
ESTIMATE	2.63	
95% CI	(1.09, 6.37)	
P-VALUE [3]	0.0316†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | AGE GROUP = <18 YEARS

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	2/4 (50.0)	7/8 (87.5)
RISK DIFFERENCE [1]		
ESTIMATE	-40.00	
95% CI	(-100.00, 20.73)	
RELATIVE RISK [2]		
ESTIMATE	1.03	
95% CI	(0.53, 2.00)	
ODDS RATIO [2]		
ESTIMATE	0.30*	
95% CI	(0.03, 2.94)*	
P-VALUE [3]	0.2059	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | AGE GROUP = >=18 YEARS

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	39/50 (78.0)	29/44 (65.9)
RISK DIFFERENCE [1]		
ESTIMATE	12.40	
95% CI	(-5.73, 30.53)	
RELATIVE RISK [2]		
ESTIMATE	1.19	
95% CI	(0.92, 1.55)	
ODDS RATIO [2]		
ESTIMATE	1.85	
95% CI	(0.73, 4.69)	
P-VALUE [3]	0.1868	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | AGE GROUP = <18 YEARS

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	2/4 (50.0)	7/8 (87.5)
RISK DIFFERENCE [1]		
ESTIMATE	-40.00	
95% CI	(-100.00, 20.73)	
RELATIVE RISK [2]		
ESTIMATE	1.03	
95% CI	(0.53, 2.00)	
ODDS RATIO [2]		
ESTIMATE	0.30*	
95% CI	(0.03, 2.94)*	
P-VALUE [3]	0.2059	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS AGE GROUP = >=18 YEARS		
TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	39/50 (78.0)	32/44 (72.7)
RISK DIFFERENCE [1]		
ESTIMATE	5.97	
95% CI	(-11.30, 23.24)	
RELATIVE RISK [2]		
ESTIMATE	1.05	
95% CI	(0.85, 1.30)	
ODDS RATIO [2]		
ESTIMATE	1.39	
95% CI	(0.53, 3.64)	
P-VALUE [3]	0.5025	

1.5.3 Region (Variante 1)

- GA-NRS=General Anxiety Numeric Rating Scale; CI=Confidence Interval
- Time to first incidence of GA-NRS reduction of ≥ 2 points within 4, 8, 12, 24, and 48 hours of the first IMP administration = Date/time of first ≥ 2 points reduction in GA-NRS score for 2 consecutive time points in a row – Date/time of first IMP administration.
- Attacks that had a baseline GA-NRS score below a cutoff point were excluded from the corresponding analysis.
- Attacks that did not have at least 1 post-baseline assessment within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | REGION 1 = US

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	8/14 (57.1)	5/11 (45.5)
RISK DIFFERENCE [1]		
ESTIMATE	6.02	
95% CI	(-33.60, 45.64)	
RELATIVE RISK [2]		
ESTIMATE	1.09	
95% CI	(0.53, 2.26)	
ODDS RATIO [2]		
ESTIMATE	1.30	
95% CI	(0.23, 7.56)	
P-VALUE [3]	0.7794	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | REGION 1 = ROW

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	27/40 (67.5)	19/40 (47.5)
RISK DIFFERENCE [1]		
ESTIMATE	20.00	
95% CI	(-1.66, 41.66)	
RELATIVE RISK [2]		
ESTIMATE	1.39	
95% CI	(0.93, 2.08)	
ODDS RATIO [2]		
ESTIMATE	2.20	
95% CI	(0.86, 5.63)	
P-VALUE [3]	0.0752	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | REGION 1 = US

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	8/14 (57.1)	7/11 (63.6)
RISK DIFFERENCE [1]		
ESTIMATE	-9.26	
95% CI	(-50.51, 31.99)	
RELATIVE RISK [2]		
ESTIMATE	0.92	
95% CI	(0.46, 1.85)	
ODDS RATIO [2]		
ESTIMATE	0.70	
95% CI	(0.12, 4.05)	
P-VALUE [3]	0.6750	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | REGION 1 = ROW

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	30/40 (75.0)	21/40 (52.5)
RISK DIFFERENCE [1]		
ESTIMATE	22.50	
95% CI	(1.86, 43.14)	
RELATIVE RISK [2]		
ESTIMATE	1.41	
95% CI	(1.00, 2.00)	
ODDS RATIO [2]		
ESTIMATE	2.65	
95% CI	(1.01, 6.95)	
P-VALUE [3]	0.0398†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | REGION 1 = US

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/14 (64.3)	8/11 (72.7)
RISK DIFFERENCE [1]		
ESTIMATE	-12.04	
95% CI	(-51.15, 27.08)	
RELATIVE RISK [2]		
ESTIMATE	0.91	
95% CI	(0.49, 1.68)	
ODDS RATIO [2]		
ESTIMATE	0.60	
95% CI	(0.10, 3.71)	
P-VALUE [3]	0.5645	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | REGION 1 = ROW

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	31/40 (77.5)	22/41 (53.7)
RISK DIFFERENCE [1]		
ESTIMATE	23.79	
95% CI	(3.70, 43.88)	
RELATIVE RISK [2]		
ESTIMATE	1.43	
95% CI	(1.03, 1.99)	
ODDS RATIO [2]		
ESTIMATE	2.93	
95% CI	(1.11, 7.72)	
P-VALUE [3]	0.0271†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | REGION 1 = US

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/14 (64.3)	9/11 (81.8)
RISK DIFFERENCE [1]		
ESTIMATE	-19.68	
95% CI	(-58.76, 19.41)	
RELATIVE RISK [2]		
ESTIMATE	0.86	
95% CI	(0.47, 1.58)	
ODDS RATIO [2]		
ESTIMATE	0.50*	
95% CI	(0.08, 3.18)*	
P-VALUE [3]	0.3315	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | REGION 1 = ROW

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	32/40 (80.0)	27/41 (65.9)
RISK DIFFERENCE [1]		
ESTIMATE	14.27	
95% CI	(-4.82, 33.36)	
RELATIVE RISK [2]		
ESTIMATE	1.21	
95% CI	(0.93, 1.58)	
ODDS RATIO [2]		
ESTIMATE	2.07	
95% CI	(0.75, 5.76)	
P-VALUE [3]	0.1553	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | REGION 1 = US

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/14 (64.3)	10/11 (90.9)
RISK DIFFERENCE [1]		
ESTIMATE	-27.31	
95% CI	(-63.61, 8.98)	
RELATIVE RISK [2]		
ESTIMATE	0.75	
95% CI	(0.43, 1.31)	
ODDS RATIO [2]		
ESTIMATE	0.34*	
95% CI	(0.05, 2.27)*	
P-VALUE [3]	0.1492	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS REGION 1 = ROW		
TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	32/40 (80.0)	29/41 (70.7)
RISK DIFFERENCE [1]		
ESTIMATE	9.52	
95% CI	(-9.03, 28.06)	
RELATIVE RISK [2]		
ESTIMATE	1.09	
95% CI	(0.86, 1.38)	
ODDS RATIO [2]		
ESTIMATE	1.67	
95% CI	(0.58, 4.77)	
P-VALUE [3]	0.3236	

1.5.4 Region (Variante 2)

- GA-NRS=General Anxiety Numeric Rating Scale; CI=Confidence Interval
- Time to first incidence of GA-NRS reduction of ≥ 2 points within 4, 8, 12, 24, and 48 hours of the first IMP administration = Date/time of first ≥ 2 points reduction in GA-NRS score for 2 consecutive time points in a row – Date/time of first IMP administration.
- Attacks that had a baseline GA-NRS score below a cutoff point were excluded from the corresponding analysis.
- Attacks that did not have at least 1 post-baseline assessment within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | REGION 2 = NORTH AMERICA

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	8/14 (57.1)	5/11 (45.5)
RISK DIFFERENCE [1]		
ESTIMATE	6.02	
95% CI	(-33.60, 45.64)	
RELATIVE RISK [2]		
ESTIMATE	1.09	
95% CI	(0.53, 2.26)	
ODDS RATIO [2]		
ESTIMATE	1.30	
95% CI	(0.23, 7.56)	
P-VALUE [3]	0.7794	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | REGION 2 = EUROPE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	20/29 (69.0)	17/33 (51.5)
RISK DIFFERENCE [1]		
ESTIMATE	17.30	
95% CI	(-7.50, 42.09)	
RELATIVE RISK [2]		
ESTIMATE	1.30	
95% CI	(0.84, 2.03)	
ODDS RATIO [2]		
ESTIMATE	1.97	
95% CI	(0.67, 5.78)	
P-VALUE [3]	0.1775	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | REGION 2 = ROW

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	7/11 (63.6)	2/7 (28.6)
RISK DIFFERENCE [1]		
ESTIMATE	44.83	
95% CI	(5.88, 83.78)	
RELATIVE RISK [2]		
ESTIMATE	2.19	
95% CI	(0.80, 6.00)	
ODDS RATIO [2]		
ESTIMATE	4.16*	
95% CI	(0.60, 29.00)*	
P-VALUE [3]	0.1028	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | REGION 2 = NORTH AMERICA

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	8/14 (57.1)	7/11 (63.6)
RISK DIFFERENCE [1]		
ESTIMATE	-9.26	
95% CI	(-50.51, 31.99)	
RELATIVE RISK [2]		
ESTIMATE	0.92	
95% CI	(0.46, 1.85)	
ODDS RATIO [2]		
ESTIMATE	0.70	
95% CI	(0.12, 4.05)	
P-VALUE [3]	0.6750	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | REGION 2 = EUROPE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	22/29 (75.9)	19/33 (57.6)
RISK DIFFERENCE [1]		
ESTIMATE	18.33	
95% CI	(-4.88, 41.55)	
RELATIVE RISK [2]		
ESTIMATE	1.30	
95% CI	(0.90, 1.87)	
ODDS RATIO [2]		
ESTIMATE	2.28	
95% CI	(0.76, 6.87)	
P-VALUE [3]	0.1385	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | REGION 2 = ROW

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	8/11 (72.7)	2/7 (28.6)
RISK DIFFERENCE [1]		
ESTIMATE	55.17	
95% CI	(19.61, 90.74)	
RELATIVE RISK [2]		
ESTIMATE	2.37	
95% CI	(0.87, 6.42)	
ODDS RATIO [2]		
ESTIMATE	5.93*	
95% CI	(0.78, 45.07)*	
P-VALUE [3]	0.0422†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | REGION 2 = NORTH AMERICA

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/14 (64.3)	8/11 (72.7)
RISK DIFFERENCE [1]		
ESTIMATE	-12.04	
95% CI	(-51.15, 27.08)	
RELATIVE RISK [2]		
ESTIMATE	0.91	
95% CI	(0.49, 1.68)	
ODDS RATIO [2]		
ESTIMATE	0.60	
95% CI	(0.10, 3.71)	
P-VALUE [3]	0.5645	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | REGION 2 = EUROPE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	23/29 (79.3)	20/34 (58.8)
RISK DIFFERENCE [1]		
ESTIMATE	20.74	
95% CI	(-1.60, 43.07)	
RELATIVE RISK [2]		
ESTIMATE	1.33	
95% CI	(0.95, 1.88)	
ODDS RATIO [2]		
ESTIMATE	2.69	
95% CI	(0.86, 8.39)	
P-VALUE [3]	0.0862	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | REGION 2 = ROW

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	8/11 (72.7)	2/7 (28.6)
RISK DIFFERENCE [1]		
ESTIMATE	55.17	
95% CI	(19.61, 90.74)	
RELATIVE RISK [2]		
ESTIMATE	2.37	
95% CI	(0.87, 6.42)	
ODDS RATIO [2]		
ESTIMATE	5.93*	
95% CI	(0.78, 45.07)*	
P-VALUE [3]	0.0422†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | REGION 2 = NORTH AMERICA

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/14 (64.3)	9/11 (81.8)
RISK DIFFERENCE [1]		
ESTIMATE	-19.68	
95% CI	(-58.76, 19.41)	
RELATIVE RISK [2]		
ESTIMATE	0.86	
95% CI	(0.47, 1.58)	
ODDS RATIO [2]		
ESTIMATE	0.50*	
95% CI	(0.08, 3.18)*	
P-VALUE [3]	0.3315	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | REGION 2 = EUROPE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	24/29 (82.8)	23/34 (67.6)
RISK DIFFERENCE [1]		
ESTIMATE	15.66	
95% CI	(-5.30, 36.62)	
RELATIVE RISK [2]		
ESTIMATE	1.22	
95% CI	(0.92, 1.63)	
ODDS RATIO [2]		
ESTIMATE	2.36	
95% CI	(0.70, 7.93)	
P-VALUE [3]	0.1662	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | REGION 2 = ROW

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	8/11 (72.7)	4/7 (57.1)
RISK DIFFERENCE [1]		
ESTIMATE	24.14	
95% CI	(-16.59, 64.86)	
RELATIVE RISK [2]		
ESTIMATE	1.27	
95% CI	(0.71, 2.29)	
ODDS RATIO [2]		
ESTIMATE	2.34*	
95% CI	(0.31, 17.79)*	
P-VALUE [3]	0.3222	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | REGION 2 = NORTH AMERICA

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/14 (64.3)	10/11 (90.9)
RISK DIFFERENCE [1]		
ESTIMATE	-27.31	
95% CI	(-63.61, 8.98)	
RELATIVE RISK [2]		
ESTIMATE	0.75	
95% CI	(0.43, 1.31)	
ODDS RATIO [2]		
ESTIMATE	0.34*	
95% CI	(0.05, 2.27)*	
P-VALUE [3]	0.1492	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | REGION 2 = EUROPE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	24/29 (82.8)	24/34 (70.6)
RISK DIFFERENCE [1]		
ESTIMATE	13.01	
95% CI	(-7.63, 33.65)	
RELATIVE RISK [2]		
ESTIMATE	1.16	
95% CI	(0.88, 1.52)	
ODDS RATIO [2]		
ESTIMATE	2.10	
95% CI	(0.62, 7.13)	
P-VALUE [3]	0.2383	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS REGION 2 = ROW		
TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	8/11 (72.7)	5/7 (71.4)
RISK DIFFERENCE [1]		
ESTIMATE	8.62	
95% CI	(-29.12, 46.36)	
RELATIVE RISK [2]		
ESTIMATE	0.89	
95% CI	(0.63, 1.26)	
ODDS RATIO [2]		
ESTIMATE	1.41*	
95% CI	(0.17, 11.64)*	
P-VALUE [3]	0.6908	

1.5.5 Prophylaxe-Status (Variante 1)

- GA-NRS=General Anxiety Numeric Rating Scale; CI=Confidence Interval
- Time to first incidence of GA-NRS reduction of ≥ 2 points within 4, 8, 12, 24, and 48 hours of the first IMP administration = Date/time of first ≥ 2 points reduction in GA-NRS score for 2 consecutive time points in a row – Date/time of first IMP administration.
- Attacks that had a baseline GA-NRS score below a cutoff point were excluded from the corresponding analysis.
- Attacks that did not have at least 1 post-baseline assessment within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/14 (64.3)	5/11 (45.5)
RISK DIFFERENCE [1]		
ESTIMATE	14.00	
95% CI	(-28.00, 56.01)	
RELATIVE RISK [2]		
ESTIMATE	0.78	
95% CI	(0.44, 1.39)	
ODDS RATIO [2]		
ESTIMATE	2.19*	
95% CI	(0.33, 14.34)*	
P-VALUE [3]	0.5132	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
DEMAND

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	26/40 (65.0)	19/40 (47.5)
RISK DIFFERENCE [1]		
ESTIMATE	17.54	
95% CI	(-4.03, 39.12)	
RELATIVE RISK [2]		
ESTIMATE	1.36	
95% CI	(0.91, 2.03)	
ODDS RATIO [2]		
ESTIMATE	2.03	
95% CI	(0.82, 5.03)	
P-VALUE [3]	0.1207	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/14 (64.3)	7/11 (63.6)
RISK DIFFERENCE [1]		
ESTIMATE	-0.74	
95% CI	(-41.06, 39.58)	
RELATIVE RISK [2]		
ESTIMATE	0.74	
95% CI	(0.44, 1.24)	
ODDS RATIO [2]		
ESTIMATE	1.07*	
95% CI	(0.16, 7.02)*	
P-VALUE [3]	0.9718	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
DEMAND

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	29/40 (72.5)	21/40 (52.5)
RISK DIFFERENCE [1]		
ESTIMATE	20.09	
95% CI	(-0.68, 40.85)	
RELATIVE RISK [2]		
ESTIMATE	1.38	
95% CI	(0.97, 1.96)	
ODDS RATIO [2]		
ESTIMATE	2.39	
95% CI	(0.94, 6.09)	
P-VALUE [3]	0.0688	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	10/14 (71.4)	8/11 (72.7)
RISK DIFFERENCE [1]		
ESTIMATE	-4.18	
95% CI	(-40.20, 31.84)	
RELATIVE RISK [2]		
ESTIMATE	0.81	
95% CI	(0.55, 1.20)	
ODDS RATIO [2]		
ESTIMATE	0.94*	
95% CI	(0.15, 5.91)*	
P-VALUE [3]	0.8324	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
DEMAND

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	30/40 (75.0)	22/41 (53.7)
RISK DIFFERENCE [1]		
ESTIMATE	21.44	
95% CI	(1.10, 41.78)	
RELATIVE RISK [2]		
ESTIMATE	1.40	
95% CI	(1.00, 1.95)	
ODDS RATIO [2]		
ESTIMATE	2.60	
95% CI	(1.01, 6.69)	
P-VALUE [3]	0.0485†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	10/14 (71.4)	9/11 (81.8)
RISK DIFFERENCE [1]		
ESTIMATE	-11.55	
95% CI	(-45.62, 22.53)	
RELATIVE RISK [2]		
ESTIMATE	0.76	
95% CI	(0.52, 1.12)	
ODDS RATIO [2]		
ESTIMATE	0.66*	
95% CI	(0.10, 4.36)*	
P-VALUE [3]	0.5319	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
DEMAND

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	31/40 (77.5)	27/41 (65.9)
RISK DIFFERENCE [1]		
ESTIMATE	12.22	
95% CI	(-7.07, 31.51)	
RELATIVE RISK [2]		
ESTIMATE	1.16	
95% CI	(0.89, 1.51)	
ODDS RATIO [2]		
ESTIMATE	1.86	
95% CI	(0.69, 5.02)	
P-VALUE [3]	0.2274	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	10/14 (71.4)	10/11 (90.9)
RISK DIFFERENCE [1]		
ESTIMATE	-20.15	
95% CI	(-50.27, 9.98)	
RELATIVE RISK [2]		
ESTIMATE	0.75	
95% CI	(0.53, 1.08)	
ODDS RATIO [2]		
ESTIMATE	0.41*	
95% CI	(0.06, 2.83)*	
P-VALUE [3]	0.2522	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS PROPHYLACTIC TREATMENT STATUS 1 = ON DEMAND		
TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	31/40 (77.5)	29/41 (70.7)
RISK DIFFERENCE [1]		
ESTIMATE	7.65	
95% CI	(-11.11, 26.41)	
RELATIVE RISK [2]		
ESTIMATE	1.02	
95% CI	(0.81, 1.29)	
ODDS RATIO [2]		
ESTIMATE	1.55	
95% CI	(0.54, 4.41)	
P-VALUE [3]	0.4293	

1.5.6 Prophylaxe-Status (Variante 2)

- GA-NRS=General Anxiety Numeric Rating Scale; CI=Confidence Interval
- Time to first incidence of GA-NRS reduction of ≥ 2 points within 4, 8, 12, 24, and 48 hours of the first IMP administration = Date/time of first ≥ 2 points reduction in GA-NRS score for 2 consecutive time points in a row – Date/time of first IMP administration.
- Attacks that had a baseline GA-NRS score below a cutoff point were excluded from the corresponding analysis.
- Attacks that did not have at least 1 post-baseline assessment within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/9 (55.6)	3/8 (37.5)
RISK DIFFERENCE [1]		
ESTIMATE	24.62	
95% CI	(-30.60, 79.83)	
RELATIVE RISK [2]		
ESTIMATE	1.25	
95% CI	(0.46, 3.36)	
ODDS RATIO [2]		
ESTIMATE	2.16*	
95% CI	(0.28, 16.70)*	
P-VALUE [3]	0.3811	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/5 (80.0)	2/3 (66.7)
RISK DIFFERENCE [1]		
ESTIMATE	17.86	
95% CI	(-22.59, 58.31)	
RELATIVE RISK [2]		
ESTIMATE	2.00	
95% CI	(0.14, 28.42)	
ODDS RATIO [2]		
ESTIMATE	3.00*	
95% CI	(0.06, 151.19)*	
P-VALUE [3]	0.4795	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
DEMAND

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	26/40 (65.0)	19/40 (47.5)
RISK DIFFERENCE [1]		
ESTIMATE	17.54	
95% CI	(-4.03, 39.12)	
RELATIVE RISK [2]		
ESTIMATE	1.36	
95% CI	(0.91, 2.03)	
ODDS RATIO [2]		
ESTIMATE	2.03	
95% CI	(0.82, 5.03)	
P-VALUE [3]	0.1207	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/9 (55.6)	5/8 (62.5)
RISK DIFFERENCE [1]		
ESTIMATE	1.54	
95% CI	(-52.69, 55.77)	
RELATIVE RISK [2]		
ESTIMATE	0.91	
95% CI	(0.43, 1.92)	
ODDS RATIO [2]		
ESTIMATE	0.93*	
95% CI	(0.12, 7.17)*	
P-VALUE [3]	0.9546	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/5 (80.0)	2/3 (66.7)
RISK DIFFERENCE [1]		
ESTIMATE	17.86	
95% CI	(-22.59, 58.31)	
RELATIVE RISK [2]		
ESTIMATE	2.00	
95% CI	(0.14, 28.42)	
ODDS RATIO [2]		
ESTIMATE	3.00*	
95% CI	(0.06, 151.19)*	
P-VALUE [3]	0.4795	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
DEMAND

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	29/40 (72.5)	21/40 (52.5)
RISK DIFFERENCE [1]		
ESTIMATE	20.09	
95% CI	(-0.68, 40.85)	
RELATIVE RISK [2]		
ESTIMATE	1.38	
95% CI	(0.97, 1.96)	
ODDS RATIO [2]		
ESTIMATE	2.39	
95% CI	(0.94, 6.09)	
P-VALUE [3]	0.0688	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	6/9 (66.7)	6/8 (75.0)
RISK DIFFERENCE [1]		
ESTIMATE	-3.85	
95% CI	(-49.69, 42.00)	
RELATIVE RISK [2]		
ESTIMATE	0.94	
95% CI	(0.56, 1.59)	
ODDS RATIO [2]		
ESTIMATE	0.86*	
95% CI	(0.11, 6.54)*	
P-VALUE [3]	0.8795	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/5 (80.0)	2/3 (66.7)
RISK DIFFERENCE [1]		
ESTIMATE	17.86	
95% CI	(-22.59, 58.31)	
RELATIVE RISK [2]		
ESTIMATE	2.00	
95% CI	(0.14, 28.42)	
ODDS RATIO [2]		
ESTIMATE	3.00*	
95% CI	(0.06, 151.19)*	
P-VALUE [3]	0.4795	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
DEMAND

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	30/40 (75.0)	22/41 (53.7)
RISK DIFFERENCE [1]		
ESTIMATE	21.44	
95% CI	(1.10, 41.78)	
RELATIVE RISK [2]		
ESTIMATE	1.40	
95% CI	(1.00, 1.95)	
ODDS RATIO [2]		
ESTIMATE	2.60	
95% CI	(1.01, 6.69)	
P-VALUE [3]	0.0485†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	6/9 (66.7)	7/8 (87.5)
RISK DIFFERENCE [1]		
ESTIMATE	-15.38	
95% CI	(-57.87, 27.10)	
RELATIVE RISK [2]		
ESTIMATE	0.84	
95% CI	(0.52, 1.37)	
ODDS RATIO [2]		
ESTIMATE	0.56*	
95% CI	(0.07, 4.51)*	
P-VALUE [3]	0.5021	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/5 (80.0)	2/3 (66.7)
RISK DIFFERENCE [1]		
ESTIMATE	17.86	
95% CI	(-22.59, 58.31)	
RELATIVE RISK [2]		
ESTIMATE	2.00	
95% CI	(0.14, 28.42)	
ODDS RATIO [2]		
ESTIMATE	3.00*	
95% CI	(0.06, 151.19)*	
P-VALUE [3]	0.4795	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
DEMAND

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	31/40 (77.5)	27/41 (65.9)
RISK DIFFERENCE [1]		
ESTIMATE	12.22	
95% CI	(-7.07, 31.51)	
RELATIVE RISK [2]		
ESTIMATE	1.16	
95% CI	(0.89, 1.51)	
ODDS RATIO [2]		
ESTIMATE	1.86	
95% CI	(0.69, 5.02)	
P-VALUE [3]	0.2274	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	6/9 (66.7)	8/8 (100.0)
RISK DIFFERENCE [1]		
ESTIMATE	-26.15	
95% CI	(-58.68, 6.38)	
RELATIVE RISK [2]		
ESTIMATE	0.59	
95% CI	(0.32, 1.10)	
ODDS RATIO [2]		
ESTIMATE	0.25*	
95% CI	(0.02, 3.15)*	
P-VALUE [3]	0.1630	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
DEMAND

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/5 (80.0)	2/3 (66.7)
RISK DIFFERENCE [1]		
ESTIMATE	17.86	
95% CI	(-22.59, 58.31)	
RELATIVE RISK [2]		
ESTIMATE	2.00	
95% CI	(0.14, 28.42)	
ODDS RATIO [2]		
ESTIMATE	3.00*	
95% CI	(0.06, 151.19)*	
P-VALUE [3]	0.4795	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	31/40 (77.5)	29/41 (70.7)
RISK DIFFERENCE [1]		
ESTIMATE	7.65	
95% CI	(-11.11, 26.41)	
RELATIVE RISK [2]		
ESTIMATE	1.02	
95% CI	(0.81, 1.29)	
ODDS RATIO [2]		
ESTIMATE	1.55	
95% CI	(0.54, 4.41)	
P-VALUE [3]	0.4293	

1.5.7 Attacken-Schwere (PGIS) zu Baseline

- GA-NRS=General Anxiety Numeric Rating Scale; CI=Confidence Interval
- Time to first incidence of GA-NRS reduction of ≥ 2 points within 4, 8, 12, 24, and 48 hours of the first IMP administration = Date/time of first ≥ 2 points reduction in GA-NRS score for 2 consecutive time points in a row – Date/time of first IMP administration.
- Attacks that had a baseline GA-NRS score below a cutoff point were excluded from the corresponding analysis.
- Attacks that did not have at least 1 post-baseline assessment within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
NONE OR MILD

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	11/21 (52.4)	8/19 (42.1)
RISK DIFFERENCE [1]		
ESTIMATE	10.52	
95% CI	(-20.85, 41.89)	
RELATIVE RISK [2]		
ESTIMATE	1.17	
95% CI	(0.58, 2.36)	
ODDS RATIO [2]		
ESTIMATE	1.49	
95% CI	(0.41, 5.41)	
P-VALUE [3]	0.5223	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
MODERATE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	15/24 (62.5)	12/22 (54.5)
RISK DIFFERENCE [1]		
ESTIMATE	8.07	
95% CI	(-20.84, 36.98)	
RELATIVE RISK [2]		
ESTIMATE	1.14	
95% CI	(0.70, 1.87)	
ODDS RATIO [2]		
ESTIMATE	1.37	
95% CI	(0.41, 4.62)	
P-VALUE [3]	0.5918	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
SEVERE OR VERY SEVERE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/9 (100.0)	4/10 (40.0)
RISK DIFFERENCE [1]		
ESTIMATE	53.63	
95% CI	(17.57, 89.68)	
RELATIVE RISK [2]		
ESTIMATE	2.77	
95% CI	(1.13, 6.78)	
ODDS RATIO [2]		
ESTIMATE	9.10*	
95% CI	(0.73, 112.67)*	
P-VALUE [3]	0.0246†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
NONE OR MILD

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	11/21 (52.4)	10/19 (52.6)
RISK DIFFERENCE [1]		
ESTIMATE	-0.47	
95% CI	(-31.62, 30.68)	
RELATIVE RISK [2]		
ESTIMATE	1.00	
95% CI	(0.55, 1.82)	
ODDS RATIO [2]		
ESTIMATE	0.98	
95% CI	(0.28, 3.43)	
P-VALUE [3]	0.9771	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
MODERATE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	18/24 (75.0)	13/22 (59.1)
RISK DIFFERENCE [1]		
ESTIMATE	15.72	
95% CI	(-11.81, 43.25)	
RELATIVE RISK [2]		
ESTIMATE	1.19	
95% CI	(0.79, 1.80)	
ODDS RATIO [2]		
ESTIMATE	1.89	
95% CI	(0.49, 7.27)	
P-VALUE [3]	0.2723	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
SEVERE OR VERY SEVERE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/9 (100.0)	5/10 (50.0)
RISK DIFFERENCE [1]		
ESTIMATE	44.56	
95% CI	(9.62, 79.50)	
RELATIVE RISK [2]		
ESTIMATE	2.24	
95% CI	(1.08, 4.63)	
ODDS RATIO [2]		
ESTIMATE	6.69*	
95% CI	(0.55, 81.25)*	
P-VALUE [3]	0.0553	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
NONE OR MILD

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	12/21 (57.1)	10/19 (52.6)
RISK DIFFERENCE [1]		
ESTIMATE	4.55	
95% CI	(-26.37, 35.47)	
RELATIVE RISK [2]		
ESTIMATE	1.08	
95% CI	(0.61, 1.91)	
ODDS RATIO [2]		
ESTIMATE	1.20	
95% CI	(0.34, 4.20)	
P-VALUE [3]	0.7813	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
MODERATE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	19/24 (79.2)	15/23 (65.2)
RISK DIFFERENCE [1]		
ESTIMATE	14.09	
95% CI	(-11.64, 39.82)	
RELATIVE RISK [2]		
ESTIMATE	1.21	
95% CI	(0.84, 1.74)	
ODDS RATIO [2]		
ESTIMATE	2.01	
95% CI	(0.50, 8.01)	
P-VALUE [3]	0.2991	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
SEVERE OR VERY SEVERE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/9 (100.0)	5/10 (50.0)
RISK DIFFERENCE [1]		
ESTIMATE	44.56	
95% CI	(9.62, 79.50)	
RELATIVE RISK [2]		
ESTIMATE	2.24	
95% CI	(1.08, 4.63)	
ODDS RATIO [2]		
ESTIMATE	6.69*	
95% CI	(0.55, 81.25)*	
P-VALUE [3]	0.0553	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
NONE OR MILD

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	12/21 (57.1)	12/19 (63.2)
RISK DIFFERENCE [1]		
ESTIMATE	-6.27	
95% CI	(-36.61, 24.07)	
RELATIVE RISK [2]		
ESTIMATE	0.87	
95% CI	(0.53, 1.43)	
ODDS RATIO [2]		
ESTIMATE	0.79	
95% CI	(0.21, 2.95)	
P-VALUE [3]	0.6954	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
MODERATE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	20/24 (83.3)	17/23 (73.9)
RISK DIFFERENCE [1]		
ESTIMATE	10.26	
95% CI	(-13.18, 33.71)	
RELATIVE RISK [2]		
ESTIMATE	1.19	
95% CI	(0.89, 1.59)	
ODDS RATIO [2]		
ESTIMATE	1.51*	
95% CI	(0.33, 6.91)*	
P-VALUE [3]	0.4065	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
SEVERE IR VERY SEVERE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/9 (100.0)	7/10 (70.0)
RISK DIFFERENCE [1]		
ESTIMATE	26.44	
95% CI	(-3.41, 56.28)	
RELATIVE RISK [2]		
ESTIMATE	1.45	
95% CI	(0.93, 2.26)	
ODDS RATIO [2]		
ESTIMATE	3.60*	
95% CI	(0.29, 44.58)*	
P-VALUE [3]	0.1845	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
NONE OR MILD

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	12/21 (57.1)	13/19 (68.4)
RISK DIFFERENCE [1]		
ESTIMATE	-11.68	
95% CI	(-41.42, 18.06)	
RELATIVE RISK [2]		
ESTIMATE	0.76	
95% CI	(0.48, 1.22)	
ODDS RATIO [2]		
ESTIMATE	0.73*	
95% CI	(0.18, 2.87)*	
P-VALUE [3]	0.4545	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
MODERATE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	20/24 (83.3)	18/23 (78.3)
RISK DIFFERENCE [1]		
ESTIMATE	6.43	
95% CI	(-15.84, 28.71)	
RELATIVE RISK [2]		
ESTIMATE	1.15	
95% CI	(0.89, 1.47)	
ODDS RATIO [2]		
ESTIMATE	1.34*	
95% CI	(0.29, 6.16)*	
P-VALUE [3]	0.5850	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
SEVERE OR VERY SEVERE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/9 (100.0)	8/10 (80.0)
RISK DIFFERENCE [1]		
ESTIMATE	18.13	
95% CI	(-7.54, 43.80)	
RELATIVE RISK [2]		
ESTIMATE	1.40	
95% CI	(0.88, 2.24)	
ODDS RATIO [2]		
ESTIMATE	4.09*	
95% CI	(0.15, 108.94)*	
P-VALUE [3]	0.2598	

1.6 Anzahl und Anteil der Attacken mit einer Verringerung des GA-NRS um ≥ 3 Punkte

1.6.1 Alter

- GA-NRS=General Anxiety Numeric Rating Scale; CI=Confidence Interval
- Time to first incidence of GA-NRS reduction of ≥ 3 points within 4, 8, 12, 24, and 48 hours of the first IMP administration = Date/time of first ≥ 3 points reduction in GA-NRS score for 2 consecutive time points in a row – Date/time of first IMP administration.
- Attacks that had a baseline GA-NRS score below a cutoff point were excluded from the corresponding analysis.
- Attacks that did not have at least 1 post-baseline assessment within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | AGE GROUP = <18 YEARS

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	1/3 (33.3)	3/5 (60.0)
RISK DIFFERENCE [1]		
ESTIMATE	-14.29	
95% CI	(-82.87, 54.30)	
RELATIVE RISK [2]		
ESTIMATE	1.34	
95% CI	(0.62, 2.88)	
ODDS RATIO [2]		
ESTIMATE	0.60*	
95% CI	(0.04, 8.73)*	
P-VALUE [3]	0.7055	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | AGE GROUP = >=18 YEARS

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	21/43 (48.8)	14/40 (35.0)
RISK DIFFERENCE [1]		
ESTIMATE	12.25	
95% CI	(-9.12, 33.62)	
RELATIVE RISK [2]		
ESTIMATE	1.27	
95% CI	(0.76, 2.13)	
ODDS RATIO [2]		
ESTIMATE	1.65	
95% CI	(0.66, 4.10)	
P-VALUE [3]	0.2632	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | AGE GROUP = <18 YEARS

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	1/3 (33.3)	3/5 (60.0)
RISK DIFFERENCE [1]		
ESTIMATE	-14.29	
95% CI	(-82.87, 54.30)	
RELATIVE RISK [2]		
ESTIMATE	1.34	
95% CI	(0.62, 2.88)	
ODDS RATIO [2]		
ESTIMATE	0.60*	
95% CI	(0.04, 8.73)*	
P-VALUE [3]	0.7055	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | AGE GROUP = >=18 YEARS

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	25/43 (58.1)	17/40 (42.5)
RISK DIFFERENCE [1]		
ESTIMATE	14.29	
95% CI	(-7.05, 35.64)	
RELATIVE RISK [2]		
ESTIMATE	1.31	
95% CI	(0.85, 2.02)	
ODDS RATIO [2]		
ESTIMATE	1.79	
95% CI	(0.74, 4.35)	
P-VALUE [3]	0.1991	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | AGE GROUP = <18 YEARS

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	2/3 (66.7)	3/5 (60.0)
RISK DIFFERENCE [1]		
ESTIMATE	14.29	
95% CI	(-50.95, 79.52)	
RELATIVE RISK [2]		
ESTIMATE	1.42	
95% CI	(0.67, 2.97)	
ODDS RATIO [2]		
ESTIMATE	1.36*	
95% CI	(0.09, 20.65)*	
P-VALUE [3]	0.7290	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | AGE GROUP = >=18 YEARS

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	29/43 (67.4)	18/40 (45.0)
RISK DIFFERENCE [1]		
ESTIMATE	21.65	
95% CI	(0.66, 42.63)	
RELATIVE RISK [2]		
ESTIMATE	1.47	
95% CI	(0.99, 2.19)	
ODDS RATIO [2]		
ESTIMATE	2.46	
95% CI	(1.00, 6.04)	
P-VALUE [3]	0.0512	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | AGE GROUP = <18 YEARS

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	2/3 (66.7)	3/5 (60.0)
RISK DIFFERENCE [1]		
ESTIMATE	14.29	
95% CI	(-50.95, 79.52)	
RELATIVE RISK [2]		
ESTIMATE	1.42	
95% CI	(0.67, 2.97)	
ODDS RATIO [2]		
ESTIMATE	1.36*	
95% CI	(0.09, 20.65)*	
P-VALUE [3]	0.7290	

 Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

 WITHIN 24 HOURS | AGE GROUP = >=18 YEARS

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	30/43 (69.8)	25/40 (62.5)
RISK DIFFERENCE [1]		
ESTIMATE	6.49	
95% CI	(-13.92, 26.90)	
RELATIVE RISK [2]		
ESTIMATE	1.10	
95% CI	(0.81, 1.50)	
ODDS RATIO [2]		
ESTIMATE	1.34	
95% CI	(0.53, 3.37)	
P-VALUE [3]	0.5402	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | AGE GROUP = <18 YEARS

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	2/3 (66.7)	3/5 (60.0)
RISK DIFFERENCE [1]		
ESTIMATE	14.29	
95% CI	(-50.95, 79.52)	
RELATIVE RISK [2]		
ESTIMATE	1.42	
95% CI	(0.67, 2.97)	
ODDS RATIO [2]		
ESTIMATE	1.36*	
95% CI	(0.09, 20.65)*	
P-VALUE [3]	0.7290	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS AGE GROUP = >=18 YEARS		
TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	31/43 (72.1)	26/40 (65.0)
RISK DIFFERENCE [1]		
ESTIMATE	7.26	
95% CI	(-12.81, 27.34)	
RELATIVE RISK [2]		
ESTIMATE	1.11	
95% CI	(0.83, 1.49)	
ODDS RATIO [2]		
ESTIMATE	1.40	
95% CI	(0.55, 3.59)	
P-VALUE [3]	0.4868	

1.6.2 Region (1)

- GA-NRS=General Anxiety Numeric Rating Scale; CI=Confidence Interval
- Time to first incidence of GA-NRS reduction of ≥ 3 points within 4, 8, 12, 24, and 48 hours of the first IMP administration = Date/time of first ≥ 3 points reduction in GA-NRS score for 2 consecutive time points in a row – Date/time of first IMP administration.
- Attacks that had a baseline GA-NRS score below a cutoff point were excluded from the corresponding analysis.
- Attacks that did not have at least 1 post-baseline assessment within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | REGION 1 = US

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	3/12 (25.0)	3/11 (27.3)
RISK DIFFERENCE [1]		
ESTIMATE	-5.09	
95% CI	(-44.78, 34.60)	
RELATIVE RISK [2]		
ESTIMATE	0.93	
95% CI	(0.25, 3.50)	
ODDS RATIO [2]		
ESTIMATE	0.90*	
95% CI	(0.14, 5.89)*	
P-VALUE [3]	0.8151	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | REGION 1 = ROW

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	19/34 (55.9)	14/34 (41.2)
RISK DIFFERENCE [1]		
ESTIMATE	14.71	
95% CI	(-8.67, 38.08)	
RELATIVE RISK [2]		
ESTIMATE	1.31	
95% CI	(0.79, 2.16)	
ODDS RATIO [2]		
ESTIMATE	1.80	
95% CI	(0.65, 4.99)	
P-VALUE [3]	0.2242	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | REGION 1 = US

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/12 (41.7)	6/11 (54.5)
RISK DIFFERENCE [1]		
ESTIMATE	-4.76	
95% CI	(-50.62, 41.11)	
RELATIVE RISK [2]		
ESTIMATE	1.33	
95% CI	(0.61, 2.86)	
ODDS RATIO [2]		
ESTIMATE	0.82*	
95% CI	(0.13, 5.16)*	
P-VALUE [3]	0.8438	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | REGION 1 = ROW

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	21/34 (61.8)	14/34 (41.2)
RISK DIFFERENCE [1]		
ESTIMATE	20.59	
95% CI	(-2.18, 43.36)	
RELATIVE RISK [2]		
ESTIMATE	1.43	
95% CI	(0.89, 2.28)	
ODDS RATIO [2]		
ESTIMATE	2.38	
95% CI	(0.85, 6.61)	
P-VALUE [3]	0.0875	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | REGION 1 = US

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	6/12 (50.0)	7/11 (63.6)
RISK DIFFERENCE [1]		
ESTIMATE	-3.21	
95% CI	(-48.00, 41.58)	
RELATIVE RISK [2]		
ESTIMATE	1.22	
95% CI	(0.73, 2.04)	
ODDS RATIO [2]		
ESTIMATE	0.83*	
95% CI	(0.13, 5.22)*	
P-VALUE [3]	0.8926	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | REGION 1 = ROW

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	25/34 (73.5)	14/34 (41.2)
RISK DIFFERENCE [1]		
ESTIMATE	32.35	
95% CI	(10.61, 54.10)	
RELATIVE RISK [2]		
ESTIMATE	1.66	
95% CI	(1.08, 2.56)	
ODDS RATIO [2]		
ESTIMATE	4.19	
95% CI	(1.42, 12.39)	
P-VALUE [3]	0.0068†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | REGION 1 = US

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	7/12 (58.3)	8/11 (72.7)
RISK DIFFERENCE [1]		
ESTIMATE	-6.53	
95% CI	(-53.53, 40.47)	
RELATIVE RISK [2]		
ESTIMATE	1.20	
95% CI	(0.72, 1.99)	
ODDS RATIO [2]		
ESTIMATE	0.86*	
95% CI	(0.13, 5.71)*	
P-VALUE [3]	0.7763	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | REGION 1 = ROW

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	25/34 (73.5)	20/34 (58.8)
RISK DIFFERENCE [1]		
ESTIMATE	14.71	
95% CI	(-7.25, 36.66)	
RELATIVE RISK [2]		
ESTIMATE	1.24	
95% CI	(0.89, 1.74)	
ODDS RATIO [2]		
ESTIMATE	1.96	
95% CI	(0.69, 5.61)	
P-VALUE [3]	0.2035	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | REGION 1 = US

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	7/12 (58.3)	8/11 (72.7)
RISK DIFFERENCE [1]		
ESTIMATE	-6.53	
95% CI	(-53.53, 40.47)	
RELATIVE RISK [2]		
ESTIMATE	1.20	
95% CI	(0.72, 1.99)	
ODDS RATIO [2]		
ESTIMATE	0.86*	
95% CI	(0.13, 5.71)*	
P-VALUE [3]	0.7763	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS REGION 1 = ROW		
TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	26/34 (76.5)	21/34 (61.8)
RISK DIFFERENCE [1]		
ESTIMATE	14.71	
95% CI	(-7.03, 36.44)	
RELATIVE RISK [2]		
ESTIMATE	1.23	
95% CI	(0.89, 1.71)	
ODDS RATIO [2]		
ESTIMATE	1.99	
95% CI	(0.69, 5.76)	
P-VALUE [3]	0.1990	

1.6.3 Region (2)

- GA-NRS=General Anxiety Numeric Rating Scale; CI=Confidence Interval
- Time to first incidence of GA-NRS reduction of ≥ 3 points within 4, 8, 12, 24, and 48 hours of the first IMP administration = Date/time of first ≥ 3 points reduction in GA-NRS score for 2 consecutive time points in a row – Date/time of first IMP administration.
- Attacks that had a baseline GA-NRS score below a cutoff point were excluded from the corresponding analysis.
- Attacks that did not have at least 1 post-baseline assessment within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | REGION 2 = NORTH AMERICA

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	3/12 (25.0)	3/11 (27.3)
RISK DIFFERENCE [1]		
ESTIMATE	-5.09	
95% CI	(-44.78, 34.60)	
RELATIVE RISK [2]		
ESTIMATE	0.93	
95% CI	(0.25, 3.50)	
ODDS RATIO [2]		
ESTIMATE	0.90*	
95% CI	(0.14, 5.89)*	
P-VALUE [3]	0.8151	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | REGION 2 = EUROPE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	15/26 (57.7)	13/29 (44.8)
RISK DIFFERENCE [1]		
ESTIMATE	12.19	
95% CI	(-14.53, 38.92)	
RELATIVE RISK [2]		
ESTIMATE	1.24	
95% CI	(0.71, 2.16)	
ODDS RATIO [2]		
ESTIMATE	1.61	
95% CI	(0.53, 4.91)	
P-VALUE [3]	0.3749	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | REGION 2 = ROW

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/8 (50.0)	1/5 (20.0)
RISK DIFFERENCE [1]		
ESTIMATE	42.50	
95% CI	(8.24, 76.76)	
RELATIVE RISK [2]		
ESTIMATE	2.04	
95% CI	(0.67, 6.24)	
ODDS RATIO [2]		
ESTIMATE	3.00*	
95% CI	(0.35, 25.89)*	
P-VALUE [3]	0.1762	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | REGION 2 = NORTH AMERICA

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/12 (41.7)	6/11 (54.5)
RISK DIFFERENCE [1]		
ESTIMATE	-4.76	
95% CI	(-50.62, 41.11)	
RELATIVE RISK [2]		
ESTIMATE	1.33	
95% CI	(0.61, 2.86)	
ODDS RATIO [2]		
ESTIMATE	0.82*	
95% CI	(0.13, 5.16)*	
P-VALUE [3]	0.8438	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | REGION 2 = EUROPE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	17/26 (65.4)	13/29 (44.8)
RISK DIFFERENCE [1]		
ESTIMATE	20.42	
95% CI	(-5.22, 46.06)	
RELATIVE RISK [2]		
ESTIMATE	1.38	
95% CI	(0.85, 2.26)	
ODDS RATIO [2]		
ESTIMATE	2.34	
95% CI	(0.76, 7.21)	
P-VALUE [3]	0.1339	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | REGION 2 = ROW

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/8 (50.0)	1/5 (20.0)
RISK DIFFERENCE [1]		
ESTIMATE	42.50	
95% CI	(8.24, 76.76)	
RELATIVE RISK [2]		
ESTIMATE	2.04	
95% CI	(0.67, 6.24)	
ODDS RATIO [2]		
ESTIMATE	3.00*	
95% CI	(0.35, 25.89)*	
P-VALUE [3]	0.1762	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | REGION 2 = NORTH AMERICA

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	6/12 (50.0)	7/11 (63.6)
RISK DIFFERENCE [1]		
ESTIMATE	-3.21	
95% CI	(-48.00, 41.58)	
RELATIVE RISK [2]		
ESTIMATE	1.22	
95% CI	(0.73, 2.04)	
ODDS RATIO [2]		
ESTIMATE	0.83*	
95% CI	(0.13, 5.22)*	
P-VALUE [3]	0.8926	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | REGION 2 = EUROPE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	21/26 (80.8)	13/29 (44.8)
RISK DIFFERENCE [1]		
ESTIMATE	36.22	
95% CI	(12.72, 59.71)	
RELATIVE RISK [2]		
ESTIMATE	1.67	
95% CI	(1.09, 2.58)	
ODDS RATIO [2]		
ESTIMATE	5.41	
95% CI	(1.55, 18.85)	
P-VALUE [3]	0.0067†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | REGION 2 = ROW

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/8 (50.0)	1/5 (20.0)
RISK DIFFERENCE [1]		
ESTIMATE	42.50	
95% CI	(8.24, 76.76)	
RELATIVE RISK [2]		
ESTIMATE	2.04	
95% CI	(0.67, 6.24)	
ODDS RATIO [2]		
ESTIMATE	3.00*	
95% CI	(0.35, 25.89)*	
P-VALUE [3]	0.1762	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | REGION 2 = NORTH AMERICA

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	7/12 (58.3)	8/11 (72.7)
RISK DIFFERENCE [1]		
ESTIMATE	-6.53	
95% CI	(-53.53, 40.47)	
RELATIVE RISK [2]		
ESTIMATE	1.20	
95% CI	(0.72, 1.99)	
ODDS RATIO [2]		
ESTIMATE	0.86*	
95% CI	(0.13, 5.71)*	
P-VALUE [3]	0.7763	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | REGION 2 = EUROPE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	21/26 (80.8)	18/29 (62.1)
RISK DIFFERENCE [1]		
ESTIMATE	18.80	
95% CI	(-4.41, 42.01)	
RELATIVE RISK [2]		
ESTIMATE	1.26	
95% CI	(0.90, 1.76)	
ODDS RATIO [2]		
ESTIMATE	2.61	
95% CI	(0.75, 9.07)	
P-VALUE [3]	0.1333	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | REGION 2 = ROW

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/8 (50.0)	2/5 (40.0)
RISK DIFFERENCE [1]		
ESTIMATE	20.00	
95% CI	(-35.70, 75.70)	
RELATIVE RISK [2]		
ESTIMATE	1.52	
95% CI	(0.53, 4.37)	
ODDS RATIO [2]		
ESTIMATE	1.61*	
95% CI	(0.19, 13.96)*	
P-VALUE [3]	0.5564	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | REGION 2 = NORTH AMERICA

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	7/12 (58.3)	8/11 (72.7)
RISK DIFFERENCE [1]		
ESTIMATE	-6.53	
95% CI	(-53.53, 40.47)	
RELATIVE RISK [2]		
ESTIMATE	1.20	
95% CI	(0.72, 1.99)	
ODDS RATIO [2]		
ESTIMATE	0.86*	
95% CI	(0.13, 5.71)*	
P-VALUE [3]	0.7763	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | REGION 2 = EUROPE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	22/26 (84.6)	18/29 (62.1)
RISK DIFFERENCE [1]		
ESTIMATE	22.88	
95% CI	(-0.00, 45.76)	
RELATIVE RISK [2]		
ESTIMATE	1.30	
95% CI	(0.94, 1.81)	
ODDS RATIO [2]		
ESTIMATE	2.95*	
95% CI	(0.82, 10.58)*	
P-VALUE [3]	0.0648	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS REGION 2 = ROW		
TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/8 (50.0)	3/5 (60.0)
RISK DIFFERENCE [1]		
ESTIMATE	-2.50	
95% CI	(-66.96, 61.96)	
RELATIVE RISK [2]		
ESTIMATE	1.04	
95% CI	(0.39, 2.73)	
ODDS RATIO [2]		
ESTIMATE	0.98*	
95% CI	(0.11, 8.42)*	
P-VALUE [3]	0.9414	

1.6.4 Prophylaxe-Status (Variant 1)

- GA-NRS=General Anxiety Numeric Rating Scale; CI=Confidence Interval
- Time to first incidence of GA-NRS reduction of ≥ 3 points within 4, 8, 12, 24, and 48 hours of the first IMP administration = Date/time of first ≥ 3 points reduction in GA-NRS score for 2 consecutive time points in a row – Date/time of first IMP administration.
- Attacks that had a baseline GA-NRS score below a cutoff point were excluded from the corresponding analysis.
- Attacks that did not have at least 1 post-baseline assessment within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/11 (45.5)	2/10 (20.0)
RISK DIFFERENCE [1]		
ESTIMATE	29.89	
95% CI	(-14.66, 74.44)	
RELATIVE RISK [2]		
ESTIMATE	2.05	
95% CI	(0.61, 6.92)	
ODDS RATIO [2]		
ESTIMATE	3.11*	
95% CI	(0.44, 21.89)*	
P-VALUE [3]	0.2067	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
DEMAND

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	17/35 (48.6)	15/35 (42.9)
RISK DIFFERENCE [1]		
ESTIMATE	5.10	
95% CI	(-18.02, 28.22)	
RELATIVE RISK [2]		
ESTIMATE	1.12	
95% CI	(0.68, 1.87)	
ODDS RATIO [2]		
ESTIMATE	1.23	
95% CI	(0.46, 3.26)	
P-VALUE [3]	0.6685	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	6/11 (54.5)	5/10 (50.0)
RISK DIFFERENCE [1]		
ESTIMATE	12.21	
95% CI	(-31.73, 56.15)	
RELATIVE RISK [2]		
ESTIMATE	1.25	
95% CI	(0.58, 2.66)	
ODDS RATIO [2]		
ESTIMATE	1.55*	
95% CI	(0.24, 10.04)*	
P-VALUE [3]	0.6137	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
DEMAND

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	20/35 (57.1)	15/35 (42.9)
RISK DIFFERENCE [1]		
ESTIMATE	13.69	
95% CI	(-9.33, 36.71)	
RELATIVE RISK [2]		
ESTIMATE	1.29	
95% CI	(0.81, 2.06)	
ODDS RATIO [2]		
ESTIMATE	1.75	
95% CI	(0.67, 4.61)	
P-VALUE [3]	0.2554	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	7/11 (63.6)	6/10 (60.0)
RISK DIFFERENCE [1]		
ESTIMATE	13.30	
95% CI	(-28.84, 55.44)	
RELATIVE RISK [2]		
ESTIMATE	1.27	
95% CI	(0.71, 2.27)	
ODDS RATIO [2]		
ESTIMATE	1.55*	
95% CI	(0.24, 10.06)*	
P-VALUE [3]	0.5761	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
DEMAND

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	24/35 (68.6)	15/35 (42.9)
RISK DIFFERENCE [1]		
ESTIMATE	25.14	
95% CI	(2.79, 47.50)	
RELATIVE RISK [2]		
ESTIMATE	1.53	
95% CI	(0.99, 2.36)	
ODDS RATIO [2]		
ESTIMATE	2.90	
95% CI	(1.07, 7.85)	
P-VALUE [3]	0.0358†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	7/11 (63.6)	8/10 (80.0)
RISK DIFFERENCE [1]		
ESTIMATE	-11.42	
95% CI	(-52.01, 29.16)	
RELATIVE RISK [2]		
ESTIMATE	0.96	
95% CI	(0.59, 1.58)	
ODDS RATIO [2]		
ESTIMATE	0.59*	
95% CI	(0.09, 4.01)*	
P-VALUE [3]	0.6007	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
DEMAND

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	25/35 (71.4)	20/35 (57.1)
RISK DIFFERENCE [1]		
ESTIMATE	13.89	
95% CI	(-8.22, 36.00)	
RELATIVE RISK [2]		
ESTIMATE	1.25	
95% CI	(0.88, 1.77)	
ODDS RATIO [2]		
ESTIMATE	1.86	
95% CI	(0.68, 5.05)	
P-VALUE [3]	0.2325	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	7/11 (63.6)	8/10 (80.0)
RISK DIFFERENCE [1]		
ESTIMATE	-11.42	
95% CI	(-52.01, 29.16)	
RELATIVE RISK [2]		
ESTIMATE	0.96	
95% CI	(0.59, 1.58)	
ODDS RATIO [2]		
ESTIMATE	0.59*	
95% CI	(0.09, 4.01)*	
P-VALUE [3]	0.6007	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS PROPHYLACTIC TREATMENT STATUS 1 = ON DEMAND		
TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	26/35 (74.3)	21/35 (60.0)
RISK DIFFERENCE [1]		
ESTIMATE	14.28	
95% CI	(-7.51, 36.06)	
RELATIVE RISK [2]		
ESTIMATE	1.24	
95% CI	(0.89, 1.73)	
ODDS RATIO [2]		
ESTIMATE	1.92	
95% CI	(0.70, 5.31)	
P-VALUE [3]	0.2139	

1.6.5 Prophylaxe-Status (Variant 2)

- GA-NRS=General Anxiety Numeric Rating Scale; CI=Confidence Interval
- Time to first incidence of GA-NRS reduction of ≥ 3 points within 4, 8, 12, 24, and 48 hours of the first IMP administration = Date/time of first ≥ 3 points reduction in GA-NRS score for 2 consecutive time points in a row – Date/time of first IMP administration.
- Attacks that had a baseline GA-NRS score below a cutoff point were excluded from the corresponding analysis.
- Attacks that did not have at least 1 post-baseline assessment within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	3/8 (37.5)	2/7 (28.6)
RISK DIFFERENCE [1]		
ESTIMATE	18.26	
95% CI	(-48.73, 85.26)	
RELATIVE RISK [2]		
ESTIMATE	1.50	
95% CI	(0.39, 5.71)	
ODDS RATIO [2]		
ESTIMATE	1.92*	
95% CI	(0.20, 18.33)*	
P-VALUE [3]	0.5339	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	2/3 (66.7)	0/3 (0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
DEMAND

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	17/35 (48.6)	15/35 (42.9)
RISK DIFFERENCE [1]		
ESTIMATE	5.10	
95% CI	(-18.02, 28.22)	
RELATIVE RISK [2]		
ESTIMATE	1.12	
95% CI	(0.68, 1.87)	
ODDS RATIO [2]		
ESTIMATE	1.23	
95% CI	(0.46, 3.26)	
P-VALUE [3]	0.6685	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/8 (50.0)	5/7 (71.4)
RISK DIFFERENCE [1]		
ESTIMATE	-12.87	
95% CI	(-68.10, 42.35)	
RELATIVE RISK [2]		
ESTIMATE	0.88	
95% CI	(0.43, 1.82)	
ODDS RATIO [2]		
ESTIMATE	0.63*	
95% CI	(0.08, 5.10)*	
P-VALUE [3]	0.6607	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	2/3 (66.7)	0/3 (0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
DEMAND

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	20/35 (57.1)	15/35 (42.9)
RISK DIFFERENCE [1]		
ESTIMATE	13.69	
95% CI	(-9.33, 36.71)	
RELATIVE RISK [2]		
ESTIMATE	1.29	
95% CI	(0.81, 2.06)	
ODDS RATIO [2]		
ESTIMATE	1.75	
95% CI	(0.67, 4.61)	
P-VALUE [3]	0.2554	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/8 (62.5)	6/7 (85.7)
RISK DIFFERENCE [1]		
ESTIMATE	-17.07	
95% CI	(-61.41, 27.28)	
RELATIVE RISK [2]		
ESTIMATE	0.67	
95% CI	(0.33, 1.33)	
ODDS RATIO [2]		
ESTIMATE	0.49*	
95% CI	(0.04, 5.64)*	
P-VALUE [3]	0.5001	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	2/3 (66.7)	0/3 (0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
DEMAND

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	24/35 (68.6)	15/35 (42.9)
RISK DIFFERENCE [1]		
ESTIMATE	25.14	
95% CI	(2.79, 47.50)	
RELATIVE RISK [2]		
ESTIMATE	1.53	
95% CI	(0.99, 2.36)	
ODDS RATIO [2]		
ESTIMATE	2.90	
95% CI	(1.07, 7.85)	
P-VALUE [3]	0.0358†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/8 (62.5)	7/7 (100.0)
RISK DIFFERENCE [1]		
ESTIMATE	-30.54	
95% CI	(-67.49, 6.41)	
RELATIVE RISK [2]		
ESTIMATE	0.59	
95% CI	(0.32, 1.10)	
ODDS RATIO [2]		
ESTIMATE	0.25*	
95% CI	(0.02, 3.15)*	
P-VALUE [3]	0.1630	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	2/3 (66.7)	1/3 (33.3)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
DEMAND

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	25/35 (71.4)	20/35 (57.1)
RISK DIFFERENCE [1]		
ESTIMATE	13.89	
95% CI	(-8.22, 36.00)	
RELATIVE RISK [2]		
ESTIMATE	1.25	
95% CI	(0.88, 1.77)	
ODDS RATIO [2]		
ESTIMATE	1.86	
95% CI	(0.68, 5.05)	
P-VALUE [3]	0.2325	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/8 (62.5)	7/7 (100.0)
RISK DIFFERENCE [1]		
ESTIMATE	-30.54	
95% CI	(-67.49, 6.41)	
RELATIVE RISK [2]		
ESTIMATE	0.59	
95% CI	(0.32, 1.10)	
ODDS RATIO [2]		
ESTIMATE	0.25*	
95% CI	(0.02, 3.15)*	
P-VALUE [3]	0.1630	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	2/3 (66.7)	1/3 (33.3)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	26/35 (74.3)	21/35 (60.0)
RISK DIFFERENCE [1]		
ESTIMATE	14.28	
95% CI	(-7.51, 36.06)	
RELATIVE RISK [2]		
ESTIMATE	1.24	
95% CI	(0.89, 1.73)	
ODDS RATIO [2]		
ESTIMATE	1.92	
95% CI	(0.70, 5.31)	
P-VALUE [3]	0.2139	

1.6.6 Attacken-Schwere (PGIS) zu Baseline

- GA-NRS=General Anxiety Numeric Rating Scale; CI=Confidence Interval
- Time to first incidence of GA-NRS reduction of ≥ 3 points within 4, 8, 12, 24, and 48 hours of the first IMP administration = Date/time of first ≥ 3 points reduction in GA-NRS score for 2 consecutive time points in a row – Date/time of first IMP administration.
- Attacks that had a baseline GA-NRS score below a cutoff point were excluded from the corresponding analysis.
- Attacks that did not have at least 1 post-baseline assessment within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
NONE OR MILD

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	6/16 (37.5)	6/15 (40.0)
RISK DIFFERENCE [1]		
ESTIMATE	-2.16	
95% CI	(-36.52, 32.20)	
RELATIVE RISK [2]		
ESTIMATE	0.93	
95% CI	(0.38, 2.29)	
ODDS RATIO [2]		
ESTIMATE	0.91	
95% CI	(0.21, 3.96)	
P-VALUE [3]	0.9067	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
MODERATE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	8/21 (38.1)	8/20 (40.0)
RISK DIFFERENCE [1]		
ESTIMATE	-5.36	
95% CI	(-33.79, 23.08)	
RELATIVE RISK [2]		
ESTIMATE	0.91	
95% CI	(0.46, 1.82)	
ODDS RATIO [2]		
ESTIMATE	0.78	
95% CI	(0.20, 3.04)	
P-VALUE [3]	0.7189	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
SEVERE OR VERY SEVERE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	8/9 (88.9)	3/10 (30.0)
RISK DIFFERENCE [1]		
ESTIMATE	56.95	
95% CI	(14.99, 98.91)	
RELATIVE RISK [2]		
ESTIMATE	1.06	
95% CI	(0.64, 1.75)	
ODDS RATIO [2]		
ESTIMATE	6.31*	
95% CI	(0.73, 54.24)*	
P-VALUE [3]	0.0276†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
NONE OR MILD

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	7/16 (43.8)	8/15 (53.3)
RISK DIFFERENCE [1]		
ESTIMATE	-9.35	
95% CI	(-44.19, 25.49)	
RELATIVE RISK [2]		
ESTIMATE	0.79	
95% CI	(0.38, 1.61)	
ODDS RATIO [2]		
ESTIMATE	0.71*	
95% CI	(0.17, 2.93)*	
P-VALUE [3]	0.6134	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
MODERATE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	10/21 (47.6)	9/20 (45.0)
RISK DIFFERENCE [1]		
ESTIMATE	-0.58	
95% CI	(-29.91, 28.76)	
RELATIVE RISK [2]		
ESTIMATE	0.90	
95% CI	(0.51, 1.58)	
ODDS RATIO [2]		
ESTIMATE	0.96	
95% CI	(0.25, 3.70)	
P-VALUE [3]	0.9698	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
SEVERE OR VERY SEVERE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/9 (100.0)	3/10 (30.0)
RISK DIFFERENCE [1]		
ESTIMATE	61.93	
95% CI	(25.37, 98.50)	
RELATIVE RISK [2]		
ESTIMATE	3.65	
95% CI	(1.25, 10.65)	
ODDS RATIO [2]		
ESTIMATE	17.94*	
95% CI	(1.29, 249.64)*	
P-VALUE [3]	0.0094†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
NONE OR MILD

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	10/16 (62.5)	8/15 (53.3)
RISK DIFFERENCE [1]		
ESTIMATE	9.35	
95% CI	(-23.37, 42.07)	
RELATIVE RISK [2]		
ESTIMATE	1.23	
95% CI	(0.59, 2.58)	
ODDS RATIO [2]		
ESTIMATE	1.54*	
95% CI	(0.34, 7.07)*	
P-VALUE [3]	0.5912	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
MODERATE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	12/21 (57.1)	10/20 (50.0)
RISK DIFFERENCE [1]		
ESTIMATE	4.11	
95% CI	(-25.49, 33.70)	
RELATIVE RISK [2]		
ESTIMATE	1.01	
95% CI	(0.60, 1.69)	
ODDS RATIO [2]		
ESTIMATE	1.21	
95% CI	(0.33, 4.48)	
P-VALUE [3]	0.7919	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
SEVERE OR VERY SEVERE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/9 (100.0)	3/10 (30.0)
RISK DIFFERENCE [1]		
ESTIMATE	61.93	
95% CI	(25.37, 98.50)	
RELATIVE RISK [2]		
ESTIMATE	3.65	
95% CI	(1.25, 10.65)	
ODDS RATIO [2]		
ESTIMATE	17.94*	
95% CI	(1.29, 249.64)*	
P-VALUE [3]	0.0094†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
NONE OR MILD

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	10/16 (62.5)	8/15 (53.3)
RISK DIFFERENCE [1]		
ESTIMATE	9.35	
95% CI	(-23.37, 42.07)	
RELATIVE RISK [2]		
ESTIMATE	1.23	
95% CI	(0.59, 2.58)	
ODDS RATIO [2]		
ESTIMATE	1.54*	
95% CI	(0.34, 7.07)*	
P-VALUE [3]	0.5912	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
MODERATE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	13/21 (61.9)	13/20 (65.0)
RISK DIFFERENCE [1]		
ESTIMATE	-6.63	
95% CI	(-34.83, 21.56)	
RELATIVE RISK [2]		
ESTIMATE	0.90	
95% CI	(0.59, 1.37)	
ODDS RATIO [2]		
ESTIMATE	0.73	
95% CI	(0.19, 2.85)	
P-VALUE [3]	0.6599	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
SEVERE OR VERY SEVERE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/9 (100.0)	7/10 (70.0)
RISK DIFFERENCE [1]		
ESTIMATE	26.44	
95% CI	(-3.41, 56.28)	
RELATIVE RISK [2]		
ESTIMATE	1.45	
95% CI	(0.93, 2.26)	
ODDS RATIO [2]		
ESTIMATE	3.60*	
95% CI	(0.29, 44.58)*	
P-VALUE [3]	0.1845	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
NONE OR MILD

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	10/16 (62.5)	8/15 (53.3)
RISK DIFFERENCE [1]		
ESTIMATE	9.35	
95% CI	(-23.37, 42.07)	
RELATIVE RISK [2]		
ESTIMATE	1.23	
95% CI	(0.59, 2.58)	
ODDS RATIO [2]		
ESTIMATE	1.54*	
95% CI	(0.34, 7.07)*	
P-VALUE [3]	0.5912	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
MODERATE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	14/21 (66.7)	14/20 (70.0)
RISK DIFFERENCE [1]		
ESTIMATE	-4.98	
95% CI	(-33.29, 23.33)	
RELATIVE RISK [2]		
ESTIMATE	0.92	
95% CI	(0.61, 1.38)	
ODDS RATIO [2]		
ESTIMATE	0.79	
95% CI	(0.20, 3.08)	
P-VALUE [3]	0.7411	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS ATTACK SEVERITY AT BASELINE PGI-S = SEVERE OR VERY SEVERE		
TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/9 (100.0)	7/10 (70.0)
RISK DIFFERENCE [1]		
ESTIMATE	26.44	
95% CI	(-3.41, 56.28)	
RELATIVE RISK [2]		
ESTIMATE	1.45	
95% CI	(0.93, 2.26)	
ODDS RATIO [2]		
ESTIMATE	3.60*	
95% CI	(0.29, 44.58)*	
P-VALUE [3]	0.1845	

1.7 Anzahl und Anteil der Attacken mit einer Verringerung des GA-NRS um ≥ 4 Punkte

1.7.1 Geschlecht

- GA-NRS=General Anxiety Numeric Rating Scale; CI=Confidence Interval
- Time to first incidence of GA-NRS reduction of ≥ 4 points within 4, 8, 12, 24, and 48 hours of the first IMP administration = Date/time of first ≥ 4 points reduction in GA-NRS score for 2 consecutive time points in a row – Date/time of first IMP administration.
- Attacks that had a baseline GA-NRS score below a cutoff point were excluded from the corresponding analysis.
- Attacks that did not have at least 1 post-baseline assessment within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | SEX = MALE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/13 (38.5)	3/9 (33.3)
RISK DIFFERENCE [1]		
ESTIMATE	9.08	
95% CI	(-31.97, 50.13)	
RELATIVE RISK [2]		
ESTIMATE	1.28	
95% CI	(0.40, 4.09)	
ODDS RATIO [2]		
ESTIMATE	1.50	
95% CI	(0.23, 9.80)	
P-VALUE [3]	0.6861	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | SEX = FEMALE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	10/25 (40.0)	12/25 (48.0)
RISK DIFFERENCE [1]		
ESTIMATE	-8.00	
95% CI	(-37.06, 21.06)	
RELATIVE RISK [2]		
ESTIMATE	1.10	
95% CI	(0.53, 2.28)	
ODDS RATIO [2]		
ESTIMATE	0.78	
95% CI	(0.22, 2.84)	
P-VALUE [3]	0.5698	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | SEX = MALE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	6/13 (46.2)	3/9 (33.3)
RISK DIFFERENCE [1]		
ESTIMATE	15.24	
95% CI	(-26.47, 56.95)	
RELATIVE RISK [2]		
ESTIMATE	1.43	
95% CI	(0.46, 4.48)	
ODDS RATIO [2]		
ESTIMATE	1.90	
95% CI	(0.30, 12.27)	
P-VALUE [3]	0.5091	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | SEX = FEMALE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	11/25 (44.0)	14/25 (56.0)
RISK DIFFERENCE [1]		
ESTIMATE	-12.00	
95% CI	(-39.70, 15.70)	
RELATIVE RISK [2]		
ESTIMATE	0.96	
95% CI	(0.55, 1.68)	
ODDS RATIO [2]		
ESTIMATE	0.62	
95% CI	(0.18, 2.08)	
P-VALUE [3]	0.3915	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | SEX = MALE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	8/13 (61.5)	3/9 (33.3)
RISK DIFFERENCE [1]		
ESTIMATE	27.57	
95% CI	(-14.81, 69.95)	
RELATIVE RISK [2]		
ESTIMATE	1.70	
95% CI	(0.55, 5.21)	
ODDS RATIO [2]		
ESTIMATE	3.00	
95% CI	(0.46, 19.59)	
P-VALUE [3]	0.2385	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | SEX = FEMALE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	13/25 (52.0)	14/25 (56.0)
RISK DIFFERENCE [1]		
ESTIMATE	-4.00	
95% CI	(-31.74, 23.74)	
RELATIVE RISK [2]		
ESTIMATE	1.00	
95% CI	(0.60, 1.67)	
ODDS RATIO [2]		
ESTIMATE	0.84	
95% CI	(0.27, 2.69)	
P-VALUE [3]	0.7778	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | SEX = MALE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/13 (69.2)	4/9 (44.4)
RISK DIFFERENCE [1]		
ESTIMATE	24.83	
95% CI	(-19.72, 69.37)	
RELATIVE RISK [2]		
ESTIMATE	1.29	
95% CI	(0.48, 3.47)	
ODDS RATIO [2]		
ESTIMATE	2.51	
95% CI	(0.37, 16.99)	
P-VALUE [3]	0.2821	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | SEX = FEMALE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	13/25 (52.0)	17/25 (68.0)
RISK DIFFERENCE [1]		
ESTIMATE	-16.00	
95% CI	(-42.35, 10.35)	
RELATIVE RISK [2]		
ESTIMATE	0.84	
95% CI	(0.55, 1.30)	
ODDS RATIO [2]		
ESTIMATE	0.50	
95% CI	(0.15, 1.64)	
P-VALUE [3]	0.2449	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | SEX = MALE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	10/13 (76.9)	4/9 (44.4)
RISK DIFFERENCE [1]		
ESTIMATE	35.96	
95% CI	(-4.31, 76.23)	
RELATIVE RISK [2]		
ESTIMATE	1.52	
95% CI	(0.68, 3.42)	
ODDS RATIO [2]		
ESTIMATE	4.76	
95% CI	(0.65, 34.92)	
P-VALUE [3]	0.1106	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS SEX = FEMALE		
TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	13/25 (52.0)	18/25 (72.0)
RISK DIFFERENCE [1]		
ESTIMATE	-20.00	
95% CI	(-46.26, 6.26)	
RELATIVE RISK [2]		
ESTIMATE	0.81	
95% CI	(0.53, 1.24)	
ODDS RATIO [2]		
ESTIMATE	0.42	
95% CI	(0.12, 1.41)	
P-VALUE [3]	0.1454	

1.7.2 Alter

- GA-NRS=General Anxiety Numeric Rating Scale; CI=Confidence Interval
- Time to first incidence of GA-NRS reduction of ≥ 4 points within 4, 8, 12, 24, and 48 hours of the first IMP administration = Date/time of first ≥ 4 points reduction in GA-NRS score for 2 consecutive time points in a row – Date/time of first IMP administration.
- Attacks that had a baseline GA-NRS score below a cutoff point were excluded from the corresponding analysis.
- Attacks that did not have at least 1 post-baseline assessment within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | AGE GROUP = <18 YEARS

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	1/3 (33.3)	3/5 (60.0)
RISK DIFFERENCE [1]		
ESTIMATE	-14.29	
95% CI	(-82.87, 54.30)	
RELATIVE RISK [2]		
ESTIMATE	1.34	
95% CI	(0.62, 2.88)	
ODDS RATIO [2]		
ESTIMATE	0.60*	
95% CI	(0.04, 8.73)*	
P-VALUE [3]	0.7055	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | AGE GROUP = >=18 YEARS

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	14/35 (40.0)	12/29 (41.4)
RISK DIFFERENCE [1]		
ESTIMATE	-0.75	
95% CI	(-25.96, 24.46)	
RELATIVE RISK [2]		
ESTIMATE	1.00	
95% CI	(0.53, 1.90)	
ODDS RATIO [2]		
ESTIMATE	0.95	
95% CI	(0.33, 2.72)	
P-VALUE [3]	0.9517	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | AGE GROUP = <18 YEARS

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	1/3 (33.3)	3/5 (60.0)
RISK DIFFERENCE [1]		
ESTIMATE	-14.29	
95% CI	(-82.87, 54.30)	
RELATIVE RISK [2]		
ESTIMATE	1.34	
95% CI	(0.62, 2.88)	
ODDS RATIO [2]		
ESTIMATE	0.60*	
95% CI	(0.04, 8.73)*	
P-VALUE [3]	0.7055	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | AGE GROUP = >=18 YEARS

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	16/35 (45.7)	14/29 (48.3)
RISK DIFFERENCE [1]		
ESTIMATE	-1.84	
95% CI	(-26.59, 22.91)	
RELATIVE RISK [2]		
ESTIMATE	1.00	
95% CI	(0.59, 1.69)	
ODDS RATIO [2]		
ESTIMATE	0.92	
95% CI	(0.34, 2.54)	
P-VALUE [3]	0.8839	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | AGE GROUP = <18 YEARS

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	1/3 (33.3)	3/5 (60.0)
RISK DIFFERENCE [1]		
ESTIMATE	-14.29	
95% CI	(-82.87, 54.30)	
RELATIVE RISK [2]		
ESTIMATE	1.34	
95% CI	(0.62, 2.88)	
ODDS RATIO [2]		
ESTIMATE	0.60*	
95% CI	(0.04, 8.73)*	
P-VALUE [3]	0.7055	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | AGE GROUP = >=18 YEARS

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	20/35 (57.1)	14/29 (48.3)
RISK DIFFERENCE [1]		
ESTIMATE	9.09	
95% CI	(-15.47, 33.65)	
RELATIVE RISK [2]		
ESTIMATE	1.19	
95% CI	(0.74, 1.91)	
ODDS RATIO [2]		
ESTIMATE	1.44	
95% CI	(0.53, 3.89)	
P-VALUE [3]	0.4753	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | AGE GROUP = <18 YEARS

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	2/3 (66.7)	3/5 (60.0)
RISK DIFFERENCE [1]		
ESTIMATE	14.29	
95% CI	(-50.95, 79.52)	
RELATIVE RISK [2]		
ESTIMATE	1.42	
95% CI	(0.67, 2.97)	
ODDS RATIO [2]		
ESTIMATE	1.36*	
95% CI	(0.09, 20.65)*	
P-VALUE [3]	0.7290	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | AGE GROUP = >=18 YEARS

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	20/35 (57.1)	18/29 (62.1)
RISK DIFFERENCE [1]		
ESTIMATE	-4.33	
95% CI	(-28.28, 19.62)	
RELATIVE RISK [2]		
ESTIMATE	0.93	
95% CI	(0.63, 1.38)	
ODDS RATIO [2]		
ESTIMATE	0.83	
95% CI	(0.30, 2.30)	
P-VALUE [3]	0.7279	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | AGE GROUP = <18 YEARS

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	2/3 (66.7)	3/5 (60.0)
RISK DIFFERENCE [1]		
ESTIMATE	14.29	
95% CI	(-50.95, 79.52)	
RELATIVE RISK [2]		
ESTIMATE	1.42	
95% CI	(0.67, 2.97)	
ODDS RATIO [2]		
ESTIMATE	1.36*	
95% CI	(0.09, 20.65)*	
P-VALUE [3]	0.7290	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS AGE GROUP = >=18 YEARS		
TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	21/35 (60.0)	19/29 (65.5)
RISK DIFFERENCE [1]		
ESTIMATE	-4.87	
95% CI	(-28.46, 18.71)	
RELATIVE RISK [2]		
ESTIMATE	0.94	
95% CI	(0.65, 1.36)	
ODDS RATIO [2]		
ESTIMATE	0.81	
95% CI	(0.29, 2.28)	
P-VALUE [3]	0.6906	

1.7.3 Region (1)

- GA-NRS=General Anxiety Numeric Rating Scale; CI=Confidence Interval
- Time to first incidence of GA-NRS reduction of ≥ 4 points within 4, 8, 12, 24, and 48 hours of the first IMP administration = Date/time of first ≥ 4 points reduction in GA-NRS score for 2 consecutive time points in a row – Date/time of first IMP administration.
- Attacks that had a baseline GA-NRS score below a cutoff point were excluded from the corresponding analysis.
- Attacks that did not have at least 1 post-baseline assessment within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | REGION 1 = US

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	3/11 (27.3)	2/7 (28.6)
RISK DIFFERENCE [1]		
ESTIMATE	-1.00	
95% CI	(-46.36, 44.36)	
RELATIVE RISK [2]		
ESTIMATE	0.96	
95% CI	(0.21, 4.37)	
ODDS RATIO [2]		
ESTIMATE	0.95	
95% CI	(0.11, 8.31)	
P-VALUE [3]	0.9669	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | REGION 1 = ROW

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	12/27 (44.4)	13/27 (48.1)
RISK DIFFERENCE [1]		
ESTIMATE	-3.70	
95% CI	(-31.12, 23.71)	
RELATIVE RISK [2]		
ESTIMATE	1.11	
95% CI	(0.60, 2.06)	
ODDS RATIO [2]		
ESTIMATE	0.86	
95% CI	(0.26, 2.83)	
P-VALUE [3]	0.7839	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | REGION 1 = US

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	3/11 (27.3)	4/7 (57.1)
RISK DIFFERENCE [1]		
ESTIMATE	-23.00	
95% CI	(-70.76, 24.76)	
RELATIVE RISK [2]		
ESTIMATE	0.55	
95% CI	(0.15, 2.02)	
ODDS RATIO [2]		
ESTIMATE	0.37	
95% CI	(0.04, 3.21)	
P-VALUE [3]	0.3619	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | REGION 1 = ROW

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	14/27 (51.9)	13/27 (48.1)
RISK DIFFERENCE [1]		
ESTIMATE	3.70	
95% CI	(-23.58, 30.99)	
RELATIVE RISK [2]		
ESTIMATE	1.14	
95% CI	(0.65, 2.01)	
ODDS RATIO [2]		
ESTIMATE	1.13	
95% CI	(0.37, 3.48)	
P-VALUE [3]	0.7871	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | REGION 1 = US

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/11 (45.5)	4/7 (57.1)
RISK DIFFERENCE [1]		
ESTIMATE	-9.00	
95% CI	(-60.25, 42.25)	
RELATIVE RISK [2]		
ESTIMATE	0.80	
95% CI	(0.24, 2.71)	
ODDS RATIO [2]		
ESTIMATE	0.72	
95% CI	(0.09, 5.97)	
P-VALUE [3]	0.7364	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | REGION 1 = ROW

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	16/27 (59.3)	13/27 (48.1)
RISK DIFFERENCE [1]		
ESTIMATE	11.11	
95% CI	(-15.76, 37.98)	
RELATIVE RISK [2]		
ESTIMATE	1.24	
95% CI	(0.74, 2.08)	
ODDS RATIO [2]		
ESTIMATE	1.53	
95% CI	(0.50, 4.61)	
P-VALUE [3]	0.4201	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | REGION 1 = US

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/11 (45.5)	5/7 (71.4)
RISK DIFFERENCE [1]		
ESTIMATE	-20.00	
95% CI	(-71.88, 31.88)	
RELATIVE RISK [2]		
ESTIMATE	0.66	
95% CI	(0.20, 2.16)	
ODDS RATIO [2]		
ESTIMATE	0.55*	
95% CI	(0.06, 4.92)*	
P-VALUE [3]	0.4366	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | REGION 1 = ROW

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	17/27 (63.0)	16/27 (59.3)
RISK DIFFERENCE [1]		
ESTIMATE	3.70	
95% CI	(-22.33, 29.74)	
RELATIVE RISK [2]		
ESTIMATE	1.09	
95% CI	(0.71, 1.66)	
ODDS RATIO [2]		
ESTIMATE	1.16	
95% CI	(0.38, 3.54)	
P-VALUE [3]	0.7830	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | REGION 1 = US

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/11 (45.5)	5/7 (71.4)
RISK DIFFERENCE [1]		
ESTIMATE	-20.00	
95% CI	(-71.88, 31.88)	
RELATIVE RISK [2]		
ESTIMATE	0.66	
95% CI	(0.20, 2.16)	
ODDS RATIO [2]		
ESTIMATE	0.55*	
95% CI	(0.06, 4.92)*	
P-VALUE [3]	0.4366	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS REGION 1 = ROW		
TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	18/27 (66.7)	17/27 (63.0)
RISK DIFFERENCE [1]		
ESTIMATE	3.70	
95% CI	(-22.09, 29.50)	
RELATIVE RISK [2]		
ESTIMATE	1.10	
95% CI	(0.74, 1.64)	
ODDS RATIO [2]		
ESTIMATE	1.14	
95% CI	(0.35, 3.65)	
P-VALUE [3]	0.7783	

1.7.4 Region (2)

- GA-NRS=General Anxiety Numeric Rating Scale; CI=Confidence Interval
- Time to first incidence of GA-NRS reduction of ≥ 4 points within 4, 8, 12, 24, and 48 hours of the first IMP administration = Date/time of first ≥ 4 points reduction in GA-NRS score for 2 consecutive time points in a row – Date/time of first IMP administration.
- Attacks that had a baseline GA-NRS score below a cutoff point were excluded from the corresponding analysis.
- Attacks that did not have at least 1 post-baseline assessment within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | REGION 2 = NORTH AMERICA

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	3/11 (27.3)	2/7 (28.6)
RISK DIFFERENCE [1]		
ESTIMATE	-1.00	
95% CI	(-46.36, 44.36)	
RELATIVE RISK [2]		
ESTIMATE	0.96	
95% CI	(0.21, 4.37)	
ODDS RATIO [2]		
ESTIMATE	0.95	
95% CI	(0.11, 8.31)	
P-VALUE [3]	0.9669	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | REGION 2 = EUROPE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	10/22 (45.5)	12/24 (50.0)
RISK DIFFERENCE [1]		
ESTIMATE	-6.02	
95% CI	(-36.20, 24.17)	
RELATIVE RISK [2]		
ESTIMATE	1.11	
95% CI	(0.54, 2.25)	
ODDS RATIO [2]		
ESTIMATE	0.84	
95% CI	(0.23, 3.09)	
P-VALUE [3]	0.6865	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | REGION 2 = ROW

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	2/5 (40.0)	1/3 (33.3)
RISK DIFFERENCE [1]		
ESTIMATE	36.36	
95% CI	(-2.38, 75.10)	
RELATIVE RISK [2]		
ESTIMATE	1.80	
95% CI	(0.52, 6.22)	
ODDS RATIO [2]		
ESTIMATE	1.92*	
95% CI	(0.13, 28.66)*	
P-VALUE [3]	0.3883	

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	3/11 (27.3)	4/7 (57.1)
RISK DIFFERENCE [1]		
ESTIMATE	-23.00	
95% CI	(-70.76, 24.76)	
RELATIVE RISK [2]		
ESTIMATE	0.55	
95% CI	(0.15, 2.02)	
ODDS RATIO [2]		
ESTIMATE	0.37	
95% CI	(0.04, 3.21)	
P-VALUE [3]	0.3619	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | REGION 2 = EUROPE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	12/22 (54.5)	12/24 (50.0)
RISK DIFFERENCE [1]		
ESTIMATE	3.81	
95% CI	(-26.08, 33.70)	
RELATIVE RISK [2]		
ESTIMATE	1.12	
95% CI	(0.60, 2.07)	
ODDS RATIO [2]		
ESTIMATE	1.14	
95% CI	(0.34, 3.85)	
P-VALUE [3]	0.8003	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | REGION 2 = ROW

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	2/5 (40.0)	1/3 (33.3)
RISK DIFFERENCE [1]		
ESTIMATE	36.36	
95% CI	(-2.38, 75.10)	
RELATIVE RISK [2]		
ESTIMATE	1.80	
95% CI	(0.52, 6.22)	
ODDS RATIO [2]		
ESTIMATE	1.92*	
95% CI	(0.13, 28.66)*	
P-VALUE [3]	0.3883	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | REGION 2 = NORTH AMERICA

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/11 (45.5)	4/7 (57.1)
RISK DIFFERENCE [1]		
ESTIMATE	-9.00	
95% CI	(-60.25, 42.25)	
RELATIVE RISK [2]		
ESTIMATE	0.80	
95% CI	(0.24, 2.71)	
ODDS RATIO [2]		
ESTIMATE	0.72	
95% CI	(0.09, 5.97)	
P-VALUE [3]	0.7364	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | REGION 2 = EUROPE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	14/22 (63.6)	12/24 (50.0)
RISK DIFFERENCE [1]		
ESTIMATE	13.64	
95% CI	(-15.34, 42.61)	
RELATIVE RISK [2]		
ESTIMATE	1.25	
95% CI	(0.73, 2.14)	
ODDS RATIO [2]		
ESTIMATE	1.71	
95% CI	(0.51, 5.68)	
P-VALUE [3]	0.3637	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | REGION 2 = ROW

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	2/5 (40.0)	1/3 (33.3)
RISK DIFFERENCE [1]		
ESTIMATE	36.36	
95% CI	(-2.38, 75.10)	
RELATIVE RISK [2]		
ESTIMATE	1.80	
95% CI	(0.52, 6.22)	
ODDS RATIO [2]		
ESTIMATE	1.92*	
95% CI	(0.13, 28.66)*	
P-VALUE [3]	0.3883	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | REGION 2 = NORTH AMERICA

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/11 (45.5)	5/7 (71.4)
RISK DIFFERENCE [1]		
ESTIMATE	-20.00	
95% CI	(-71.88, 31.88)	
RELATIVE RISK [2]		
ESTIMATE	0.66	
95% CI	(0.20, 2.16)	
ODDS RATIO [2]		
ESTIMATE	0.55*	
95% CI	(0.06, 4.92)*	
P-VALUE [3]	0.4366	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | REGION 2 = EUROPE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	15/22 (68.2)	15/24 (62.5)
RISK DIFFERENCE [1]		
ESTIMATE	5.50	
95% CI	(-22.17, 33.17)	
RELATIVE RISK [2]		
ESTIMATE	1.09	
95% CI	(0.71, 1.67)	
ODDS RATIO [2]		
ESTIMATE	1.27	
95% CI	(0.37, 4.33)	
P-VALUE [3]	0.7030	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | REGION 2 = ROW

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	2/5 (40.0)	1/3 (33.3)
RISK DIFFERENCE [1]		
ESTIMATE	36.36	
95% CI	(-2.38, 75.10)	
RELATIVE RISK [2]		
ESTIMATE	1.80	
95% CI	(0.52, 6.22)	
ODDS RATIO [2]		
ESTIMATE	1.92*	
95% CI	(0.13, 28.66)*	
P-VALUE [3]	0.3883	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | REGION 2 = NORTH AMERICA

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/11 (45.5)	5/7 (71.4)
RISK DIFFERENCE [1]		
ESTIMATE	-20.00	
95% CI	(-71.88, 31.88)	
RELATIVE RISK [2]		
ESTIMATE	0.66	
95% CI	(0.20, 2.16)	
ODDS RATIO [2]		
ESTIMATE	0.55*	
95% CI	(0.06, 4.92)*	
P-VALUE [3]	0.4366	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | REGION 2 = EUROPE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	16/22 (72.7)	16/24 (66.7)
RISK DIFFERENCE [1]		
ESTIMATE	5.82	
95% CI	(-21.26, 32.89)	
RELATIVE RISK [2]		
ESTIMATE	1.09	
95% CI	(0.73, 1.63)	
ODDS RATIO [2]		
ESTIMATE	1.29	
95% CI	(0.36, 4.67)	
P-VALUE [3]	0.6762	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS REGION 2 = ROW		
TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	2/5 (40.0)	1/3 (33.3)
RISK DIFFERENCE [1]		
ESTIMATE	36.36	
95% CI	(-2.38, 75.10)	
RELATIVE RISK [2]		
ESTIMATE	1.80	
95% CI	(0.52, 6.22)	
ODDS RATIO [2]		
ESTIMATE	1.92*	
95% CI	(0.13, 28.66)*	
P-VALUE [3]	0.3883	

1.7.5 Prophylaxe-Status (Variante 1)

- GA-NRS=General Anxiety Numeric Rating Scale; CI=Confidence Interval
- Time to first incidence of GA-NRS reduction of ≥ 4 points within 4, 8, 12, 24, and 48 hours of the first IMP administration = Date/time of first ≥ 4 points reduction in GA-NRS score for 2 consecutive time points in a row – Date/time of first IMP administration.
- Attacks that had a baseline GA-NRS score below a cutoff point were excluded from the corresponding analysis.
- Attacks that did not have at least 1 post-baseline assessment within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	3/10 (30.0)	2/7 (28.6)
RISK DIFFERENCE [1]		
ESTIMATE	8.24	
95% CI	(-39.68, 56.16)	
RELATIVE RISK [2]		
ESTIMATE	1.34	
95% CI	(0.30, 5.91)	
ODDS RATIO [2]		
ESTIMATE	1.35	
95% CI	(0.14, 13.46)	
P-VALUE [3]	0.7351	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
DEMAND

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	12/28 (42.9)	13/27 (48.1)
RISK DIFFERENCE [1]		
ESTIMATE	-5.05	
95% CI	(-31.98, 21.89)	
RELATIVE RISK [2]		
ESTIMATE	0.99	
95% CI	(0.54, 1.82)	
ODDS RATIO [2]		
ESTIMATE	0.82	
95% CI	(0.27, 2.51)	
P-VALUE [3]	0.7090	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	3/10 (30.0)	4/7 (57.1)
RISK DIFFERENCE [1]		
ESTIMATE	-14.23	
95% CI	(-58.94, 30.48)	
RELATIVE RISK [2]		
ESTIMATE	0.80	
95% CI	(0.32, 1.99)	
ODDS RATIO [2]		
ESTIMATE	0.47	
95% CI	(0.05, 4.64)	
P-VALUE [3]	0.5392	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
DEMAND

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	14/28 (50.0)	13/27 (48.1)
RISK DIFFERENCE [1]		
ESTIMATE	2.00	
95% CI	(-24.87, 28.86)	
RELATIVE RISK [2]		
ESTIMATE	1.07	
95% CI	(0.61, 1.86)	
ODDS RATIO [2]		
ESTIMATE	1.07	
95% CI	(0.36, 3.17)	
P-VALUE [3]	0.8841	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	6/10 (60.0)	4/7 (57.1)
RISK DIFFERENCE [1]		
ESTIMATE	9.36	
95% CI	(-38.89, 57.62)	
RELATIVE RISK [2]		
ESTIMATE	1.04	
95% CI	(0.45, 2.45)	
ODDS RATIO [2]		
ESTIMATE	1.48	
95% CI	(0.17, 12.69)	
P-VALUE [3]	0.7198	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
DEMAND

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	15/28 (53.6)	13/27 (48.1)
RISK DIFFERENCE [1]		
ESTIMATE	5.52	
95% CI	(-21.22, 32.25)	
RELATIVE RISK [2]		
ESTIMATE	1.12	
95% CI	(0.66, 1.91)	
ODDS RATIO [2]		
ESTIMATE	1.23	
95% CI	(0.42, 3.63)	
P-VALUE [3]	0.6875	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	6/10 (60.0)	6/7 (85.7)
RISK DIFFERENCE [1]		
ESTIMATE	-20.22	
95% CI	(-63.34, 22.89)	
RELATIVE RISK [2]		
ESTIMATE	0.73	
95% CI	(0.39, 1.38)	
ODDS RATIO [2]		
ESTIMATE	0.41*	
95% CI	(0.04, 3.71)*	
P-VALUE [3]	0.3899	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
DEMAND

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	16/28 (57.1)	15/27 (55.6)
RISK DIFFERENCE [1]		
ESTIMATE	1.76	
95% CI	(-24.34, 27.87)	
RELATIVE RISK [2]		
ESTIMATE	1.04	
95% CI	(0.66, 1.65)	
ODDS RATIO [2]		
ESTIMATE	1.07	
95% CI	(0.37, 3.15)	
P-VALUE [3]	0.8966	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	6/10 (60.0)	6/7 (85.7)
RISK DIFFERENCE [1]		
ESTIMATE	-20.22	
95% CI	(-63.34, 22.89)	
RELATIVE RISK [2]		
ESTIMATE	0.73	
95% CI	(0.39, 1.38)	
ODDS RATIO [2]		
ESTIMATE	0.41*	
95% CI	(0.04, 3.71)*	
P-VALUE [3]	0.3899	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS PROPHYLACTIC TREATMENT STATUS 1 = ON DEMAND		
TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	17/28 (60.7)	16/27 (59.3)
RISK DIFFERENCE [1]		
ESTIMATE	1.64	
95% CI	(-24.30, 27.59)	
RELATIVE RISK [2]		
ESTIMATE	1.06	
95% CI	(0.69, 1.63)	
ODDS RATIO [2]		
ESTIMATE	1.07	
95% CI	(0.35, 3.21)	
P-VALUE [3]	0.9021	

1.7.6 Prophylaxe-Status (Variante 2)

- GA-NRS=General Anxiety Numeric Rating Scale; CI=Confidence Interval
- Time to first incidence of GA-NRS reduction of ≥ 4 points within 4, 8, 12, 24, and 48 hours of the first IMP administration = Date/time of first ≥ 4 points reduction in GA-NRS score for 2 consecutive time points in a row – Date/time of first IMP administration.
- Attacks that had a baseline GA-NRS score below a cutoff point were excluded from the corresponding analysis.
- Attacks that did not have at least 1 post-baseline assessment within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	2/7 (28.6)	2/5 (40.0)
RISK DIFFERENCE [1]		
ESTIMATE	-3.41	
95% CI	(-77.29, 70.47)	
RELATIVE RISK [2]		
ESTIMATE	1.03	
95% CI	(0.22, 4.85)	
ODDS RATIO [2]		
ESTIMATE	0.93*	
95% CI	(0.07, 12.81)*	
P-VALUE [3]	0.9153	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	1/3 (33.3)	0/2 (0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
DEMAND

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	12/28 (42.9)	13/27 (48.1)
RISK DIFFERENCE [1]		
ESTIMATE	-5.05	
95% CI	(-31.98, 21.89)	
RELATIVE RISK [2]		
ESTIMATE	0.99	
95% CI	(0.54, 1.82)	
ODDS RATIO [2]		
ESTIMATE	0.82	
95% CI	(0.27, 2.51)	
P-VALUE [3]	0.7090	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	2/7 (28.6)	4/5 (80.0)
RISK DIFFERENCE [1]		
ESTIMATE	-37.50	
95% CI	(-97.86, 22.86)	
RELATIVE RISK [2]		
ESTIMATE	0.72	
95% CI	(0.29, 1.81)	
ODDS RATIO [2]		
ESTIMATE	0.23*	
95% CI	(0.02, 3.19)*	
P-VALUE [3]	0.2110	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	1/3 (33.3)	0/2 (0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
DEMAND

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	14/28 (50.0)	13/27 (48.1)
RISK DIFFERENCE [1]		
ESTIMATE	2.00	
95% CI	(-24.87, 28.86)	
RELATIVE RISK [2]		
ESTIMATE	1.07	
95% CI	(0.61, 1.86)	
ODDS RATIO [2]		
ESTIMATE	1.07	
95% CI	(0.36, 3.17)	
P-VALUE [3]	0.8841	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/7 (57.1)	4/5 (80.0)
RISK DIFFERENCE [1]		
ESTIMATE	-21.59	
95% CI	(-75.80, 32.62)	
RELATIVE RISK [2]		
ESTIMATE	0.67	
95% CI	(0.33, 1.33)	
ODDS RATIO [2]		
ESTIMATE	0.49*	
95% CI	(0.04, 5.64)*	
P-VALUE [3]	0.5001	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	2/3 (66.7)	0/2 (0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
DEMAND

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	15/28 (53.6)	13/27 (48.1)
RISK DIFFERENCE [1]		
ESTIMATE	5.52	
95% CI	(-21.22, 32.25)	
RELATIVE RISK [2]		
ESTIMATE	1.12	
95% CI	(0.66, 1.91)	
ODDS RATIO [2]		
ESTIMATE	1.23	
95% CI	(0.42, 3.63)	
P-VALUE [3]	0.6875	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/7 (57.1)	5/5 (100.0)
RISK DIFFERENCE [1]		
ESTIMATE	-38.64	
95% CI	(-80.12, 2.85)	
RELATIVE RISK [2]		
ESTIMATE	0.59	
95% CI	(0.32, 1.10)	
ODDS RATIO [2]		
ESTIMATE	0.25*	
95% CI	(0.02, 3.15)*	
P-VALUE [3]	0.1630	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	2/3 (66.7)	1/2 (50.0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
DEMAND

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	16/28 (57.1)	15/27 (55.6)
RISK DIFFERENCE [1]		
ESTIMATE	1.76	
95% CI	(-24.34, 27.87)	
RELATIVE RISK [2]		
ESTIMATE	1.04	
95% CI	(0.66, 1.65)	
ODDS RATIO [2]		
ESTIMATE	1.07	
95% CI	(0.37, 3.15)	
P-VALUE [3]	0.8966	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/7 (57.1)	5/5 (100.0)
RISK DIFFERENCE [1]		
ESTIMATE	-38.64	
95% CI	(-80.12, 2.85)	
RELATIVE RISK [2]		
ESTIMATE	0.59	
95% CI	(0.32, 1.10)	
ODDS RATIO [2]		
ESTIMATE	0.25*	
95% CI	(0.02, 3.15)*	
P-VALUE [3]	0.1630	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	2/3 (66.7)	1/2 (50.0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	17/28 (60.7)	16/27 (59.3)
RISK DIFFERENCE [1]		
ESTIMATE	1.64	
95% CI	(-24.30, 27.59)	
RELATIVE RISK [2]		
ESTIMATE	1.06	
95% CI	(0.69, 1.63)	
ODDS RATIO [2]		
ESTIMATE	1.07	
95% CI	(0.35, 3.21)	
P-VALUE [3]	0.9021	

1.8 Anzahl und Anteil der Attacken mit einer Verringerung des GA-NRS um ≥ 5 Punkte

1.8.1 Geschlecht

- GA-NRS=General Anxiety Numeric Rating Scale; CI=Confidence Interval
- Time to first incidence of GA-NRS reduction of ≥ 5 points within 4, 8, 12, 24, and 48 hours of the first IMP administration = Date/time of first ≥ 5 points reduction in GA-NRS score for 2 consecutive time points in a row – Date/time of first IMP administration.
- Attacks that had a baseline GA-NRS score below a cutoff point were excluded from the corresponding analysis.
- Attacks that did not have at least 1 post-baseline assessment within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | SEX = MALE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/11 (36.4)	2/7 (28.6)
RISK DIFFERENCE [1]		
ESTIMATE	17.65	
95% CI	(-24.71, 60.01)	
RELATIVE RISK [2]		
ESTIMATE	1.37	
95% CI	(0.38, 4.93)	
ODDS RATIO [2]		
ESTIMATE	1.76*	
95% CI	(0.22, 14.18)*	
P-VALUE [3]	0.4870	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | SEX = FEMALE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	10/21 (47.6)	9/20 (45.0)
RISK DIFFERENCE [1]		
ESTIMATE	3.08	
95% CI	(-28.97, 35.14)	
RELATIVE RISK [2]		
ESTIMATE	1.23	
95% CI	(0.59, 2.55)	
ODDS RATIO [2]		
ESTIMATE	1.16	
95% CI	(0.30, 4.48)	
P-VALUE [3]	0.8445	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | SEX = MALE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/11 (45.5)	2/7 (28.6)
RISK DIFFERENCE [1]		
ESTIMATE	23.53	
95% CI	(-20.77, 67.83)	
RELATIVE RISK [2]		
ESTIMATE	1.48	
95% CI	(0.41, 5.31)	
ODDS RATIO [2]		
ESTIMATE	2.17*	
95% CI	(0.27, 17.33)*	
P-VALUE [3]	0.3755	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | SEX = FEMALE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	11/21 (52.4)	9/20 (45.0)
RISK DIFFERENCE [1]		
ESTIMATE	7.71	
95% CI	(-24.04, 39.47)	
RELATIVE RISK [2]		
ESTIMATE	1.22	
95% CI	(0.62, 2.42)	
ODDS RATIO [2]		
ESTIMATE	1.34	
95% CI	(0.36, 4.93)	
P-VALUE [3]	0.6275	

 Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

 WITHIN 12 HOURS | SEX = MALE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	6/11 (54.5)	2/7 (28.6)
RISK DIFFERENCE [1]		
ESTIMATE	29.41	
95% CI	(-16.58, 75.40)	
RELATIVE RISK [2]		
ESTIMATE	1.58	
95% CI	(0.44, 5.63)	
ODDS RATIO [2]		
ESTIMATE	2.63*	
95% CI	(0.33, 21.04)*	
P-VALUE [3]	0.2781	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | SEX = FEMALE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	12/21 (57.1)	11/20 (55.0)
RISK DIFFERENCE [1]		
ESTIMATE	2.31	
95% CI	(-29.10, 33.73)	
RELATIVE RISK [2]		
ESTIMATE	1.07	
95% CI	(0.61, 1.89)	
ODDS RATIO [2]		
ESTIMATE	1.10	
95% CI	(0.30, 3.99)	
P-VALUE [3]	0.8841	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | SEX = MALE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	6/11 (54.5)	3/7 (42.9)
RISK DIFFERENCE [1]		
ESTIMATE	17.65	
95% CI	(-31.74, 67.04)	
RELATIVE RISK [2]		
ESTIMATE	1.07	
95% CI	(0.36, 3.21)	
ODDS RATIO [2]		
ESTIMATE	1.60*	
95% CI	(0.20, 12.80)*	
P-VALUE [3]	0.5152	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | SEX = FEMALE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	12/21 (57.1)	14/20 (70.0)
RISK DIFFERENCE [1]		
ESTIMATE	-12.60	
95% CI	(-42.48, 17.29)	
RELATIVE RISK [2]		
ESTIMATE	0.88	
95% CI	(0.55, 1.42)	
ODDS RATIO [2]		
ESTIMATE	0.60	
95% CI	(0.16, 2.32)	
P-VALUE [3]	0.4118	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | SEX = MALE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	8/11 (72.7)	3/7 (42.9)
RISK DIFFERENCE [1]		
ESTIMATE	38.24	
95% CI	(-5.66, 82.13)	
RELATIVE RISK [2]		
ESTIMATE	1.43	
95% CI	(0.60, 3.37)	
ODDS RATIO [2]		
ESTIMATE	4.10*	
95% CI	(0.46, 36.82)*	
P-VALUE [3]	0.1461	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS SEX = FEMALE		
TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	12/21 (57.1)	15/20 (75.0)
RISK DIFFERENCE [1]		
ESTIMATE	-17.74	
95% CI	(-47.43, 11.96)	
RELATIVE RISK [2]		
ESTIMATE	0.83	
95% CI	(0.52, 1.32)	
ODDS RATIO [2]		
ESTIMATE	0.54	
95% CI	(0.13, 2.31)	
P-VALUE [3]	0.2425	

1.8.2 Alter

- GA-NRS=General Anxiety Numeric Rating Scale; CI=Confidence Interval
- Time to first incidence of GA-NRS reduction of ≥ 5 points within 4, 8, 12, 24, and 48 hours of the first IMP administration = Date/time of first ≥ 5 points reduction in GA-NRS score for 2 consecutive time points in a row – Date/time of first IMP administration.
- Attacks that had a baseline GA-NRS score below a cutoff point were excluded from the corresponding analysis.
- Attacks that did not have at least 1 post-baseline assessment within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | AGE GROUP = <18 YEARS

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)

NUMBER OF ATTACKS n/N (%)	1/3 (33.3)	2/3 (66.7)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | AGE GROUP = >=18 YEARS

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	13/29 (44.8)	9/24 (37.5)
RISK DIFFERENCE [1]		
ESTIMATE	8.15	
95% CI	(-19.20, 35.50)	
RELATIVE RISK [2]		
ESTIMATE	1.22	
95% CI	(0.62, 2.43)	
ODDS RATIO [2]		
ESTIMATE	1.37	
95% CI	(0.43, 4.32)	
P-VALUE [3]	0.5534	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | AGE GROUP = <18 YEARS

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)

NUMBER OF ATTACKS n/N (%)	1/3 (33.3)	2/3 (66.7)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | AGE GROUP = >=18 YEARS

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	15/29 (51.7)	9/24 (37.5)
RISK DIFFERENCE [1]		
ESTIMATE	14.62	
95% CI	(-12.49, 41.73)	
RELATIVE RISK [2]		
ESTIMATE	1.35	
95% CI	(0.71, 2.55)	
ODDS RATIO [2]		
ESTIMATE	1.77	
95% CI	(0.57, 5.45)	
P-VALUE [3]	0.2965	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | AGE GROUP = <18 YEARS

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)

NUMBER OF ATTACKS n/N (%)	1/3 (33.3)	2/3 (66.7)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | AGE GROUP = >=18 YEARS

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	17/29 (58.6)	11/24 (45.8)
RISK DIFFERENCE [1]		
ESTIMATE	12.71	
95% CI	(-14.38, 39.81)	
RELATIVE RISK [2]		
ESTIMATE	1.25	
95% CI	(0.73, 2.12)	
ODDS RATIO [2]		
ESTIMATE	1.66	
95% CI	(0.55, 5.00)	
P-VALUE [3]	0.3660	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | AGE GROUP = <18 YEARS

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)

NUMBER OF ATTACKS n/N (%)	1/3 (33.3)	2/3 (66.7)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | AGE GROUP = >=18 YEARS

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	17/29 (58.6)	15/24 (62.5)
RISK DIFFERENCE [1]		
ESTIMATE	-3.58	
95% CI	(-30.03, 22.87)	
RELATIVE RISK [2]		
ESTIMATE	0.95	
95% CI	(0.61, 1.46)	
ODDS RATIO [2]		
ESTIMATE	0.86	
95% CI	(0.28, 2.63)	
P-VALUE [3]	0.7947	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | AGE GROUP = <18 YEARS

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)

NUMBER OF ATTACKS n/N (%)	2/3 (66.7)	2/3 (66.7)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS AGE GROUP = >=18 YEARS		
TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	18/29 (62.1)	16/24 (66.7)
RISK DIFFERENCE [1]		
ESTIMATE	-4.31	
95% CI	(-30.41, 21.79)	
RELATIVE RISK [2]		
ESTIMATE	0.94	
95% CI	(0.63, 1.41)	
ODDS RATIO [2]		
ESTIMATE	0.84	
95% CI	(0.26, 2.67)	
P-VALUE [3]	0.7494	

1.8.3 Region (Variante 1)

- GA-NRS=General Anxiety Numeric Rating Scale; CI=Confidence Interval
- Time to first incidence of GA-NRS reduction of ≥ 5 points within 4, 8, 12, 24, and 48 hours of the first IMP administration = Date/time of first ≥ 5 points reduction in GA-NRS score for 2 consecutive time points in a row – Date/time of first IMP administration.
- Attacks that had a baseline GA-NRS score below a cutoff point were excluded from the corresponding analysis.
- Attacks that did not have at least 1 post-baseline assessment within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | REGION 1 = US

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	3/10 (30.0)	1/4 (25.0)
RISK DIFFERENCE [1]		
ESTIMATE	8.33	
95% CI	(-59.83, 76.50)	
RELATIVE RISK [2]		
ESTIMATE	1.33	
95% CI	(0.13, 13.74)	
ODDS RATIO [2]		
ESTIMATE	1.50	
95% CI	(0.06, 40.63)	
P-VALUE [3]	0.8231	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | REGION 1 = ROW

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	11/22 (50.0)	10/23 (43.5)
RISK DIFFERENCE [1]		
ESTIMATE	5.93	
95% CI	(-23.49, 35.35)	
RELATIVE RISK [2]		
ESTIMATE	1.32	
95% CI	(0.68, 2.54)	
ODDS RATIO [2]		
ESTIMATE	1.31	
95% CI	(0.36, 4.79)	
P-VALUE [3]	0.6873	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | REGION 1 = US

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	3/10 (30.0)	1/4 (25.0)
RISK DIFFERENCE [1]		
ESTIMATE	8.33	
95% CI	(-59.83, 76.50)	
RELATIVE RISK [2]		
ESTIMATE	1.33	
95% CI	(0.13, 13.74)	
ODDS RATIO [2]		
ESTIMATE	1.50	
95% CI	(0.06, 40.63)	
P-VALUE [3]	0.8231	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | REGION 1 = ROW

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	13/22 (59.1)	10/23 (43.5)
RISK DIFFERENCE [1]		
ESTIMATE	15.25	
95% CI	(-13.84, 44.35)	
RELATIVE RISK [2]		
ESTIMATE	1.39	
95% CI	(0.77, 2.53)	
ODDS RATIO [2]		
ESTIMATE	1.83	
95% CI	(0.54, 6.25)	
P-VALUE [3]	0.3115	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | REGION 1 = US

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/10 (40.0)	2/4 (50.0)
RISK DIFFERENCE [1]		
ESTIMATE	-16.67	
95% CI	(-89.10, 55.77)	
RELATIVE RISK [2]		
ESTIMATE	0.67	
95% CI	(0.10, 4.35)	
ODDS RATIO [2]		
ESTIMATE	0.50	
95% CI	(0.02, 11.09)	
P-VALUE [3]	0.6831	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | REGION 1 = ROW

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	14/22 (63.6)	11/23 (47.8)
RISK DIFFERENCE [1]		
ESTIMATE	15.68	
95% CI	(-13.48, 44.84)	
RELATIVE RISK [2]		
ESTIMATE	1.33	
95% CI	(0.76, 2.31)	
ODDS RATIO [2]		
ESTIMATE	1.85	
95% CI	(0.55, 6.28)	
P-VALUE [3]	0.3003	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | REGION 1 = US

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/10 (40.0)	3/4 (75.0)
RISK DIFFERENCE [1]		
ESTIMATE	-41.67	
95% CI	(-100.00, 26.50)	
RELATIVE RISK [2]		
ESTIMATE	0.44	
95% CI	(0.08, 2.43)	
ODDS RATIO [2]		
ESTIMATE	0.17	
95% CI	(0.01, 4.51)	
P-VALUE [3]	0.3074	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | REGION 1 = ROW

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	14/22 (63.6)	14/23 (60.9)
RISK DIFFERENCE [1]		
ESTIMATE	2.54	
95% CI	(-26.01, 31.10)	
RELATIVE RISK [2]		
ESTIMATE	1.07	
95% CI	(0.68, 1.70)	
ODDS RATIO [2]		
ESTIMATE	1.11	
95% CI	(0.32, 3.80)	
P-VALUE [3]	0.8629	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | REGION 1 = US

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/10 (40.0)	3/4 (75.0)
RISK DIFFERENCE [1]		
ESTIMATE	-41.67	
95% CI	(-100.00, 26.50)	
RELATIVE RISK [2]		
ESTIMATE	0.44	
95% CI	(0.08, 2.43)	
ODDS RATIO [2]		
ESTIMATE	0.17	
95% CI	(0.01, 4.51)	
P-VALUE [3]	0.3074	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS REGION 1 = ROW		
TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	16/22 (72.7)	15/23 (65.2)
RISK DIFFERENCE [1]		
ESTIMATE	7.42	
95% CI	(-20.10, 34.94)	
RELATIVE RISK [2]		
ESTIMATE	1.13	
95% CI	(0.75, 1.70)	
ODDS RATIO [2]		
ESTIMATE	1.37	
95% CI	(0.37, 5.13)	
P-VALUE [3]	0.5993	

1.8.4 Region (Variante 2)

- GA-NRS=General Anxiety Numeric Rating Scale; CI=Confidence Interval
- Time to first incidence of GA-NRS reduction of ≥ 5 points within 4, 8, 12, 24, and 48 hours of the first IMP administration = Date/time of first ≥ 5 points reduction in GA-NRS score for 2 consecutive time points in a row – Date/time of first IMP administration.
- Attacks that had a baseline GA-NRS score below a cutoff point were excluded from the corresponding analysis.
- Attacks that did not have at least 1 post-baseline assessment within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | REGION 2 = NORTH AMERICA

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	3/10 (30.0)	1/4 (25.0)
RISK DIFFERENCE [1]		
ESTIMATE	8.33	
95% CI	(-59.83, 76.50)	
RELATIVE RISK [2]		
ESTIMATE	1.33	
95% CI	(0.13, 13.74)	
ODDS RATIO [2]		
ESTIMATE	1.50	
95% CI	(0.06, 40.63)	
P-VALUE [3]	0.8231	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | REGION 2 = EUROPE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	10/18 (55.6)	9/20 (45.0)
RISK DIFFERENCE [1]		
ESTIMATE	8.89	
95% CI	(-23.76, 41.54)	
RELATIVE RISK [2]		
ESTIMATE	1.30	
95% CI	(0.64, 2.65)	
ODDS RATIO [2]		
ESTIMATE	1.44	
95% CI	(0.37, 5.67)	
P-VALUE [3]	0.5918	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | REGION 2 = ROW

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	1/4 (25.0)	1/3 (33.3)
RISK DIFFERENCE [1]		
ESTIMATE	23.53	
95% CI	(-13.14, 60.20)	
RELATIVE RISK [2]		
ESTIMATE	2.00	
95% CI	(0.50, 8.00)	
ODDS RATIO [2]		
ESTIMATE	3.00*	
95% CI	(0.06, 151.19)*	
P-VALUE [3]	0.4795	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | REGION 2 = NORTH AMERICA

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	3/10 (30.0)	1/4 (25.0)
RISK DIFFERENCE [1]		
ESTIMATE	8.33	
95% CI	(-59.83, 76.50)	
RELATIVE RISK [2]		
ESTIMATE	1.33	
95% CI	(0.13, 13.74)	
ODDS RATIO [2]		
ESTIMATE	1.50	
95% CI	(0.06, 40.63)	
P-VALUE [3]	0.8231	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | REGION 2 = EUROPE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	12/18 (66.7)	9/20 (45.0)
RISK DIFFERENCE [1]		
ESTIMATE	21.47	
95% CI	(-9.89, 52.82)	
RELATIVE RISK [2]		
ESTIMATE	1.46	
95% CI	(0.79, 2.69)	
ODDS RATIO [2]		
ESTIMATE	2.38	
95% CI	(0.63, 9.05)	
P-VALUE [3]	0.1982	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | REGION 2 = ROW

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	1/4 (25.0)	1/3 (33.3)
RISK DIFFERENCE [1]		
ESTIMATE	23.53	
95% CI	(-13.14, 60.20)	
RELATIVE RISK [2]		
ESTIMATE	2.00	
95% CI	(0.50, 8.00)	
ODDS RATIO [2]		
ESTIMATE	3.00*	
95% CI	(0.06, 151.19)*	
P-VALUE [3]	0.4795	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | REGION 2 = NORTH AMERICA

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/10 (40.0)	2/4 (50.0)
RISK DIFFERENCE [1]		
ESTIMATE	-16.67	
95% CI	(-89.10, 55.77)	
RELATIVE RISK [2]		
ESTIMATE	0.67	
95% CI	(0.10, 4.35)	
ODDS RATIO [2]		
ESTIMATE	0.50	
95% CI	(0.02, 11.09)	
P-VALUE [3]	0.6831	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | REGION 2 = EUROPE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	13/18 (72.2)	10/20 (50.0)
RISK DIFFERENCE [1]		
ESTIMATE	23.35	
95% CI	(-6.94, 53.65)	
RELATIVE RISK [2]		
ESTIMATE	1.41	
95% CI	(0.83, 2.41)	
ODDS RATIO [2]		
ESTIMATE	2.72	
95% CI	(0.69, 10.75)	
P-VALUE [3]	0.1537	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | REGION 2 = ROW

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	1/4 (25.0)	1/3 (33.3)
RISK DIFFERENCE [1]		
ESTIMATE	23.53	
95% CI	(-13.14, 60.20)	
RELATIVE RISK [2]		
ESTIMATE	2.00	
95% CI	(0.50, 8.00)	
ODDS RATIO [2]		
ESTIMATE	3.00*	
95% CI	(0.06, 151.19)*	
P-VALUE [3]	0.4795	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | REGION 2 = NORTH AMERICA

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/10 (40.0)	3/4 (75.0)
RISK DIFFERENCE [1]		
ESTIMATE	-41.67	
95% CI	(-100.00, 26.50)	
RELATIVE RISK [2]		
ESTIMATE	0.44	
95% CI	(0.08, 2.43)	
ODDS RATIO [2]		
ESTIMATE	0.17	
95% CI	(0.01, 4.51)	
P-VALUE [3]	0.3074	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | REGION 2 = EUROPE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	13/18 (72.2)	13/20 (65.0)
RISK DIFFERENCE [1]		
ESTIMATE	7.75	
95% CI	(-21.92, 37.43)	
RELATIVE RISK [2]		
ESTIMATE	1.11	
95% CI	(0.72, 1.72)	
ODDS RATIO [2]		
ESTIMATE	1.43	
95% CI	(0.36, 5.74)	
P-VALUE [3]	0.6192	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | REGION 2 = ROW

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	1/4 (25.0)	1/3 (33.3)
RISK DIFFERENCE [1]		
ESTIMATE	23.53	
95% CI	(-13.14, 60.20)	
RELATIVE RISK [2]		
ESTIMATE	2.00	
95% CI	(0.50, 8.00)	
ODDS RATIO [2]		
ESTIMATE	3.00*	
95% CI	(0.06, 151.19)*	
P-VALUE [3]	0.4795	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | REGION 2 = NORTH AMERICA

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/10 (40.0)	3/4 (75.0)
RISK DIFFERENCE [1]		
ESTIMATE	-41.67	
95% CI	(-100.00, 26.50)	
RELATIVE RISK [2]		
ESTIMATE	0.44	
95% CI	(0.08, 2.43)	
ODDS RATIO [2]		
ESTIMATE	0.17	
95% CI	(0.01, 4.51)	
P-VALUE [3]	0.3074	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | REGION 2 = EUROPE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	15/18 (83.3)	14/20 (70.0)
RISK DIFFERENCE [1]		
ESTIMATE	14.73	
95% CI	(-11.79, 41.25)	
RELATIVE RISK [2]		
ESTIMATE	1.17	
95% CI	(0.83, 1.65)	
ODDS RATIO [2]		
ESTIMATE	2.33	
95% CI	(0.48, 11.36)	
P-VALUE [3]	0.2986	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS REGION 2 = ROW		
TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	1/4 (25.0)	1/3 (33.3)
RISK DIFFERENCE [1]		
ESTIMATE	23.53	
95% CI	(-13.14, 60.20)	
RELATIVE RISK [2]		
ESTIMATE	2.00	
95% CI	(0.50, 8.00)	
ODDS RATIO [2]		
ESTIMATE	3.00*	
95% CI	(0.06, 151.19)*	
P-VALUE [3]	0.4795	

1.8.5 Prophylaxe-Status (Variante 1)

- GA-NRS=General Anxiety Numeric Rating Scale; CI=Confidence Interval
- Time to first incidence of GA-NRS reduction of ≥ 5 points within 4, 8, 12, 24, and 48 hours of the first IMP administration = Date/time of first ≥ 5 points reduction in GA-NRS score for 2 consecutive time points in a row – Date/time of first IMP administration.
- Attacks that had a baseline GA-NRS score below a cutoff point were excluded from the corresponding analysis.
- Attacks that did not have at least 1 post-baseline assessment within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	3/8 (37.5)	2/6 (33.3)
RISK DIFFERENCE [1]		
ESTIMATE	9.09	
95% CI	(-47.95, 66.14)	
RELATIVE RISK [2]		
ESTIMATE	1.22	
95% CI	(0.29, 5.12)	
ODDS RATIO [2]		
ESTIMATE	1.37	
95% CI	(0.12, 15.23)	
P-VALUE [3]	0.7538	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
DEMAND

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	11/24 (45.8)	9/21 (42.9)
RISK DIFFERENCE [1]		
ESTIMATE	4.49	
95% CI	(-24.85, 33.82)	
RELATIVE RISK [2]		
ESTIMATE	1.18	
95% CI	(0.61, 2.28)	
ODDS RATIO [2]		
ESTIMATE	1.20	
95% CI	(0.35, 4.13)	
P-VALUE [3]	0.7632	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	3/8 (37.5)	2/6 (33.3)
RISK DIFFERENCE [1]		
ESTIMATE	9.09	
95% CI	(-47.95, 66.14)	
RELATIVE RISK [2]		
ESTIMATE	1.22	
95% CI	(0.29, 5.12)	
ODDS RATIO [2]		
ESTIMATE	1.37	
95% CI	(0.12, 15.23)	
P-VALUE [3]	0.7538	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
DEMAND

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	13/24 (54.2)	9/21 (42.9)
RISK DIFFERENCE [1]		
ESTIMATE	12.18	
95% CI	(-17.02, 41.38)	
RELATIVE RISK [2]		
ESTIMATE	1.30	
95% CI	(0.71, 2.41)	
ODDS RATIO [2]		
ESTIMATE	1.63	
95% CI	(0.49, 5.42)	
P-VALUE [3]	0.4236	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/8 (50.0)	3/6 (50.0)
RISK DIFFERENCE [1]		
ESTIMATE	4.55	
95% CI	(-50.54, 59.63)	
RELATIVE RISK [2]		
ESTIMATE	1.12	
95% CI	(0.40, 3.12)	
ODDS RATIO [2]		
ESTIMATE	1.20	
95% CI	(0.12, 11.44)	
P-VALUE [3]	0.8802	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
DEMAND

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	14/24 (58.3)	10/21 (47.6)
RISK DIFFERENCE [1]		
ESTIMATE	10.90	
95% CI	(-18.56, 40.36)	
RELATIVE RISK [2]		
ESTIMATE	1.21	
95% CI	(0.69, 2.13)	
ODDS RATIO [2]		
ESTIMATE	1.54	
95% CI	(0.46, 5.10)	
P-VALUE [3]	0.4759	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/8 (50.0)	4/6 (66.7)
RISK DIFFERENCE [1]		
ESTIMATE	-9.09	
95% CI	(-61.59, 43.41)	
RELATIVE RISK [2]		
ESTIMATE	0.87	
95% CI	(0.37, 2.04)	
ODDS RATIO [2]		
ESTIMATE	0.67	
95% CI	(0.06, 6.87)	
P-VALUE [3]	0.7518	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
DEMAND

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	14/24 (58.3)	13/21 (61.9)
RISK DIFFERENCE [1]		
ESTIMATE	-3.21	
95% CI	(-32.08, 25.67)	
RELATIVE RISK [2]		
ESTIMATE	0.96	
95% CI	(0.60, 1.54)	
ODDS RATIO [2]		
ESTIMATE	0.88	
95% CI	(0.26, 2.97)	
P-VALUE [3]	0.8307	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/8 (50.0)	5/6 (83.3)
RISK DIFFERENCE [1]		
ESTIMATE	-31.82	
95% CI	(-80.28, 16.64)	
RELATIVE RISK [2]		
ESTIMATE	0.62	
95% CI	(0.30, 1.28)	
ODDS RATIO [2]		
ESTIMATE	0.32*	
95% CI	(0.03, 3.45)*	
P-VALUE [3]	0.2684	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS PROPHYLACTIC TREATMENT STATUS 1 = ON DEMAND		
TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	16/24 (66.7)	13/21 (61.9)
RISK DIFFERENCE [1]		
ESTIMATE	5.13	
95% CI	(-23.12, 33.38)	
RELATIVE RISK [2]		
ESTIMATE	1.09	
95% CI	(0.70, 1.69)	
ODDS RATIO [2]		
ESTIMATE	1.25	
95% CI	(0.36, 4.36)	
P-VALUE [3]	0.7263	

1.8.6 Prophylaxe-Status (Variante 2)

- GA-NRS=General Anxiety Numeric Rating Scale; CI=Confidence Interval
- Time to first incidence of GA-NRS reduction of ≥ 5 points within 4, 8, 12, 24, and 48 hours of the first IMP administration = Date/time of first ≥ 5 points reduction in GA-NRS score for 2 consecutive time points in a row – Date/time of first IMP administration.
- Attacks that had a baseline GA-NRS score below a cutoff point were excluded from the corresponding analysis.
- Attacks that did not have at least 1 post-baseline assessment within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	2/6 (33.3)	2/5 (40.0)
RISK DIFFERENCE [1]		
ESTIMATE	-1.45	
95% CI	(-75.83, 72.93)	
RELATIVE RISK [2]		
ESTIMATE	1.09	
95% CI	(0.23, 5.09)	
ODDS RATIO [2]		
ESTIMATE	1.03*	
95% CI	(0.07, 14.34)*	
P-VALUE [3]	0.9654	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	1/2 (50.0)	0/1 (0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
DEMAND

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	11/24 (45.8)	9/21 (42.9)
RISK DIFFERENCE [1]		
ESTIMATE	4.49	
95% CI	(-24.85, 33.82)	
RELATIVE RISK [2]		
ESTIMATE	1.18	
95% CI	(0.61, 2.28)	
ODDS RATIO [2]		
ESTIMATE	1.20	
95% CI	(0.35, 4.13)	
P-VALUE [3]	0.7632	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	2/6 (33.3)	2/5 (40.0)
RISK DIFFERENCE [1]		
ESTIMATE	-1.45	
95% CI	(-75.83, 72.93)	
RELATIVE RISK [2]		
ESTIMATE	1.09	
95% CI	(0.23, 5.09)	
ODDS RATIO [2]		
ESTIMATE	1.03*	
95% CI	(0.07, 14.34)*	
P-VALUE [3]	0.9654	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	1/2 (50.0)	0/1 (0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
DEMAND

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	13/24 (54.2)	9/21 (42.9)
RISK DIFFERENCE [1]		
ESTIMATE	12.18	
95% CI	(-17.02, 41.38)	
RELATIVE RISK [2]		
ESTIMATE	1.30	
95% CI	(0.71, 2.41)	
ODDS RATIO [2]		
ESTIMATE	1.63	
95% CI	(0.49, 5.42)	
P-VALUE [3]	0.4236	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	3/6 (50.0)	3/5 (60.0)
RISK DIFFERENCE [1]		
ESTIMATE	-8.70	
95% CI	(-73.58, 56.19)	
RELATIVE RISK [2]		
ESTIMATE	0.78	
95% CI	(0.29, 2.11)	
ODDS RATIO [2]		
ESTIMATE	0.79*	
95% CI	(0.07, 8.74)*	
P-VALUE [3]	0.8033	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	1/2 (50.0)	0/1 (0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
DEMAND

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	14/24 (58.3)	10/21 (47.6)
RISK DIFFERENCE [1]		
ESTIMATE	10.90	
95% CI	(-18.56, 40.36)	
RELATIVE RISK [2]		
ESTIMATE	1.21	
95% CI	(0.69, 2.13)	
ODDS RATIO [2]		
ESTIMATE	1.54	
95% CI	(0.46, 5.10)	
P-VALUE [3]	0.4759	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	3/6 (50.0)	4/5 (80.0)
RISK DIFFERENCE [1]		
ESTIMATE	-26.09	
95% CI	(-83.46, 31.28)	
RELATIVE RISK [2]		
ESTIMATE	0.68	
95% CI	(0.29, 1.57)	
ODDS RATIO [2]		
ESTIMATE	0.40*	
95% CI	(0.03, 4.77)*	
P-VALUE [3]	0.4281	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	1/2 (50.0)	0/1 (0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
DEMAND

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	14/24 (58.3)	13/21 (61.9)
RISK DIFFERENCE [1]		
ESTIMATE	-3.21	
95% CI	(-32.08, 25.67)	
RELATIVE RISK [2]		
ESTIMATE	0.96	
95% CI	(0.60, 1.54)	
ODDS RATIO [2]		
ESTIMATE	0.88	
95% CI	(0.26, 2.97)	
P-VALUE [3]	0.8307	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	3/6 (50.0)	4/5 (80.0)
RISK DIFFERENCE [1]		
ESTIMATE	-26.09	
95% CI	(-83.46, 31.28)	
RELATIVE RISK [2]		
ESTIMATE	0.68	
95% CI	(0.29, 1.57)	
ODDS RATIO [2]		
ESTIMATE	0.40*	
95% CI	(0.03, 4.77)*	
P-VALUE [3]	0.4281	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	1/2 (50.0)	1/1 (100.0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	16/24 (66.7)	13/21 (61.9)
RISK DIFFERENCE [1]		
ESTIMATE	5.13	
95% CI	(-23.12, 33.38)	
RELATIVE RISK [2]		
ESTIMATE	1.09	
95% CI	(0.70, 1.69)	
ODDS RATIO [2]		
ESTIMATE	1.25	
95% CI	(0.36, 4.36)	
P-VALUE [3]	0.7263	

1.8.7 Attacken-Schwere (PGIS) zu Baseline

- GA-NRS=General Anxiety Numeric Rating Scale; CI=Confidence Interval
- Time to first incidence of GA-NRS reduction of ≥ 5 points within 4, 8, 12, 24, and 48 hours of the first IMP administration = Date/time of first ≥ 5 points reduction in GA-NRS score for 2 consecutive time points in a row – Date/time of first IMP administration.
- Attacks that had a baseline GA-NRS score below a cutoff point were excluded from the corresponding analysis.
- Attacks that did not have at least 1 post-baseline assessment within the analyzed period were excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline GA-NRS (not at all anxious, mildly anxious, moderately anxious, extremely anxious).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
NONE OR MILD

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	2/11 (18.2)	5/10 (50.0)
RISK DIFFERENCE [1]		
ESTIMATE	-31.91	
95% CI	(-73.84, 10.01)	
RELATIVE RISK [2]		
ESTIMATE	0.63	
95% CI	(0.12, 3.16)	
ODDS RATIO [2]		
ESTIMATE	0.37*	
95% CI	(0.04, 3.22)*	
P-VALUE [3]	0.1412	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
MODERATE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	7/15 (46.7)	3/9 (33.3)
RISK DIFFERENCE [1]		
ESTIMATE	20.10	
95% CI	(-14.14, 54.34)	
RELATIVE RISK [2]		
ESTIMATE	1.24	
95% CI	(0.52, 2.96)	
ODDS RATIO [2]		
ESTIMATE	2.16*	
95% CI	(0.31, 15.21)*	
P-VALUE [3]	0.3185	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
SEVERE OR VERY SEVERE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/6 (83.3)	3/8 (37.5)
RISK DIFFERENCE [1]		
ESTIMATE	46.23	
95% CI	(-5.27, 97.73)	
RELATIVE RISK [2]		
ESTIMATE	1.56	
95% CI	(0.64, 3.81)	
ODDS RATIO [2]		
ESTIMATE	3.68*	
95% CI	(0.30, 45.56)*	
P-VALUE [3]	0.1209	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
NONE OR MILD

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	3/11 (27.3)	5/10 (50.0)
RISK DIFFERENCE [1]		
ESTIMATE	-22.34	
95% CI	(-65.07, 20.39)	
RELATIVE RISK [2]		
ESTIMATE	0.59	
95% CI	(0.15, 2.34)	
ODDS RATIO [2]		
ESTIMATE	0.41	
95% CI	(0.06, 3.01)	
P-VALUE [3]	0.3155	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
MODERATE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	8/15 (53.3)	3/9 (33.3)
RISK DIFFERENCE [1]		
ESTIMATE	25.70	
95% CI	(-10.01, 61.41)	
RELATIVE RISK [2]		
ESTIMATE	1.28	
95% CI	(0.54, 3.04)	
ODDS RATIO [2]		
ESTIMATE	2.54*	
95% CI	(0.36, 17.79)*	
P-VALUE [3]	0.2212	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
SEVERE OR VERY SEVERE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/6 (83.3)	3/8 (37.5)
RISK DIFFERENCE [1]		
ESTIMATE	46.23	
95% CI	(-5.27, 97.73)	
RELATIVE RISK [2]		
ESTIMATE	1.56	
95% CI	(0.64, 3.81)	
ODDS RATIO [2]		
ESTIMATE	3.68*	
95% CI	(0.30, 45.56)*	
P-VALUE [3]	0.1209	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
NONE OR MILD

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/11 (36.4)	5/10 (50.0)
RISK DIFFERENCE [1]		
ESTIMATE	-12.77	
95% CI	(-55.50, 29.97)	
RELATIVE RISK [2]		
ESTIMATE	0.70	
95% CI	(0.24, 2.03)	
ODDS RATIO [2]		
ESTIMATE	0.59	
95% CI	(0.09, 3.70)	
P-VALUE [3]	0.5695	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
MODERATE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/15 (60.0)	5/9 (55.6)
RISK DIFFERENCE [1]		
ESTIMATE	8.78	
95% CI	(-31.11, 48.66)	
RELATIVE RISK [2]		
ESTIMATE	0.95	
95% CI	(0.49, 1.85)	
ODDS RATIO [2]		
ESTIMATE	1.45	
95% CI	(0.22, 9.73)	
P-VALUE [3]	0.6769	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
SEVERE OR VERY SEVERE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/6 (83.3)	3/8 (37.5)
RISK DIFFERENCE [1]		
ESTIMATE	46.23	
95% CI	(-5.27, 97.73)	
RELATIVE RISK [2]		
ESTIMATE	1.56	
95% CI	(0.64, 3.81)	
ODDS RATIO [2]		
ESTIMATE	3.68*	
95% CI	(0.30, 45.56)*	
P-VALUE [3]	0.1209	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
NONE OR MILD

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/11 (36.4)	5/10 (50.0)
RISK DIFFERENCE [1]		
ESTIMATE	-12.77	
95% CI	(-55.50, 29.97)	
RELATIVE RISK [2]		
ESTIMATE	0.70	
95% CI	(0.24, 2.03)	
ODDS RATIO [2]		
ESTIMATE	0.59	
95% CI	(0.09, 3.70)	
P-VALUE [3]	0.5695	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
MODERATE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/15 (60.0)	6/9 (66.7)
RISK DIFFERENCE [1]		
ESTIMATE	-3.82	
95% CI	(-43.37, 35.74)	
RELATIVE RISK [2]		
ESTIMATE	0.90	
95% CI	(0.49, 1.66)	
ODDS RATIO [2]		
ESTIMATE	0.85	
95% CI	(0.14, 5.13)	
P-VALUE [3]	0.8562	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
SEVERE OR VERY SEVERE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/6 (83.3)	6/8 (75.0)
RISK DIFFERENCE [1]		
ESTIMATE	12.26	
95% CI	(-30.12, 54.65)	
RELATIVE RISK [2]		
ESTIMATE	1.26	
95% CI	(0.81, 1.96)	
ODDS RATIO [2]		
ESTIMATE	1.46*	
95% CI	(0.12, 18.03)*	
P-VALUE [3]	0.6221	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
NONE OR MILD

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/11 (45.5)	5/10 (50.0)
RISK DIFFERENCE [1]		
ESTIMATE	-4.26	
95% CI	(-49.30, 40.79)	
RELATIVE RISK [2]		
ESTIMATE	0.83	
95% CI	(0.29, 2.35)	
ODDS RATIO [2]		
ESTIMATE	0.82	
95% CI	(0.13, 5.16)	
P-VALUE [3]	0.8529	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
MODERATE

TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	10/15 (66.7)	7/9 (77.8)
RISK DIFFERENCE [1]		
ESTIMATE	-10.81	
95% CI	(-47.53, 25.90)	
RELATIVE RISK [2]		
ESTIMATE	0.86	
95% CI	(0.52, 1.43)	
ODDS RATIO [2]		
ESTIMATE	0.58	
95% CI	(0.09, 3.95)	
P-VALUE [3]	0.5926	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS ATTACK SEVERITY AT BASELINE PGI-S = SEVERE OR VERY SEVERE		
TIME TO FIRST INCIDENCE OF GA-NRS REDUCTION	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/6 (83.3)	6/8 (75.0)
RISK DIFFERENCE [1]		
ESTIMATE	12.26	
95% CI	(-30.12, 54.65)	
RELATIVE RISK [2]		
ESTIMATE	1.26	
95% CI	(0.81, 1.96)	
ODDS RATIO [2]		
ESTIMATE	1.46*	
95% CI	(0.12, 18.03)*	
P-VALUE [3]	0.6221	

1.9 Anzahl und Anteil der Attacken mit einer Verringerung des VAS um mindestens 15 % der Gesamtskala

1.9.1 Geschlecht

- VAS=Visual Analogic Scale; PGI-S=Patient Global Impression of Severity; CI=Confidence Interval
- Composite VAS score is defined as the mean score across all 3 symptom scores.
- Time to at least 15 points decrease (hours) = Date/time of first ≥ 15 points decrease from baseline in composite VAS score for 3 consecutive time points (with possible missing values in between) – Date/time of first IMP administration.
- Attacks that did not have at least 3 post-baseline assessments within the analyzed period will be excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline PGI-S category (none or mild, moderate, and severe or very severe).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline PGI-S category (none or mild, moderate, and severe or very severe).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | SEX = MALE

TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	6/30 (20.0)	3/24 (12.5)
RISK DIFFERENCE [1]		
ESTIMATE	6.36	
95% CI	(-11.12, 23.84)	
RELATIVE RISK [2]		
ESTIMATE	1.36	
95% CI	(0.46, 4.00)	
ODDS RATIO [2]		
ESTIMATE	1.54*	
95% CI	(0.30, 7.91)*	
P-VALUE [3]	0.4903	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | SEX = FEMALE

TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	12/47 (25.5)	10/48 (20.8)
RISK DIFFERENCE [1]		
ESTIMATE	4.52	
95% CI	(-12.47, 21.51)	
RELATIVE RISK [2]		
ESTIMATE	1.20	
95% CI	(0.55, 2.61)	
ODDS RATIO [2]		
ESTIMATE	1.25	
95% CI	(0.45, 3.45)	
P-VALUE [3]	0.6015	

 Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | SEX = MALE

TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/31 (29.0)	3/24 (12.5)
RISK DIFFERENCE [1]		
ESTIMATE	15.25	
95% CI	(-3.57, 34.07)	
RELATIVE RISK [2]		
ESTIMATE	1.75	
95% CI	(0.63, 4.85)	
ODDS RATIO [2]		
ESTIMATE	2.56*	
95% CI	(0.49, 13.35)*	
P-VALUE [3]	0.1284	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | SEX = FEMALE

TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	14/47 (29.8)	13/48 (27.1)
RISK DIFFERENCE [1]		
ESTIMATE	2.52	
95% CI	(-15.46, 20.50)	
RELATIVE RISK [2]		
ESTIMATE	1.14	
95% CI	(0.60, 2.16)	
ODDS RATIO [2]		
ESTIMATE	1.13	
95% CI	(0.45, 2.86)	
P-VALUE [3]	0.7855	

 Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | SEX = MALE

TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	12/31 (38.7)	3/24 (12.5)
RISK DIFFERENCE [1]		
ESTIMATE	24.84	
95% CI	(5.15, 44.54)	
RELATIVE RISK [2]		
ESTIMATE	2.23	
95% CI	(0.85, 5.85)	
ODDS RATIO [2]		
ESTIMATE	4.66*	
95% CI	(0.87, 24.94)*	
P-VALUE [3]	0.0215†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | SEX = FEMALE

TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	19/47 (40.4)	15/49 (30.6)
RISK DIFFERENCE [1]		
ESTIMATE	9.33	
95% CI	(-9.32, 27.99)	
RELATIVE RISK [2]		
ESTIMATE	1.32	
95% CI	(0.78, 2.24)	
ODDS RATIO [2]		
ESTIMATE	1.54	
95% CI	(0.65, 3.64)	
P-VALUE [3]	0.3353	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | SEX = MALE

TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	16/31 (51.6)	9/25 (36.0)
RISK DIFFERENCE [1]		
ESTIMATE	15.34	
95% CI	(-6.78, 37.47)	
RELATIVE RISK [2]		
ESTIMATE	1.48	
95% CI	(0.92, 2.38)	
ODDS RATIO [2]		
ESTIMATE	2.17*	
95% CI	(0.59, 7.95)*	
P-VALUE [3]	0.1831	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | SEX = FEMALE

TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	21/48 (43.8)	20/49 (40.8)
RISK DIFFERENCE [1]		
ESTIMATE	2.14	
95% CI	(-16.98, 21.25)	
RELATIVE RISK [2]		
ESTIMATE	1.04	
95% CI	(0.67, 1.62)	
ODDS RATIO [2]		
ESTIMATE	1.10	
95% CI	(0.48, 2.52)	
P-VALUE [3]	0.8291	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | SEX = MALE

TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	16/31 (51.6)	9/25 (36.0)
RISK DIFFERENCE [1]		
ESTIMATE	15.34	
95% CI	(-6.78, 37.47)	
RELATIVE RISK [2]		
ESTIMATE	1.48	
95% CI	(0.92, 2.38)	
ODDS RATIO [2]		
ESTIMATE	2.17*	
95% CI	(0.59, 7.95)*	
P-VALUE [3]	0.1831	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS SEX = FEMALE		
TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	21/49 (42.9)	20/49 (40.8)
RISK DIFFERENCE [1]		
ESTIMATE	1.52	
95% CI	(-17.43, 20.46)	
RELATIVE RISK [2]		
ESTIMATE	1.03	
95% CI	(0.66, 1.61)	
ODDS RATIO [2]		
ESTIMATE	1.07	
95% CI	(0.47, 2.45)	
P-VALUE [3]	0.8771	

1.9.2 Alter

- VAS=Visual Analogic Scale; PGI-S=Patient Global Impression of Severity; CI=Confidence Interval
- Composite VAS score is defined as the mean score across all 3 symptom scores.
- Time to at least 15 points decrease (hours) = Date/time of first ≥ 15 points decrease from baseline in composite VAS score for 3 consecutive time points (with possible missing values in between) – Date/time of first IMP administration.
- Attacks that did not have at least 3 post-baseline assessments within the analyzed period will be excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline PGI-S category (none or mild, moderate, and severe or very severe).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline PGI-S category (none or mild, moderate, and severe or very severe).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | AGE GROUP = <18 YEARS

**TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT
OF 15 % OF THE SCALE (15 POINTS)**
**300 mg KVD900
(ATTACK=87)**
**Placebo
(ATTACK=84)**

NUMBER OF ATTACKS n/N (%)

1/9 (11.1)

1/8 (12.5)

RISK DIFFERENCE [1]

ESTIMATE

1.39

95% CI

(-46.07, 48.85)

RELATIVE RISK [2]

ESTIMATE

1.11

95% CI

(0.14, 8.78)

ODDS RATIO [2]

ESTIMATE

1.08*

95% CI

(0.08, 13.67)*

P-VALUE [3]

0.9419

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | AGE GROUP = >=18 YEARS

TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	17/68 (25.0)	12/64 (18.8)
RISK DIFFERENCE [1]		
ESTIMATE	5.48	
95% CI	(-8.24, 19.19)	
RELATIVE RISK [2]		
ESTIMATE	1.36	
95% CI	(0.70, 2.65)	
ODDS RATIO [2]		
ESTIMATE	1.40	
95% CI	(0.57, 3.45)	
P-VALUE [3]	0.4337	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | AGE GROUP = <18 YEARS

TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	1/9 (11.1)	1/8 (12.5)
RISK DIFFERENCE [1]		
ESTIMATE	1.39	
95% CI	(-46.07, 48.85)	
RELATIVE RISK [2]		
ESTIMATE	1.11	
95% CI	(0.14, 8.78)	
ODDS RATIO [2]		
ESTIMATE	1.08*	
95% CI	(0.08, 13.67)*	
P-VALUE [3]	0.9419	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | AGE GROUP = >=18 YEARS

TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	22/69 (31.9)	15/64 (23.4)
RISK DIFFERENCE [1]		
ESTIMATE	7.44	
95% CI	(-7.21, 22.10)	
RELATIVE RISK [2]		
ESTIMATE	1.40	
95% CI	(0.80, 2.44)	
ODDS RATIO [2]		
ESTIMATE	1.50	
95% CI	(0.66, 3.42)	
P-VALUE [3]	0.3213	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | AGE GROUP = <18 YEARS

TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	1/9 (11.1)	1/9 (11.1)
RISK DIFFERENCE [1]		
ESTIMATE	2.99	
95% CI	(-38.43, 44.41)	
RELATIVE RISK [2]		
ESTIMATE	1.26	
95% CI	(0.16, 10.08)	
ODDS RATIO [2]		
ESTIMATE	1.24*	
95% CI	(0.10, 15.33)*	
P-VALUE [3]	0.8638	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | AGE GROUP = >=18 YEARS

TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	30/69 (43.5)	17/64 (26.6)
RISK DIFFERENCE [1]		
ESTIMATE	15.69	
95% CI	(0.36, 31.02)	
RELATIVE RISK [2]		
ESTIMATE	1.62	
95% CI	(1.02, 2.58)	
ODDS RATIO [2]		
ESTIMATE	2.15	
95% CI	(0.99, 4.66)	
P-VALUE [3]	0.0493†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | AGE GROUP = <18 YEARS

TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	3/10 (30.0)	3/9 (33.3)
RISK DIFFERENCE [1]		
ESTIMATE	-2.34	
95% CI	(-43.43, 38.75)	
RELATIVE RISK [2]		
ESTIMATE	1.20	
95% CI	(0.35, 4.08)	
ODDS RATIO [2]		
ESTIMATE	0.90*	
95% CI	(0.09, 8.61)*	
P-VALUE [3]	0.9096	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | AGE GROUP = >=18 YEARS

TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	34/69 (49.3)	26/65 (40.0)
RISK DIFFERENCE [1]		
ESTIMATE	7.96	
95% CI	(-8.06, 23.99)	
RELATIVE RISK [2]		
ESTIMATE	1.21	
95% CI	(0.85, 1.72)	
ODDS RATIO [2]		
ESTIMATE	1.42	
95% CI	(0.69, 2.94)	
P-VALUE [3]	0.3351	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | AGE GROUP = <18 YEARS

TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	3/10 (30.0)	3/9 (33.3)
RISK DIFFERENCE [1]		
ESTIMATE	-2.34	
95% CI	(-43.43, 38.75)	
RELATIVE RISK [2]		
ESTIMATE	1.20	
95% CI	(0.35, 4.08)	
ODDS RATIO [2]		
ESTIMATE	0.90*	
95% CI	(0.09, 8.61)*	
P-VALUE [3]	0.9096	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS AGE GROUP = >=18 YEARS		
TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	34/70 (48.6)	26/65 (40.0)
RISK DIFFERENCE [1]		
ESTIMATE	7.49	
95% CI	(-8.43, 23.41)	
RELATIVE RISK [2]		
ESTIMATE	1.20	
95% CI	(0.84, 1.71)	
ODDS RATIO [2]		
ESTIMATE	1.40	
95% CI	(0.68, 2.88)	
P-VALUE [3]	0.3611	

1.9.3 Region (Variante 1)

- VAS=Visual Analogic Scale; PGI-S=Patient Global Impression of Severity; CI=Confidence Interval
- Composite VAS score is defined as the mean score across all 3 symptom scores.
- Time to at least 15 points decrease (hours) = Date/time of first ≥ 15 points decrease from baseline in composite VAS score for 3 consecutive time points (with possible missing values in between) – Date/time of first IMP administration.
- Attacks that did not have at least 3 post-baseline assessments within the analyzed period will be excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline PGI-S category (none or mild, moderate, and severe or very severe).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline PGI-S category (none or mild, moderate, and severe or very severe).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | REGION 1 = US

TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/23 (21.7)	3/20 (15.0)
RISK DIFFERENCE [1]		
ESTIMATE	3.47	
95% CI	(-19.98, 26.92)	
RELATIVE RISK [2]		
ESTIMATE	1.35	
95% CI	(0.33, 5.54)	
ODDS RATIO [2]		
ESTIMATE	1.38*	
95% CI	(0.24, 7.82)*	
P-VALUE [3]	0.7770	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | REGION 1 = ROW

TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	13/54 (24.1)	10/52 (19.2)
RISK DIFFERENCE [1]		
ESTIMATE	5.27	
95% CI	(-10.03, 20.57)	
RELATIVE RISK [2]		
ESTIMATE	1.34	
95% CI	(0.65, 2.76)	
ODDS RATIO [2]		
ESTIMATE	1.40	
95% CI	(0.52, 3.73)	
P-VALUE [3]	0.5014	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | REGION 1 = US

TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/23 (21.7)	6/20 (30.0)
RISK DIFFERENCE [1]		
ESTIMATE	-12.92	
95% CI	(-37.70, 11.87)	
RELATIVE RISK [2]		
ESTIMATE	0.82	
95% CI	(0.30, 2.28)	
ODDS RATIO [2]		
ESTIMATE	0.58*	
95% CI	(0.12, 2.86)*	
P-VALUE [3]	0.3350	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | REGION 1 = ROW

TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	18/55 (32.7)	10/52 (19.2)
RISK DIFFERENCE [1]		
ESTIMATE	14.18	
95% CI	(-1.83, 30.19)	
RELATIVE RISK [2]		
ESTIMATE	1.79	
95% CI	(0.93, 3.46)	
ODDS RATIO [2]		
ESTIMATE	2.21	
95% CI	(0.87, 5.63)	
P-VALUE [3]	0.0874	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | REGION 1 = US

TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	8/23 (34.8)	7/20 (35.0)
RISK DIFFERENCE [1]		
ESTIMATE	-6.76	
95% CI	(-33.98, 20.47)	
RELATIVE RISK [2]		
ESTIMATE	0.90	
95% CI	(0.40, 2.00)	
ODDS RATIO [2]		
ESTIMATE	0.73	
95% CI	(0.17, 3.02)	
P-VALUE [3]	0.6430	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | REGION 1 = ROW

TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	23/55 (41.8)	11/53 (20.8)
RISK DIFFERENCE [1]		
ESTIMATE	21.48	
95% CI	(5.15, 37.81)	
RELATIVE RISK [2]		
ESTIMATE	2.00	
95% CI	(1.13, 3.56)	
ODDS RATIO [2]		
ESTIMATE	3.08	
95% CI	(1.25, 7.63)	
P-VALUE [3]	0.0129†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | REGION 1 = US

TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/23 (39.1)	9/20 (45.0)
RISK DIFFERENCE [1]		
ESTIMATE	-9.55	
95% CI	(-39.11, 20.01)	
RELATIVE RISK [2]		
ESTIMATE	0.85	
95% CI	(0.41, 1.77)	
ODDS RATIO [2]		
ESTIMATE	0.67	
95% CI	(0.18, 2.46)	
P-VALUE [3]	0.5438	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | REGION 1 = ROW

TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	28/56 (50.0)	20/54 (37.0)
RISK DIFFERENCE [1]		
ESTIMATE	14.50	
95% CI	(-2.19, 31.18)	
RELATIVE RISK [2]		
ESTIMATE	1.38	
95% CI	(0.94, 2.02)	
ODDS RATIO [2]		
ESTIMATE	2.04	
95% CI	(0.87, 4.79)	
P-VALUE [3]	0.0984	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | REGION 1 = US

TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/23 (39.1)	9/20 (45.0)
RISK DIFFERENCE [1]		
ESTIMATE	-9.55	
95% CI	(-39.11, 20.01)	
RELATIVE RISK [2]		
ESTIMATE	0.85	
95% CI	(0.41, 1.77)	
ODDS RATIO [2]		
ESTIMATE	0.67	
95% CI	(0.18, 2.46)	
P-VALUE [3]	0.5438	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS REGION 1 = ROW		
TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	28/57 (49.1)	20/54 (37.0)
RISK DIFFERENCE [1]		
ESTIMATE	14.06	
95% CI	(-2.50, 30.61)	
RELATIVE RISK [2]		
ESTIMATE	1.37	
95% CI	(0.94, 2.02)	
ODDS RATIO [2]		
ESTIMATE	2.00	
95% CI	(0.85, 4.71)	
P-VALUE [3]	0.1064	

1.9.4 Region (Variante 2)

- VAS=Visual Analogic Scale; PGI-S=Patient Global Impression of Severity; CI=Confidence Interval
- Composite VAS score is defined as the mean score across all 3 symptom scores.
- Time to at least 15 points decrease (hours) = Date/time of first ≥ 15 points decrease from baseline in composite VAS score for 3 consecutive time points (with possible missing values in between) – Date/time of first IMP administration.
- Attacks that did not have at least 3 post-baseline assessments within the analyzed period will be excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline PGI-S category (none or mild, moderate, and severe or very severe).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline PGI-S category (none or mild, moderate, and severe or very severe).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | REGION 2 = NORTH AMERICA

TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	5/23 (21.7)	3/20 (15.0)
RISK DIFFERENCE [1]		
ESTIMATE	3.47	
95% CI	(-19.98, 26.92)	
RELATIVE RISK [2]		
ESTIMATE	1.35	
95% CI	(0.33, 5.54)	
ODDS RATIO [2]		
ESTIMATE	1.38*	
95% CI	(0.24, 7.82)*	
P-VALUE [3]	0.7770	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | REGION 2 = EUROPE

TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	12/40 (30.0)	8/41 (19.5)
RISK DIFFERENCE [1]		
ESTIMATE	9.18	
95% CI	(-8.60, 26.97)	
RELATIVE RISK [2]		
ESTIMATE	1.48	
95% CI	(0.70, 3.12)	
ODDS RATIO [2]		
ESTIMATE	1.74	
95% CI	(0.59, 5.17)	
P-VALUE [3]	0.3201	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | REGION 2 = ROW

TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	1/14 (7.1)	2/11 (18.2)
RISK DIFFERENCE [1]		
ESTIMATE	-16.82	
95% CI	(-45.30, 11.66)	
RELATIVE RISK [2]		
ESTIMATE	0.27	
95% CI	(0.03, 2.42)	
ODDS RATIO [2]		
ESTIMATE	0.20*	
95% CI	(0.01, 2.88)*	
P-VALUE [3]	0.2241	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | REGION 2 = NORTH AMERICA

**TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT
OF 15 % OF THE SCALE (15 POINTS)**
**300 mg KVD900
(ATTACK=87)**
**Placebo
(ATTACK=84)**

NUMBER OF ATTACKS n/N (%)

5/23 (21.7)

6/20 (30.0)

RISK DIFFERENCE [1]

ESTIMATE

-12.92

95% CI

(-37.70, 11.87)

RELATIVE RISK [2]

ESTIMATE

0.82

95% CI

(0.30, 2.28)

ODDS RATIO [2]

ESTIMATE

0.58*

95% CI

(0.12, 2.86)*

P-VALUE [3]

0.3350

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | REGION 2 = EUROPE

TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	15/40 (37.5)	8/41 (19.5)
RISK DIFFERENCE [1]		
ESTIMATE	16.67	
95% CI	(-1.61, 34.94)	
RELATIVE RISK [2]		
ESTIMATE	1.86	
95% CI	(0.92, 3.75)	
ODDS RATIO [2]		
ESTIMATE	2.61	
95% CI	(0.89, 7.64)	
P-VALUE [3]	0.0803	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | REGION 2 = ROW

TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	3/15 (20.0)	2/11 (18.2)
RISK DIFFERENCE [1]		
ESTIMATE	-1.50	
95% CI	(-35.12, 32.12)	
RELATIVE RISK [2]		
ESTIMATE	0.83	
95% CI	(0.19, 3.60)	
ODDS RATIO [2]		
ESTIMATE	0.85*	
95% CI	(0.13, 5.76)*	
P-VALUE [3]	0.9294	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

 WITHIN 12 HOURS | REGION 2 = NORTH AMERICA

TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	8/23 (34.8)	7/20 (35.0)
RISK DIFFERENCE [1]		
ESTIMATE	-6.76	
95% CI	(-33.98, 20.47)	
RELATIVE RISK [2]		
ESTIMATE	0.90	
95% CI	(0.40, 2.00)	
ODDS RATIO [2]		
ESTIMATE	0.73	
95% CI	(0.17, 3.02)	
P-VALUE [3]	0.6430	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | REGION 2 = EUROPE

TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	20/40 (50.0)	9/41 (22.0)
RISK DIFFERENCE [1]		
ESTIMATE	26.57	
95% CI	(7.59, 45.54)	
RELATIVE RISK [2]		
ESTIMATE	2.04	
95% CI	(1.12, 3.71)	
ODDS RATIO [2]		
ESTIMATE	3.99	
95% CI	(1.40, 11.36)	
P-VALUE [3]	0.0089†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | REGION 2 = ROW

**TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT
OF 15 % OF THE SCALE (15 POINTS)**
**300 mg KVD900
(ATTACK=87)**
**Placebo
(ATTACK=84)**

NUMBER OF ATTACKS n/N (%)

3/15 (20.0)

2/12 (16.7)

RISK DIFFERENCE [1]

ESTIMATE

0.88

95% CI

(-30.73, 32.50)

RELATIVE RISK [2]

ESTIMATE

0.94

95% CI

(0.21, 4.15)

ODDS RATIO [2]

ESTIMATE

0.98*

95% CI

(0.15, 6.47)*

P-VALUE [3]

0.9564

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | REGION 2 = NORTH AMERICA

TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/23 (39.1)	9/20 (45.0)
RISK DIFFERENCE [1]		
ESTIMATE	-9.55	
95% CI	(-39.11, 20.01)	
RELATIVE RISK [2]		
ESTIMATE	0.85	
95% CI	(0.41, 1.77)	
ODDS RATIO [2]		
ESTIMATE	0.67	
95% CI	(0.18, 2.46)	
P-VALUE [3]	0.5438	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | REGION 2 = EUROPE

**TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT
OF 15 % OF THE SCALE (15 POINTS)**
**300 mg KVD900
(ATTACK=87)**
**Placebo
(ATTACK=84)**

NUMBER OF ATTACKS n/N (%)

24/41 (58.5)

18/42 (42.9)

RISK DIFFERENCE [1]

ESTIMATE

14.72

95% CI

(-4.45, 33.88)

RELATIVE RISK [2]

ESTIMATE

1.23

95% CI

(0.85, 1.80)

ODDS RATIO [2]

ESTIMATE

2.02

95% CI

(0.73, 5.59)

P-VALUE [3]

0.1404

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | REGION 2 = ROW

TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/15 (26.7)	2/12 (16.7)
RISK DIFFERENCE [1]		
ESTIMATE	8.85	
95% CI	(-25.79, 43.49)	
RELATIVE RISK [2]		
ESTIMATE	1.13	
95% CI	(0.26, 4.84)	
ODDS RATIO [2]		
ESTIMATE	1.29*	
95% CI	(0.20, 8.41)*	
P-VALUE [3]	0.6137	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | REGION 2 = NORTH AMERICA

**TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT
OF 15 % OF THE SCALE (15 POINTS)****300 mg KVD900
(ATTACK=87)****Placebo
(ATTACK=84)**

NUMBER OF ATTACKS n/N (%)

9/23 (39.1)

9/20 (45.0)

RISK DIFFERENCE [1]

ESTIMATE

-9.55

95% CI

(-39.11, 20.01)

RELATIVE RISK [2]

ESTIMATE

0.85

95% CI

(0.41, 1.77)

ODDS RATIO [2]

ESTIMATE

0.67

95% CI

(0.18, 2.46)

P-VALUE [3]

0.5438

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | REGION 2 = EUROPE

TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	24/42 (57.1)	18/42 (42.9)
RISK DIFFERENCE [1]		
ESTIMATE	14.09	
95% CI	(-4.79, 32.98)	
RELATIVE RISK [2]		
ESTIMATE	1.23	
95% CI	(0.85, 1.79)	
ODDS RATIO [2]		
ESTIMATE	1.98	
95% CI	(0.72, 5.48)	
P-VALUE [3]	0.1533	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS REGION 2 = ROW		
TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	4/15 (26.7)	2/12 (16.7)
RISK DIFFERENCE [1]		
ESTIMATE	8.85	
95% CI	(-25.79, 43.49)	
RELATIVE RISK [2]		
ESTIMATE	1.13	
95% CI	(0.26, 4.84)	
ODDS RATIO [2]		
ESTIMATE	1.29*	
95% CI	(0.20, 8.41)*	
P-VALUE [3]	0.6137	

1.9.5 Prophylaxe-Status (Variante 1)

- VAS=Visual Analogic Scale; PGI-S=Patient Global Impression of Severity; CI=Confidence Interval
- Composite VAS score is defined as the mean score across all 3 symptom scores.
- Time to at least 15 points decrease (hours) = Date/time of first ≥ 15 points decrease from baseline in composite VAS score for 3 consecutive time points (with possible missing values in between) – Date/time of first IMP administration.
- Attacks that did not have at least 3 post-baseline assessments within the analyzed period will be excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline PGI-S category (none or mild, moderate, and severe or very severe).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline PGI-S category (none or mild, moderate, and severe or very severe).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

**TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT
OF 15 % OF THE SCALE (15 POINTS)**

**300 mg KVD900
(ATTACK=87)**

**Placebo
(ATTACK=84)**

NUMBER OF ATTACKS n/N (%)

5/18 (27.8)

5/18 (27.8)

RISK DIFFERENCE [1]

ESTIMATE

-1.52

95% CI

(-32.70, 29.66)

RELATIVE RISK [2]

ESTIMATE

1.33

95% CI

(0.33, 5.29)

ODDS RATIO [2]

ESTIMATE

1.28*

95% CI

(0.22, 7.32)*

P-VALUE [3]

0.9233

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
DEMAND

**TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT
OF 15 % OF THE SCALE (15 POINTS)**

**300 mg KVD900
(ATTACK=87)**

**Placebo
(ATTACK=84)**

NUMBER OF ATTACKS n/N (%)

13/59 (22.0)

8/54 (14.8)

RISK DIFFERENCE [1]

ESTIMATE

7.67

95% CI

(-5.76, 21.11)

RELATIVE RISK [2]

ESTIMATE

1.55

95% CI

(0.73, 3.29)

ODDS RATIO [2]

ESTIMATE

1.78

95% CI

(0.63, 5.01)

P-VALUE [3]

0.2734

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

**TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT
OF 15 % OF THE SCALE (15 POINTS)**

**300 mg KVD900
(ATTACK=87)**

**Placebo
(ATTACK=84)**

NUMBER OF ATTACKS n/N (%)

6/18 (33.3)

8/18 (44.4)

RISK DIFFERENCE [1]

ESTIMATE

-12.89

95% CI

(-44.84, 19.05)

RELATIVE RISK [2]

ESTIMATE

0.86

95% CI

(0.34, 2.19)

ODDS RATIO [2]

ESTIMATE

0.62

95% CI

(0.14, 2.80)

P-VALUE [3]

0.4478

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON DEMAND

TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)

300 mg KVD900 (ATTACK=87)

Placebo (ATTACK=84)

NUMBER OF ATTACKS n/N (%)

17/60 (28.3)

8/54 (14.8)

RISK DIFFERENCE [1]

ESTIMATE

14.10

95% CI

(0.20, 27.99)

RELATIVE RISK [2]

ESTIMATE

1.98

95% CI

(0.98, 4.02)

ODDS RATIO [2]

ESTIMATE

2.68

95% CI

(0.98, 7.32)

P-VALUE [3]

0.0545

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

**TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT
OF 15 % OF THE SCALE (15 POINTS)**

**300 mg KVD900
(ATTACK=87)**

**Placebo
(ATTACK=84)**

NUMBER OF ATTACKS n/N (%)

9/18 (50.0)

8/18 (44.4)

RISK DIFFERENCE [1]

ESTIMATE

3.63

95% CI

(-30.02, 37.29)

RELATIVE RISK [2]

ESTIMATE

1.13

95% CI

(0.51, 2.49)

ODDS RATIO [2]

ESTIMATE

1.17

95% CI

(0.29, 4.70)

P-VALUE [3]

0.8356

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON DEMAND

TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	22/60 (36.7)	10/55 (18.2)
RISK DIFFERENCE [1]		
ESTIMATE	18.81	
95% CI	(4.16, 33.45)	
RELATIVE RISK [2]		
ESTIMATE	1.96	
95% CI	(1.08, 3.53)	
ODDS RATIO [2]		
ESTIMATE	3.17	
95% CI	(1.22, 8.26)	
P-VALUE [3]	0.0163†	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

**TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT
OF 15 % OF THE SCALE (15 POINTS)**

**300 mg KVD900
(ATTACK=87)**

**Placebo
(ATTACK=84)**

NUMBER OF ATTACKS n/N (%)

9/18 (50.0)

10/18 (55.6)

RISK DIFFERENCE [1]

ESTIMATE

-7.61

95% CI

(-41.17, 25.95)

RELATIVE RISK [2]

ESTIMATE

0.95

95% CI

(0.48, 1.90)

ODDS RATIO [2]

ESTIMATE

0.76

95% CI

(0.19, 3.01)

P-VALUE [3]

0.6645

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
DEMAND

TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	28/61 (45.9)	19/56 (33.9)
RISK DIFFERENCE [1]		
ESTIMATE	12.79	
95% CI	(-3.08, 28.67)	
RELATIVE RISK [2]		
ESTIMATE	1.32	
95% CI	(0.89, 1.97)	
ODDS RATIO [2]		
ESTIMATE	1.90	
95% CI	(0.80, 4.49)	
P-VALUE [3]	0.1236	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | PROPHYLACTIC TREATMENT STATUS 1 = ON
PROPHYLACTIC TREATMENT

**TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT
OF 15 % OF THE SCALE (15 POINTS)****300 mg KVD900
(ATTACK=87)****Placebo
(ATTACK=84)**

NUMBER OF ATTACKS n/N (%)

9/18 (50.0)

10/18 (55.6)

RISK DIFFERENCE [1]

ESTIMATE

-7.61

95% CI

(-41.17, 25.95)

RELATIVE RISK [2]

ESTIMATE

0.95

95% CI

(0.48, 1.90)

ODDS RATIO [2]

ESTIMATE

0.76

95% CI

(0.19, 3.01)

P-VALUE [3]

0.6645

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS PROPHYLACTIC TREATMENT STATUS 1 = ON DEMAND		
TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	28/62 (45.2)	19/56 (33.9)
RISK DIFFERENCE [1]		
ESTIMATE	12.44	
95% CI	(-3.30, 28.19)	
RELATIVE RISK [2]		
ESTIMATE	1.32	
95% CI	(0.89, 1.96)	
ODDS RATIO [2]		
ESTIMATE	1.88	
95% CI	(0.79, 4.44)	
P-VALUE [3]	0.1314	

1.9.6 Prophylaxe-Status (Variante 2)

- VAS=Visual Analogic Scale; PGI-S=Patient Global Impression of Severity; CI=Confidence Interval
- Composite VAS score is defined as the mean score across all 3 symptom scores.
- Time to at least 15 points decrease (hours) = Date/time of first ≥ 15 points decrease from baseline in composite VAS score for 3 consecutive time points (with possible missing values in between) – Date/time of first IMP administration.
- Attacks that did not have at least 3 post-baseline assessments within the analyzed period will be excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline PGI-S category (none or mild, moderate, and severe or very severe).
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test by adjusting the confounding variable of the baseline PGI-S category (none or mild, moderate, and severe or very severe).
- [3] P-value from Cochran-Mantel-Haenszel test after controlling for baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	3/13 (23.1)	5/14 (35.7)
RISK DIFFERENCE [1]		
ESTIMATE	-13.25	
95% CI	(-49.80, 23.30)	
RELATIVE RISK [2]		
ESTIMATE	1.00	
95% CI	(0.25, 4.07)	
ODDS RATIO [2]		
ESTIMATE	0.81*	
95% CI	(0.13, 5.18)*	
P-VALUE [3]	0.4805	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

**TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT
OF 15 % OF THE SCALE (15 POINTS)**

**300 mg KVD900
(ATTACK=87)****Placebo
(ATTACK=84)**

NUMBER OF ATTACKS n/N (%)

2/5 (40.0)

0/4 (0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND

TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)

300 mg KVD900 (ATTACK=87)

Placebo (ATTACK=84)

NUMBER OF ATTACKS n/N (%)

13/59 (22.0)

8/54 (14.8)

RISK DIFFERENCE [1]

ESTIMATE

7.67

95% CI

(-5.76, 21.11)

RELATIVE RISK [2]

ESTIMATE

1.55

95% CI

(0.73, 3.29)

ODDS RATIO [2]

ESTIMATE

1.78

95% CI

(0.63, 5.01)

P-VALUE [3]

0.2734

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

**TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT
OF 15 % OF THE SCALE (15 POINTS)**

**300 mg KVD900
(ATTACK=87)**

**Placebo
(ATTACK=84)**

NUMBER OF ATTACKS n/N (%)

4/13 (30.8)

8/14 (57.1)

RISK DIFFERENCE [1]

ESTIMATE

-26.97

95% CI

(-63.70, 9.76)

RELATIVE RISK [2]

ESTIMATE

0.62

95% CI

(0.23, 1.67)

ODDS RATIO [2]

ESTIMATE

0.35

95% CI

(0.07, 1.86)

P-VALUE [3]

0.1878

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

**TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT
OF 15 % OF THE SCALE (15 POINTS)**

**300 mg KVD900
(ATTACK=87)**

**Placebo
(ATTACK=84)**

NUMBER OF ATTACKS n/N (%)

2/5 (40.0)

0/4 (0)

RISK DIFFERENCE [1]

ESTIMATE

21.43

95% CI

(-21.07, 63.92)

RELATIVE RISK [2]

ESTIMATE

2.25

95% CI

(0.13, 38.09)

ODDS RATIO [2]

ESTIMATE

3.00*

95% CI

(0.08, 115.34)*

P-VALUE [3]

0.4142

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
DEMAND

TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	17/60 (28.3)	8/54 (14.8)
RISK DIFFERENCE [1]		
ESTIMATE	14.10	
95% CI	(0.20, 27.99)	
RELATIVE RISK [2]		
ESTIMATE	1.98	
95% CI	(0.98, 4.02)	
ODDS RATIO [2]		
ESTIMATE	2.68	
95% CI	(0.98, 7.32)	
P-VALUE [3]	0.0545	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

**TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT
OF 15 % OF THE SCALE (15 POINTS)**

**300 mg KVD900
(ATTACK=87)**

**Placebo
(ATTACK=84)**

NUMBER OF ATTACKS n/N (%)

6/13 (46.2)

8/14 (57.1)

RISK DIFFERENCE [1]

ESTIMATE

-11.69

95% CI

(-49.96, 26.57)

RELATIVE RISK [2]

ESTIMATE

0.84

95% CI

(0.38, 1.86)

ODDS RATIO [2]

ESTIMATE

0.63

95% CI

(0.13, 3.02)

P-VALUE [3]

0.5699

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

**TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT
OF 15 % OF THE SCALE (15 POINTS)**

**300 mg KVD900
(ATTACK=87)**

**Placebo
(ATTACK=84)**

NUMBER OF ATTACKS n/N (%)

3/5 (60.0)

0/4 (0)

RISK DIFFERENCE [1]

ESTIMATE

42.86

95% CI

(-10.58, 96.30)

RELATIVE RISK [2]

ESTIMATE

3.75

95% CI

(0.27, 52.64)

ODDS RATIO [2]

ESTIMATE

8.33*

95% CI

(0.22, 320.38)*

P-VALUE [3]

0.1824

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND

TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)

300 mg KVD900 (ATTACK=87)

Placebo (ATTACK=84)

NUMBER OF ATTACKS n/N (%)

22/60 (36.7)

10/55 (18.2)

RISK DIFFERENCE [1]

ESTIMATE

18.81

95% CI

(4.16, 33.45)

RELATIVE RISK [2]

ESTIMATE

1.96

95% CI

(1.08, 3.53)

ODDS RATIO [2]

ESTIMATE

3.17

95% CI

(1.22, 8.26)

P-VALUE [3]

0.0163†

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	6/13 (46.2)	8/14 (57.1)
RISK DIFFERENCE [1]		
ESTIMATE	-11.69	
95% CI	(-49.96, 26.57)	
RELATIVE RISK [2]		
ESTIMATE	0.84	
95% CI	(0.38, 1.86)	
ODDS RATIO [2]		
ESTIMATE	0.63	
95% CI	(0.13, 3.02)	
P-VALUE [3]	0.5699	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

**TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT
OF 15 % OF THE SCALE (15 POINTS)**

**300 mg KVD900
(ATTACK=87)**

**Placebo
(ATTACK=84)**

NUMBER OF ATTACKS n/N (%)

3/5 (60.0)

2/4 (50.0)

RISK DIFFERENCE [1]

ESTIMATE

-7.14

95% CI

(-78.09, 63.80)

RELATIVE RISK [2]

ESTIMATE

1.03

95% CI

(0.26, 4.04)

ODDS RATIO [2]

ESTIMATE

0.87*

95% CI

(0.06, 12.61)*

P-VALUE [3]

0.8613

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND

**TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT
OF 15 % OF THE SCALE (15 POINTS)**

**300 mg KVD900
(ATTACK=87)****Placebo
(ATTACK=84)**

NUMBER OF ATTACKS n/N (%)

28/61 (45.9)

19/56 (33.9)

RISK DIFFERENCE [1]

ESTIMATE

12.79

95% CI

(-3.08, 28.67)

RELATIVE RISK [2]

ESTIMATE

1.32

95% CI

(0.89, 1.97)

ODDS RATIO [2]

ESTIMATE

1.90

95% CI

(0.80, 4.49)

P-VALUE [3]

0.1236

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
KALLIKREIN

**TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT
OF 15 % OF THE SCALE (15 POINTS)**

**300 mg KVD900
(ATTACK=87)**

**Placebo
(ATTACK=84)**

NUMBER OF ATTACKS n/N (%)

6/13 (46.2)

8/14 (57.1)

RISK DIFFERENCE [1]

ESTIMATE

-11.69

95% CI

(-49.96, 26.57)

RELATIVE RISK [2]

ESTIMATE

0.84

95% CI

(0.38, 1.86)

ODDS RATIO [2]

ESTIMATE

0.63

95% CI

(0.13, 3.02)

P-VALUE [3]

0.5699

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | PROPHYLACTIC TREATMENT STATUS 2 = ON
OTHER

**TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT
OF 15 % OF THE SCALE (15 POINTS)**

**300 mg KVD900
(ATTACK=87)**

**Placebo
(ATTACK=84)**

NUMBER OF ATTACKS n/N (%)

3/5 (60.0)

2/4 (50.0)

RISK DIFFERENCE [1]

ESTIMATE

-7.14

95% CI

(-78.09, 63.80)

RELATIVE RISK [2]

ESTIMATE

1.03

95% CI

(0.26, 4.04)

ODDS RATIO [2]

ESTIMATE

0.87*

95% CI

(0.06, 12.61)*

P-VALUE [3]

0.8613

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	28/62 (45.2)	19/56 (33.9)
RISK DIFFERENCE [1]		
ESTIMATE	12.44	
95% CI	(-3.30, 28.19)	
RELATIVE RISK [2]		
ESTIMATE	1.32	
95% CI	(0.89, 1.96)	
ODDS RATIO [2]		
ESTIMATE	1.88	
95% CI	(0.79, 4.44)	
P-VALUE [3]	0.1314	

1.9.7 Attacken-Schwere (PGIS) zu Baseline

- VAS=Visual Analogic Scale; CI=Confidence Interval
- Composite VAS score is defined as the mean score across all 3 symptom scores.
- Time to at least 15 points decrease (hours) = Date/time of first ≥ 15 points decrease from baseline in composite VAS score for 3 consecutive time points (with possible missing values in between) – Date/time of first IMP administration.
- Attacks that did not have at least 3 post-baseline assessments within the analyzed period will be excluded from this analysis.
- Patients who discontinued or received conventional attack treatment prior to time to event during a time period are considered as non-responders for that period.
- *: a correction of 0.5 was applied to the cells of the table that contains 0.
- †: p-value < 0.05.
- [1] Risk difference was derived from Mantel-Haenszel estimate of the common risk difference using Cochran-Mantel-Haenszel test.
- [2] Relative risk and odds ratio were derived from adjusted logit estimate of the common relative risks odds ratio using Cochran-Mantel-Haenszel test.
- [3] P-value from Cochran-Mantel-Haenszel test.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
NONE OR MILD

**TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT
OF 15 % OF THE SCALE (15 POINTS)**

**300 mg KVD900
(ATTACK=87)**

**Placebo
(ATTACK=84)**

NUMBER OF ATTACKS n/N (%)

2/33 (6.1)

5/32 (15.6)

RISK DIFFERENCE [1]

ESTIMATE

-9.56

95% CI

(-24.55, 5.42)

RELATIVE RISK [2]

ESTIMATE

0.39

95% CI

(0.08, 1.86)

ODDS RATIO [2]

ESTIMATE

0.35

95% CI

(0.06, 1.94)

P-VALUE [3]

0.2172

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
MODERATE

**TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT
OF 15 % OF THE SCALE (15 POINTS)**

**300 mg KVD900
(ATTACK=87)**

**Placebo
(ATTACK=84)**

NUMBER OF ATTACKS n/N (%)

8/30 (26.7)

5/28 (17.9)

RISK DIFFERENCE [1]

ESTIMATE

8.81

95% CI

(-12.44, 30.06)

RELATIVE RISK [2]

ESTIMATE

1.49

95% CI

(0.55, 4.03)

ODDS RATIO [2]

ESTIMATE

1.67

95% CI

(0.47, 5.90)

P-VALUE [3]

0.4255

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
SEVERE OR VERY SEVERE

**TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT
OF 15 % OF THE SCALE (15 POINTS)**

**300 mg KVD900
(ATTACK=87)**

**Placebo
(ATTACK=84)**

NUMBER OF ATTACKS n/N (%)

8/14 (57.1)

3/12 (25.0)

RISK DIFFERENCE [1]

ESTIMATE

32.14

95% CI

(-3.53, 67.81)

RELATIVE RISK [2]

ESTIMATE

2.29

95% CI

(0.78, 6.73)

ODDS RATIO [2]

ESTIMATE

4.00

95% CI

(0.74, 21.50)

P-VALUE [3]

0.1049

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
NONE OR MILD

TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	3/33 (9.1)	6/32 (18.8)
RISK DIFFERENCE [1]		
ESTIMATE	-9.66	
95% CI	(-26.36, 7.05)	
RELATIVE RISK [2]		
ESTIMATE	0.48	
95% CI	(0.13, 1.78)	
ODDS RATIO [2]		
ESTIMATE	0.43	
95% CI	(0.10, 1.91)	
P-VALUE [3]	0.2633	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
MODERATE

**TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT
OF 15 % OF THE SCALE (15 POINTS)**

**300 mg KVD900
(ATTACK=87)**

**Placebo
(ATTACK=84)**

NUMBER OF ATTACKS n/N (%)

11/31 (35.5)

6/28 (21.4)

RISK DIFFERENCE [1]

ESTIMATE

14.06

95% CI

(-8.63, 36.74)

RELATIVE RISK [2]

ESTIMATE

1.66

95% CI

(0.71, 3.89)

ODDS RATIO [2]

ESTIMATE

2.02

95% CI

(0.63, 6.46)

P-VALUE [3]

0.2379

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
SEVERE OR VERY SEVERE

TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	9/14 (64.3)	4/12 (33.3)
RISK DIFFERENCE [1]		
ESTIMATE	30.95	
95% CI	(-5.67, 67.58)	
RELATIVE RISK [2]		
ESTIMATE	1.93	
95% CI	(0.79, 4.70)	
ODDS RATIO [2]		
ESTIMATE	3.60	
95% CI	(0.71, 18.25)	
P-VALUE [3]	0.1228	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
NONE OR MILD

**TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT
OF 15 % OF THE SCALE (15 POINTS)**

**300 mg KVD900
(ATTACK=87)**

**Placebo
(ATTACK=84)**

NUMBER OF ATTACKS n/N (%)

6/33 (18.2)

6/33 (18.2)

RISK DIFFERENCE [1]

ESTIMATE

0.00

95% CI

(-18.61, 18.61)

RELATIVE RISK [2]

ESTIMATE

1.00

95% CI

(0.36, 2.78)

ODDS RATIO [2]

ESTIMATE

1.00

95% CI

(0.29, 3.49)

P-VALUE [3]

1.0000

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
MODERATE

**TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT
OF 15 % OF THE SCALE (15 POINTS)**

**300 mg KVD900
(ATTACK=87)**

**Placebo
(ATTACK=84)**

NUMBER OF ATTACKS n/N (%)

15/31 (48.4)

7/28 (25.0)

RISK DIFFERENCE [1]

ESTIMATE

23.39

95% CI

(-0.42, 47.19)

RELATIVE RISK [2]

ESTIMATE

1.94

95% CI

(0.93, 4.05)

ODDS RATIO [2]

ESTIMATE

2.81

95% CI

(0.93, 8.52)

P-VALUE [3]

0.0659

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
SEVERE OR VERY SEVERE

**TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT
OF 15 % OF THE SCALE (15 POINTS)**

**300 mg KVD900
(ATTACK=87)**

**Placebo
(ATTACK=84)**

NUMBER OF ATTACKS n/N (%)

10/14 (71.4)

5/12 (41.7)

RISK DIFFERENCE [1]

ESTIMATE

29.76

95% CI

(-6.82, 66.34)

RELATIVE RISK [2]

ESTIMATE

1.71

95% CI

(0.81, 3.62)

ODDS RATIO [2]

ESTIMATE

3.50

95% CI

(0.68, 17.89)

P-VALUE [3]

0.1332

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
NONE OR MILD

TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	8/33 (24.2)	8/33 (24.2)
RISK DIFFERENCE [1]		
ESTIMATE	0.00	
95% CI	(-20.68, 20.68)	
RELATIVE RISK [2]		
ESTIMATE	1.00	
95% CI	(0.43, 2.35)	
ODDS RATIO [2]		
ESTIMATE	1.00	
95% CI	(0.32, 3.08)	
P-VALUE [3]	1.0000	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
MODERATE

**TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT
OF 15 % OF THE SCALE (15 POINTS)**

**300 mg KVD900
(ATTACK=87)**

**Placebo
(ATTACK=84)**

NUMBER OF ATTACKS n/N (%)

18/32 (56.3)

14/28 (50.0)

RISK DIFFERENCE [1]

ESTIMATE

6.25

95% CI

(-19.02, 31.52)

RELATIVE RISK [2]

ESTIMATE

1.13

95% CI

(0.70, 1.82)

ODDS RATIO [2]

ESTIMATE

1.29

95% CI

(0.46, 3.56)

P-VALUE [3]

0.6312

 Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

 WITHIN 24 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
 SEVERE OR VERY SEVERE

TIME TO FIRST INCIDENT IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	11/14 (78.6)	7/13 (53.8)
RISK DIFFERENCE [1]		
ESTIMATE	24.73	
95% CI	(-9.86, 59.31)	
RELATIVE RISK [2]		
ESTIMATE	1.46	
95% CI	(0.82, 2.59)	
ODDS RATIO [2]		
ESTIMATE	3.14	
95% CI	(0.59, 16.84)	
P-VALUE [3]	0.1814	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
NONE OR MILD

**TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT
OF 15 % OF THE SCALE (15 POINTS)**

**300 mg KVD900
(ATTACK=87)**

**Placebo
(ATTACK=84)**

NUMBER OF ATTACKS n/N (%)

8/34 (23.5)

8/33 (24.2)

RISK DIFFERENCE [1]

ESTIMATE

-0.71

95% CI

(-21.14, 19.71)

RELATIVE RISK [2]

ESTIMATE

0.97

95% CI

(0.41, 2.28)

ODDS RATIO [2]

ESTIMATE

0.96

95% CI

(0.31, 2.96)

P-VALUE [3]

0.9458

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS | ATTACK SEVERITY AT BASELINE PGI-S =
MODERATE

TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	18/32 (56.3)	14/28 (50.0)
RISK DIFFERENCE [1]		
ESTIMATE	6.25	
95% CI	(-19.02, 31.52)	
RELATIVE RISK [2]		
ESTIMATE	1.13	
95% CI	(0.70, 1.82)	
ODDS RATIO [2]		
ESTIMATE	1.29	
95% CI	(0.46, 3.56)	
P-VALUE [3]	0.6312	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS ATTACK SEVERITY AT BASELINE PGI-S = SEVERE OR VERY SEVERE		
TIME TO FIRST INCIDENCE IN COMPOSITE VAS IMPROVEMENT OF 15 % OF THE SCALE (15 POINTS)	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
NUMBER OF ATTACKS n/N (%)	11/14 (78.6)	7/13 (53.8)
RISK DIFFERENCE [1]		
ESTIMATE	24.73	
95% CI	(-9.86, 59.31)	
RELATIVE RISK [2]		
ESTIMATE	1.46	
95% CI	(0.82, 2.59)	
ODDS RATIO [2]		
ESTIMATE	3.14	
95% CI	(0.59, 16.84)	
P-VALUE [3]	0.1814	

2 Ereigniszeitanalysen

2.1 Zeit bis zum Beginn der Symptomverbesserung definiert als mindestens „ein wenig besser“ im PGI-C

2.1.1 Geschlecht

- PGI-C=Patient Global Impression of Change; CI=Confidence Interval; NE=Not Evaluable
- Time to beginning of symptom relief within 12 hours is defined as an HAE attack being rated “a little better” or higher on the PGI-C for two time points in a row within 12 hours of the first IMP administration.
- Time to beginning of symptom relief is calculated as Date/time of first rating of “a little better” or higher (i.e. better or much better) which is immediately followed by another rating of “a little better” or higher (without missing values in between) – Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for treatment, subgroup, and subgroup*treatment interaction in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that achieved the described event within 12 hours.
- [2] Attacks are treated as right-censored at 12 hours if they did not achieve beginning of symptom relief defined by PGI-C as at least “a little better” (2 time points in a row) or received conventional attack treatment within 12 hours of the first IMP administration. In the case of discontinuation that prevented event “a little better” or higher HAE attack rating occurrence, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 2 consecutive post-baseline assessments, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to beginning of symptom relief within 12 hours.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment in the model as a fixed effect and patient as a random effect.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 1 HOUR	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.4003	
SEX = MALE		
NUMBER OF IMP-TREATED HAE ATTACKS	33	29
EVENTS [1]	6 (18.2)	4 (13.8)
CENSORED [2]	27 (81.8)	25 (86.2)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	NE (0.28, NE)	NE (0.28, NE)
MEDIAN	NE (NE, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.9455	
HAZARD RATIO (95 % CI) [4]	1.00 (0.27, 3.65)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 1 HOUR	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
SEX = FEMALE		
NUMBER OF IMP-TREATED HAE ATTACKS	54	55
EVENTS [1]	5 (9.3)	2 (3.6)
CENSORED [2]	49 (90.7)	53 (96.4)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
MEDIAN	NE (NE, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.2760	
HAZARD RATIO (95 % CI) [4]	2.42 (0.47, 12.46)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.5184	
SEX = MALE		
NUMBER OF IMP-TREATED HAE ATTACKS	33	29
EVENTS [1]	19 (57.6)	8 (27.6)
CENSORED [2]	14 (42.4)	21 (72.4)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.77 (0.28, 0.84)	1.34 (0.28, NE)
MEDIAN	1.28 (0.78, NE)	NE (1.54, NE)
75TH PERCENTILE	NE (1.30, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0174†	
HAZARD RATIO (95 % CI) [4]	2.64 (1.15, 6.07)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
SEX = FEMALE		
NUMBER OF IMP-TREATED HAE ATTACKS	54	55
EVENTS [1]	23 (42.6)	13 (23.6)
CENSORED [2]	31 (57.4)	42 (76.4)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.79 (0.77, 1.29)	1.33 (0.79, NE)
MEDIAN	NE (1.28, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0516	
HAZARD RATIO (95 % CI) [4]	2.16 (1.06, 4.43)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.3448	
SEX = MALE		
NUMBER OF IMP-TREATED HAE ATTACKS	33	29
EVENTS [1]	25 (75.8)	11 (37.9)
CENSORED [2]	8 (24.2)	18 (62.1)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.77 (0.28, 0.84)	1.30 (0.28, 3.60)
MEDIAN	1.28 (0.78, 1.83)	NE (1.34, NE)
75TH PERCENTILE	2.28 (1.35, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0042†	
HAZARD RATIO (95 % CI) [4]	2.74 (1.34, 5.62)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
SEX = FEMALE		
NUMBER OF IMP-TREATED HAE ATTACKS	54	55
EVENTS [1]	33 (61.1)	22 (40.0)
CENSORED [2]	21 (38.9)	33 (60.0)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.81 (0.77, 1.29)	1.55 (0.82, 2.33)
MEDIAN	1.78 (1.29, 2.78)	NE (2.28, NE)
75TH PERCENTILE	NE (2.78, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0151†	
HAZARD RATIO (95 % CI) [4]	2.18 (1.23, 3.86)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.3139	
SEX = MALE		
NUMBER OF IMP-TREATED HAE ATTACKS	33	29
EVENTS [1]	26 (78.8)	11 (37.9)
CENSORED [2]	7 (21.2)	18 (62.1)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.77 (0.28, 0.85)	1.30 (0.28, 3.60)
MEDIAN	1.28 (0.78, 1.83)	NE (1.34, NE)
75TH PERCENTILE	3.24 (1.35, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0042†	
HAZARD RATIO (95 % CI) [4]	2.72 (1.33, 5.55)	

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WITHIN 6 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
SEX = FEMALE		
NUMBER OF IMP-TREATED HAE ATTACKS	54	55
EVENTS [1]	33 (61.1)	23 (41.8)
CENSORED [2]	21 (38.9)	32 (58.2)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.81 (0.77, 1.29)	1.55 (0.82, 2.33)
MEDIAN	1.78 (1.29, 2.78)	NE (2.28, NE)
75TH PERCENTILE	NE (2.78, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0209†	
HAZARD RATIO (95 % CI) [4]	2.08 (1.18, 3.66)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.2092	
SEX = MALE		
NUMBER OF IMP-TREATED HAE ATTACKS	33	29
EVENTS [1]	26 (78.8)	12 (41.4)
CENSORED [2]	7 (21.2)	17 (58.6)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.77 (0.28, 0.85)	1.30 (0.28, 3.60)
MEDIAN	1.28 (0.78, 1.83)	NE (1.34, NE)
75TH PERCENTILE	3.24 (1.35, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0060†	
HAZARD RATIO (95 % CI) [4]	2.56 (1.28, 5.11)	

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WITHIN 8 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
SEX = FEMALE		
NUMBER OF IMP-TREATED HAE ATTACKS	54	55
EVENTS [1]	34 (63.0)	28 (50.9)
CENSORED [2]	20 (37.0)	27 (49.1)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.81 (0.77, 1.29)	1.55 (0.85, 2.33)
MEDIAN	1.78 (1.29, 2.78)	5.55 (2.28, NE)
75TH PERCENTILE	NE (2.78, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0517	
HAZARD RATIO (95 % CI) [4]	1.76 (1.05, 2.97)	

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WITHIN 10 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.1726	
SEX = MALE		
NUMBER OF IMP-TREATED HAE ATTACKS	33	29
EVENTS [1]	27 (81.8)	12 (41.4)
CENSORED [2]	6 (18.2)	17 (58.6)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.77 (0.28, 0.85)	1.30 (0.28, 3.60)
MEDIAN	1.28 (0.78, 1.83)	NE (1.34, NE)
75TH PERCENTILE	3.24 (1.35, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0031†	
HAZARD RATIO (95 % CI) [4]	2.72 (1.36, 5.42)	

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WITHIN 10 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
SEX = FEMALE		
NUMBER OF IMP-TREATED HAE ATTACKS	54	55
EVENTS [1]	36 (66.7)	29 (52.7)
CENSORED [2]	18 (33.3)	26 (47.3)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.81 (0.77, 1.29)	1.55 (0.85, 2.33)
MEDIAN	1.78 (1.29, 2.78)	5.55 (2.28, NE)
75TH PERCENTILE	NE (2.78, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0348†	
HAZARD RATIO (95 % CI) [4]	1.83 (1.10, 3.07)	

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WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.1481	
SEX = MALE		
NUMBER OF IMP-TREATED HAE ATTACKS	33	29
EVENTS [1]	29 (87.9)	12 (41.4)
CENSORED [2]	4 (12.1)	17 (58.6)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.77 (0.28, 0.85)	1.30 (0.28, 3.60)
MEDIAN	1.28 (0.78, 1.83)	NE (1.34, NE)
75TH PERCENTILE	3.24 (1.35, 9.54)	NE (NE, NE)
LOG-RANK P-VALUE	0.0007†	
HAZARD RATIO (95 % CI) [4]	3.12 (1.57, 6.21)	

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WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
SEX = FEMALE		
NUMBER OF IMP-TREATED HAE ATTACKS	54	55
EVENTS [1]	37 (68.5)	29 (52.7)
CENSORED [2]	17 (31.5)	26 (47.3)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.81 (0.77, 1.29)	1.55 (0.85, 2.33)
MEDIAN	1.78 (1.29, 2.78)	5.57 (2.28, NE)
75TH PERCENTILE	10.12 (2.78, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0180†	
HAZARD RATIO (95 % CI) [4]	1.92 (1.16, 3.20)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.0691	
SEX = MALE		
NUMBER OF IMP-TREATED HAE ATTACKS	33	29
EVENTS [1]	30 (90.9)	16 (55.2)
CENSORED [2]	3 (9.1)	13 (44.8)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.77 (0.28, 0.85)	1.30 (0.28, 3.60)
MEDIAN	1.28 (0.78, 1.83)	16.71 (1.34, NE)
75TH PERCENTILE	3.24 (1.35, 9.54)	NE (21.02, NE)
LOG-RANK P-VALUE	0.0002†	
HAZARD RATIO (95 % CI) [4]	3.27 (1.71, 6.25)	

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WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
SEX = FEMALE		
NUMBER OF IMP-TREATED HAE ATTACKS	54	55
EVENTS [1]	39 (72.2)	32 (58.2)
CENSORED [2]	15 (27.8)	23 (41.8)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.86 (0.77, 1.29)	1.55 (0.85, 2.33)
MEDIAN	1.82 (1.29, 3.47)	5.57 (2.28, NE)
75TH PERCENTILE	NE (3.47, NE)	NE (22.78, NE)
LOG-RANK P-VALUE	0.0683	
HAZARD RATIO (95 % CI) [4]	1.66 (1.01, 2.72)	

2.1.2 Alter

- PGI-C=Patient Global Impression of Change; CI=Confidence Interval; NE=Not Evaluable
- Time to beginning of symptom relief within 12 hours is defined as an HAE attack being rated “a little better” or higher on the PGI-C for two time points in a row within 12 hours of the first IMP administration.
- Time to beginning of symptom relief is calculated as Date/time of first rating of “a little better” or higher (i.e. better or much better) which is immediately followed by another rating of “a little better” or higher (without missing values in between) – Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for treatment, subgroup, and subgroup*treatment interaction in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that achieved the described event within 12 hours.
- [2] Attacks are treated as right-censored at 12 hours if they did not achieve beginning of symptom relief defined by PGI-C as at least “a little better” (2 time points in a row) or received conventional attack treatment within 12 hours of the first IMP administration. In the case of discontinuation that prevented event “a little better” or higher HAE attack rating occurrence, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 2 consecutive post-baseline assessments, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to beginning of symptom relief within 12 hours.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment in the model as a fixed effect and patient as a random effect.

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WITHIN 1 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.5639	
AGE GROUP = <18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	10	9
EVENTS [1]	1 (10.0)	1 (11.1)
CENSORED [2]	9 (90.0)	8 (88.9)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	NE (0.28, NE)	NE (0.56, NE)
MEDIAN	NE (0.28, NE)	NE (0.56, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.8757	
HAZARD RATIO (95 % CI) [4]	0.79 (0.05, 12.87)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 1 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
AGE GROUP = >=18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	77	75
EVENTS [1]	10 (13.0)	5 (6.7)
CENSORED [2]	67 (87.0)	70 (93.3)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	NE (0.77, NE)	NE (NE, NE)
MEDIAN	NE (NE, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.3022	
HAZARD RATIO (95 % CI) [4]	1.76 (0.59, 5.20)	

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WITHIN 2 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.1969	
AGE GROUP = <18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	10	9
EVENTS [1]	4 (40.0)	4 (44.4)
CENSORED [2]	6 (60.0)	5 (55.6)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	1.04 (0.28, NE)	1.09 (0.56, NE)
MEDIAN	NE (0.28, NE)	NE (0.56, NE)
75TH PERCENTILE	NE (1.29, NE)	NE (1.34, NE)
LOG-RANK P-VALUE	0.9651	
HAZARD RATIO (95 % CI) [4]	1.03 (0.26, 4.13)	

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WITHIN 2 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
AGE GROUP = >=18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	77	75
EVENTS [1]	38 (49.4)	17 (22.7)
CENSORED [2]	39 (50.6)	58 (77.3)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.78 (0.77, 0.85)	1.33 (0.79, NE)
MEDIAN	1.33 (0.98, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0013†	
HAZARD RATIO (95 % CI) [4]	2.68 (1.48, 4.85)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.3234	
AGE GROUP = <18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	10	9
EVENTS [1]	6 (60.0)	4 (44.4)
CENSORED [2]	4 (40.0)	5 (55.6)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	1.29 (0.28, 2.27)	1.09 (0.56, NE)
MEDIAN	2.27 (0.28, NE)	NE (0.56, NE)
75TH PERCENTILE	NE (1.70, NE)	NE (1.34, NE)
LOG-RANK P-VALUE	0.6578	
HAZARD RATIO (95 % CI) [4]	1.33 (0.37, 4.73)	

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WITHIN 4 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
AGE GROUP = >=18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	77	75
EVENTS [1]	52 (67.5)	29 (38.7)
CENSORED [2]	25 (32.5)	46 (61.3)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.78 (0.77, 0.91)	1.33 (0.82, 2.28)
MEDIAN	1.35 (1.03, 1.83)	NE (2.33, NE)
75TH PERCENTILE	NE (2.27, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0001†	
HAZARD RATIO (95 % CI) [4]	2.61 (1.62, 4.22)	

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WITHIN 6 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.3545	
AGE GROUP = <18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	10	9
EVENTS [1]	6 (60.0)	4 (44.4)
CENSORED [2]	4 (40.0)	5 (55.6)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	1.29 (0.28, 2.27)	1.09 (0.56, NE)
MEDIAN	2.27 (0.28, NE)	NE (0.56, NE)
75TH PERCENTILE	NE (1.70, NE)	NE (1.34, NE)
LOG-RANK P-VALUE	0.6578	
HAZARD RATIO (95 % CI) [4]	1.33 (0.37, 4.73)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
AGE GROUP = >=18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	77	75
EVENTS [1]	53 (68.8)	30 (40.0)
CENSORED [2]	24 (31.2)	45 (60.0)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.78 (0.77, 0.91)	1.33 (0.82, 2.28)
MEDIAN	1.35 (1.03, 1.85)	NE (2.33, NE)
75TH PERCENTILE	NE (2.27, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0002†	
HAZARD RATIO (95 % CI) [4]	2.53 (1.58, 4.05)	

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WITHIN 8 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.2522	
AGE GROUP = <18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	10	9
EVENTS [1]	6 (60.0)	5 (55.6)
CENSORED [2]	4 (40.0)	4 (44.4)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	1.29 (0.28, 2.27)	1.09 (0.56, 5.54)
MEDIAN	2.27 (0.28, NE)	3.55 (0.56, NE)
75TH PERCENTILE	NE (1.70, NE)	NE (1.34, NE)
LOG-RANK P-VALUE	0.8705	
HAZARD RATIO (95 % CI) [4]	1.10 (0.34, 3.63)	

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WITHIN 8 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
AGE GROUP = >=18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	77	75
EVENTS [1]	54 (70.1)	35 (46.7)
CENSORED [2]	23 (29.9)	40 (53.3)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.78 (0.77, 0.91)	1.33 (0.82, 2.28)
MEDIAN	1.35 (1.03, 1.85)	7.22 (2.33, NE)
75TH PERCENTILE	6.54 (2.27, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0005†	
HAZARD RATIO (95 % CI) [4]	2.31 (1.48, 3.62)	

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WITHIN 10 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.4518	
AGE GROUP = <18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	10	9
EVENTS [1]	8 (80.0)	5 (55.6)
CENSORED [2]	2 (20.0)	4 (44.4)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	1.29 (0.28, 2.27)	1.09 (0.56, 5.54)
MEDIAN	2.27 (0.28, 9.36)	3.55 (0.56, NE)
75TH PERCENTILE	7.55 (1.70, NE)	NE (1.34, NE)
LOG-RANK P-VALUE	0.4452	
HAZARD RATIO (95 % CI) [4]	1.54 (0.50, 4.74)	

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WITHIN 10 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
AGE GROUP = >=18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	77	75
EVENTS [1]	55 (71.4)	36 (48.0)
CENSORED [2]	22 (28.6)	39 (52.0)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.78 (0.77, 0.91)	1.33 (0.82, 2.28)
MEDIAN	1.35 (1.03, 1.85)	7.22 (2.33, NE)
75TH PERCENTILE	6.54 (2.27, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0004†	
HAZARD RATIO (95 % CI) [4]	2.32 (1.49, 3.62)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.6653	
AGE GROUP = <18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	10	9
EVENTS [1]	8 (80.0)	5 (55.6)
CENSORED [2]	2 (20.0)	4 (44.4)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	1.29 (0.28, 2.27)	1.34 (0.56, 5.54)
MEDIAN	2.27 (0.28, 9.36)	5.54 (0.56, NE)
75TH PERCENTILE	7.55 (1.70, NE)	NE (1.55, NE)
LOG-RANK P-VALUE	0.2692	
HAZARD RATIO (95 % CI) [4]	1.87 (0.61, 5.75)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
AGE GROUP = >=18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	77	75
EVENTS [1]	58 (75.3)	36 (48.0)
CENSORED [2]	19 (24.7)	39 (52.0)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.78 (0.77, 0.91)	1.33 (0.82, 2.28)
MEDIAN	1.35 (1.03, 1.85)	7.22 (2.33, NE)
75TH PERCENTILE	6.54 (2.27, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0001†	
HAZARD RATIO (95 % CI) [4]	2.47 (1.59, 3.84)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.5751	
AGE GROUP = <18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	10	9
EVENTS [1]	10 (100)	6 (66.7)
CENSORED [2]	0	3 (33.3)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	1.29 (0.28, 3.47)	1.34 (0.56, 5.54)
MEDIAN	2.87 (0.28, 9.36)	5.54 (0.56, NE)
75TH PERCENTILE	9.36 (2.27, NE)	NE (1.55, NE)
LOG-RANK P-VALUE	0.1843	
HAZARD RATIO (95 % CI) [4]	2.00 (0.71, 5.66)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
AGE GROUP = >=18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	77	75
EVENTS [1]	59 (76.6)	42 (56.0)
CENSORED [2]	18 (23.4)	33 (44.0)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.78 (0.77, 0.98)	1.54 (0.82, 2.33)
MEDIAN	1.53 (1.28, 2.27)	7.32 (2.59, NE)
75TH PERCENTILE	7.65 (2.28, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0006†	
HAZARD RATIO (95 % CI) [4]	2.28 (1.48, 3.51)	

2.1.3 Region (Variante 1)

- PGI-C=Patient Global Impression of Change; CI=Confidence Interval; NE=Not Evaluable
- Time to beginning of symptom relief within 12 hours is defined as an HAE attack being rated “a little better” or higher on the PGI-C for two time points in a row within 12 hours of the first IMP administration.
- Time to beginning of symptom relief is calculated as Date/time of first rating of “a little better” or higher (i.e. better or much better) which is immediately followed by another rating of “a little better” or higher (without missing values in between) – Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for treatment, subgroup, and subgroup*treatment interaction in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that achieved the described event within 12 hours.
- [2] Attacks are treated as right-censored at 12 hours if they did not achieve beginning of symptom relief defined by PGI-C as at least “a little better” (2 time points in a row) or received conventional attack treatment within 12 hours of the first IMP administration. In the case of discontinuation that prevented event “a little better” or higher HAE attack rating occurrence, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 2 consecutive post-baseline assessments, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to beginning of symptom relief within 12 hours.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment in the model as a fixed effect and patient as a random effect.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 1 HOUR	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	1.0000	
REGION 1 = US		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	5 (18.5)	0
CENSORED [2]	22 (81.5)	23 (100)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	NE (0.28, NE)	NE (NE, NE)
MEDIAN	NE (NE, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0389†	
HAZARD RATIO (95 % CI) [4]	4.91E8 (0.00, NE)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 1 HOUR	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 1 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	60	61
EVENTS [1]	6 (10.0)	6 (9.8)
CENSORED [2]	54 (90.0)	55 (90.2)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	NE (NE, NE)	NE (0.56, NE)
MEDIAN	NE (NE, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.8196	
HAZARD RATIO (95 % CI) [4]	0.79 (0.25, 2.50)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.0941	
REGION 1 = US		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	16 (59.3)	4 (17.4)
CENSORED [2]	11 (40.7)	19 (82.6)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.77 (0.28, 0.79)	NE (0.78, NE)
MEDIAN	1.28 (0.78, 1.69)	NE (1.27, NE)
75TH PERCENTILE	NE (1.28, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0055†	
HAZARD RATIO (95 % CI) [4]	4.19 (1.40, 12.58)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 1 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	60	61
EVENTS [1]	26 (43.3)	17 (27.9)
CENSORED [2]	34 (56.7)	44 (72.1)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.81 (0.77, 1.28)	1.33 (0.77, NE)
MEDIAN	NE (1.28, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0832	
HAZARD RATIO (95 % CI) [4]	1.75 (0.93, 3.30)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.1988	
REGION 1 = US		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	19 (70.4)	8 (34.8)
CENSORED [2]	8 (29.6)	15 (65.2)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.77 (0.28, 0.79)	2.03 (0.78, NE)
MEDIAN	1.28 (0.78, 2.78)	NE (1.78, NE)
75TH PERCENTILE	3.12 (1.29, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0042†	
HAZARD RATIO (95 % CI) [4]	3.17 (1.38, 7.29)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 1 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	60	61
EVENTS [1]	39 (65.0)	25 (41.0)
CENSORED [2]	21 (35.0)	36 (59.0)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.81 (0.77, 1.28)	1.32 (0.77, 1.88)
MEDIAN	1.77 (1.28, 2.27)	NE (1.88, NE)
75TH PERCENTILE	NE (2.27, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0108†	
HAZARD RATIO (95 % CI) [4]	2.00 (1.18, 3.39)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.2850	
REGION 1 = US		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	19 (70.4)	9 (39.1)
CENSORED [2]	8 (29.6)	14 (60.9)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.77 (0.28, 0.79)	2.03 (0.78, 3.85)
MEDIAN	1.28 (0.78, 2.78)	NE (1.78, NE)
75TH PERCENTILE	3.12 (1.29, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0068†	
HAZARD RATIO (95 % CI) [4]	2.88 (1.29, 6.41)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 1 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	60	61
EVENTS [1]	40 (66.7)	25 (41.0)
CENSORED [2]	20 (33.3)	36 (59.0)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.82 (0.77, 1.30)	1.32 (0.77, 1.88)
MEDIAN	1.78 (1.30, 2.27)	NE (1.88, NE)
75TH PERCENTILE	NE (2.28, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0104†	
HAZARD RATIO (95 % CI) [4]	2.01 (1.19, 3.40)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.4434	
REGION 1 = US		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	19 (70.4)	12 (52.2)
CENSORED [2]	8 (29.6)	11 (47.8)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.77 (0.28, 0.79)	2.28 (0.78, 3.85)
MEDIAN	1.28 (0.78, 2.78)	6.23 (2.28, NE)
75TH PERCENTILE	3.12 (1.29, NE)	NE (7.32, NE)
LOG-RANK P-VALUE	0.0167†	
HAZARD RATIO (95 % CI) [4]	2.38 (1.15, 4.94)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 1 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	60	61
EVENTS [1]	41 (68.3)	28 (45.9)
CENSORED [2]	19 (31.7)	33 (54.1)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.82 (0.77, 1.30)	1.32 (0.77, 1.88)
MEDIAN	1.78 (1.30, 2.27)	6.38 (1.88, NE)
75TH PERCENTILE	NE (2.28, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0172†	
HAZARD RATIO (95 % CI) [4]	1.87 (1.13, 3.08)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.4756	
REGION 1 = US		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	19 (70.4)	12 (52.2)
CENSORED [2]	8 (29.6)	11 (47.8)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.77 (0.28, 0.79)	2.28 (0.78, 3.85)
MEDIAN	1.28 (0.78, 2.78)	6.23 (2.28, NE)
75TH PERCENTILE	3.12 (1.29, NE)	NE (7.32, NE)
LOG-RANK P-VALUE	0.0167†	
HAZARD RATIO (95 % CI) [4]	2.38 (1.15, 4.94)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 1 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	60	61
EVENTS [1]	44 (73.3)	29 (47.5)
CENSORED [2]	16 (26.7)	32 (52.5)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.82 (0.77, 1.30)	1.32 (0.77, 1.88)
MEDIAN	1.78 (1.30, 2.27)	6.38 (1.88, NE)
75TH PERCENTILE	7.60 (2.28, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0069†	
HAZARD RATIO (95 % CI) [4]	2.01 (1.22, 3.29)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.5443	
REGION 1 = US		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	20 (74.1)	12 (52.2)
CENSORED [2]	7 (25.9)	11 (47.8)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.77 (0.28, 0.79)	2.28 (0.78, 3.85)
MEDIAN	1.28 (0.78, 2.78)	6.23 (2.28, NE)
75TH PERCENTILE	3.12 (1.29, NE)	NE (7.32, NE)
LOG-RANK P-VALUE	0.0096†	
HAZARD RATIO (95 % CI) [4]	2.52 (1.22, 5.20)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 1 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	60	61
EVENTS [1]	46 (76.7)	29 (47.5)
CENSORED [2]	14 (23.3)	32 (52.5)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.82 (0.77, 1.30)	1.32 (0.78, 1.88)
MEDIAN	1.78 (1.30, 2.27)	7.22 (1.88, NE)
75TH PERCENTILE	7.60 (2.28, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0019†	
HAZARD RATIO (95 % CI) [4]	2.16 (1.33, 3.52)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.3969	
REGION 1 = US		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	21 (77.8)	14 (60.9)
CENSORED [2]	6 (22.2)	9 (39.1)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.77 (0.28, 0.79)	2.28 (0.78, 3.85)
MEDIAN	1.28 (0.78, 2.78)	6.23 (2.28, NE)
75TH PERCENTILE	3.12 (1.29, NE)	NE (7.32, NE)
LOG-RANK P-VALUE	0.0118†	
HAZARD RATIO (95 % CI) [4]	2.35 (1.19, 4.66)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 1 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	60	61
EVENTS [1]	48 (80.0)	34 (55.7)
CENSORED [2]	12 (20.0)	27 (44.3)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.84 (0.77, 1.31)	1.33 (0.78, 2.04)
MEDIAN	1.79 (1.31, 2.44)	8.30 (2.04, NE)
75TH PERCENTILE	9.54 (3.24, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0071†	
HAZARD RATIO (95 % CI) [4]	1.94 (1.21, 3.10)	

2.1.4 Region (Variante 2)

- PGI-C=Patient Global Impression of Change; CI=Confidence Interval; NE=Not Evaluable
- Time to beginning of symptom relief within 12 hours is defined as an HAE attack being rated “a little better” or higher on the PGI-C for two time points in a row within 12 hours of the first IMP administration.
- Time to beginning of symptom relief is calculated as Date/time of first rating of “a little better” or higher (i.e. better or much better) which is immediately followed by another rating of “a little better” or higher (without missing values in between) – Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for treatment, subgroup, and subgroup*treatment interaction in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that achieved the described event within 12 hours.
- [2] Attacks are treated as right-censored at 12 hours if they did not achieve beginning of symptom relief defined by PGI-C as at least “a little better” (2 time points in a row) or received conventional attack treatment within 12 hours of the first IMP administration. In the case of discontinuation that prevented event “a little better” or higher HAE attack rating occurrence, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 2 consecutive post-baseline assessments, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to beginning of symptom relief within 12 hours.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment in the model as a fixed effect and patient as a random effect.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 1 HOUR	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = NORTH AMERICA		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	5 (18.5)	0
CENSORED [2]	22 (81.5)	23 (100)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 1 HOUR	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = EUROPE		
NUMBER OF IMP-TREATED HAE ATTACKS	44	48
EVENTS [1]	3 (6.8)	5 (10.4)
CENSORED [2]	41 (93.2)	43 (89.6)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 1 HOUR	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	16	13
EVENTS [1]	3 (18.8)	1 (7.7)
CENSORED [2]	13 (81.3)	12 (92.3)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.1869	
REGION 2 = NORTH AMERICA		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	16 (59.3)	4 (17.4)
CENSORED [2]	11 (40.7)	19 (82.6)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.77 (0.28, 0.79)	NE (0.78, NE)
MEDIAN	1.28 (0.78, 1.69)	NE (1.27, NE)
75TH PERCENTILE	NE (1.28, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0055†	
HAZARD RATIO (95 % CI) [4]	4.19 (1.40, 12.58)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = EUROPE		
NUMBER OF IMP-TREATED HAE ATTACKS	44	48
EVENTS [1]	18 (40.9)	13 (27.1)
CENSORED [2]	26 (59.1)	35 (72.9)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.91 (0.77, 1.35)	1.33 (0.56, NE)
MEDIAN	NE (1.28, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.2023	
HAZARD RATIO (95 % CI) [4]	1.59 (0.77, 3.26)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	16	13
EVENTS [1]	8 (50.0)	4 (30.8)
CENSORED [2]	8 (50.0)	9 (69.2)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.77 (0.28, 1.31)	0.78 (0.28, NE)
MEDIAN	1.31 (0.34, NE)	NE (0.77, NE)
75TH PERCENTILE	NE (0.91, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.2453	
HAZARD RATIO (95 % CI) [4]	2.81 (0.73, 10.79)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.2728	
REGION 2 = NORTH AMERICA		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	19 (70.4)	8 (34.8)
CENSORED [2]	8 (29.6)	15 (65.2)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.77 (0.28, 0.79)	2.03 (0.78, NE)
MEDIAN	1.28 (0.78, 2.78)	NE (1.78, NE)
75TH PERCENTILE	3.12 (1.29, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0042†	
HAZARD RATIO (95 % CI) [4]	3.17 (1.38, 7.29)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = EUROPE		
NUMBER OF IMP-TREATED HAE ATTACKS	44	48
EVENTS [1]	27 (61.4)	20 (41.7)
CENSORED [2]	17 (38.6)	28 (58.3)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.98 (0.77, 1.35)	1.32 (0.56, 2.04)
MEDIAN	1.78 (1.28, 3.60)	NE (1.85, NE)
75TH PERCENTILE	NE (2.44, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0730	
HAZARD RATIO (95 % CI) [4]	1.76 (0.96, 3.21)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	16	13
EVENTS [1]	12 (75.0)	5 (38.5)
CENSORED [2]	4 (25.0)	8 (61.5)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.77 (0.28, 1.31)	0.78 (0.28, NE)
MEDIAN	1.50 (0.34, 2.27)	NE (0.77, NE)
75TH PERCENTILE	2.27 (1.31, NE)	NE (3.28, NE)
LOG-RANK P-VALUE	0.0524	
HAZARD RATIO (95 % CI) [4]	3.22 (0.99, 10.45)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.3751	
REGION 2 = NORTH AMERICA		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	19 (70.4)	9 (39.1)
CENSORED [2]	8 (29.6)	14 (60.9)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.77 (0.28, 0.79)	2.03 (0.78, 3.85)
MEDIAN	1.28 (0.78, 2.78)	NE (1.78, NE)
75TH PERCENTILE	3.12 (1.29, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0068†	
HAZARD RATIO (95 % CI) [4]	2.88 (1.29, 6.41)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = EUROPE		
NUMBER OF IMP-TREATED HAE ATTACKS	44	48
EVENTS [1]	27 (61.4)	20 (41.7)
CENSORED [2]	17 (38.6)	28 (58.3)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.98 (0.77, 1.35)	1.32 (0.56, 2.04)
MEDIAN	1.78 (1.28, 3.60)	NE (1.85, NE)
75TH PERCENTILE	NE (2.44, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0730	
HAZARD RATIO (95 % CI) [4]	1.76 (0.96, 3.21)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	16	13
EVENTS [1]	13 (81.3)	5 (38.5)
CENSORED [2]	3 (18.8)	8 (61.5)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.77 (0.28, 1.31)	0.78 (0.28, NE)
MEDIAN	1.70 (0.34, 2.27)	NE (0.77, NE)
75TH PERCENTILE	2.27 (1.70, NE)	NE (3.28, NE)
LOG-RANK P-VALUE	0.0543	
HAZARD RATIO (95 % CI) [4]	3.25 (1.03, 10.29)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.5382	
REGION 2 = NORTH AMERICA		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	19 (70.4)	12 (52.2)
CENSORED [2]	8 (29.6)	11 (47.8)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.77 (0.28, 0.79)	2.28 (0.78, 3.85)
MEDIAN	1.28 (0.78, 2.78)	6.23 (2.28, NE)
75TH PERCENTILE	3.12 (1.29, NE)	NE (7.32, NE)
LOG-RANK P-VALUE	0.0167†	
HAZARD RATIO (95 % CI) [4]	2.38 (1.15, 4.94)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = EUROPE		
NUMBER OF IMP-TREATED HAE ATTACKS	44	48
EVENTS [1]	28 (63.6)	22 (45.8)
CENSORED [2]	16 (36.4)	26 (54.2)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.98 (0.77, 1.35)	1.32 (0.56, 2.04)
MEDIAN	1.78 (1.28, 3.60)	5.54 (1.85, NE)
75TH PERCENTILE	NE (2.44, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0906	
HAZARD RATIO (95 % CI) [4]	1.66 (0.94, 2.95)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	16	13
EVENTS [1]	13 (81.3)	6 (46.2)
CENSORED [2]	3 (18.8)	7 (53.8)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.77 (0.28, 1.31)	0.78 (0.28, 7.22)
MEDIAN	1.70 (0.34, 2.27)	7.22 (0.77, NE)
75TH PERCENTILE	2.27 (1.70, NE)	NE (3.28, NE)
LOG-RANK P-VALUE	0.0771	
HAZARD RATIO (95 % CI) [4]	3.02 (1.00, 9.16)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.6990	
REGION 2 = NORTH AMERICA		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	19 (70.4)	12 (52.2)
CENSORED [2]	8 (29.6)	11 (47.8)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.77 (0.28, 0.79)	2.28 (0.78, 3.85)
MEDIAN	1.28 (0.78, 2.78)	6.23 (2.28, NE)
75TH PERCENTILE	3.12 (1.29, NE)	NE (7.32, NE)
LOG-RANK P-VALUE	0.0167†	
HAZARD RATIO (95 % CI) [4]	2.38 (1.15, 4.94)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = EUROPE		
NUMBER OF IMP-TREATED HAE ATTACKS	44	48
EVENTS [1]	31 (70.5)	22 (45.8)
CENSORED [2]	13 (29.5)	26 (54.2)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.98 (0.77, 1.35)	1.32 (0.56, 2.04)
MEDIAN	1.78 (1.28, 3.60)	5.54 (1.85, NE)
75TH PERCENTILE	9.36 (2.44, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0295†	
HAZARD RATIO (95 % CI) [4]	1.89 (1.07, 3.34)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	16	13
EVENTS [1]	13 (81.3)	7 (53.8)
CENSORED [2]	3 (18.8)	6 (46.2)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.77 (0.28, 1.31)	0.78 (0.28, 7.22)
MEDIAN	1.70 (0.34, 2.27)	7.22 (0.77, NE)
75TH PERCENTILE	2.27 (1.70, NE)	NE (3.28, NE)
LOG-RANK P-VALUE	0.1100	
HAZARD RATIO (95 % CI) [4]	2.67 (0.92, 7.74)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.7209	
REGION 2 = NORTH AMERICA		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	20 (74.1)	12 (52.2)
CENSORED [2]	7 (25.9)	11 (47.8)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.77 (0.28, 0.79)	2.28 (0.78, 3.85)
MEDIAN	1.28 (0.78, 2.78)	6.23 (2.28, NE)
75TH PERCENTILE	3.12 (1.29, NE)	NE (7.32, NE)
LOG-RANK P-VALUE	0.0096†	
HAZARD RATIO (95 % CI) [4]	2.52 (1.22, 5.20)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = EUROPE		
NUMBER OF IMP-TREATED HAE ATTACKS	44	48
EVENTS [1]	33 (75.0)	22 (45.8)
CENSORED [2]	11 (25.0)	26 (54.2)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.98 (0.77, 1.35)	1.32 (0.56, 2.04)
MEDIAN	1.78 (1.28, 3.60)	5.54 (1.85, NE)
75TH PERCENTILE	9.36 (2.44, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0118†	
HAZARD RATIO (95 % CI) [4]	2.05 (1.17, 3.60)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	16	13
EVENTS [1]	13 (81.3)	7 (53.8)
CENSORED [2]	3 (18.8)	6 (46.2)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.77 (0.28, 1.31)	1.17 (0.28, 7.22)
MEDIAN	1.70 (0.34, 2.27)	7.76 (0.77, NE)
75TH PERCENTILE	2.27 (1.70, NE)	NE (7.22, NE)
LOG-RANK P-VALUE	0.0617	
HAZARD RATIO (95 % CI) [4]	2.95 (1.04, 8.34)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.6367	
REGION 2 = NORTH AMERICA		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	21 (77.8)	14 (60.9)
CENSORED [2]	6 (22.2)	9 (39.1)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.77 (0.28, 0.79)	2.28 (0.78, 3.85)
MEDIAN	1.28 (0.78, 2.78)	6.23 (2.28, NE)
75TH PERCENTILE	3.12 (1.29, NE)	NE (7.32, NE)
LOG-RANK P-VALUE	0.0118†	
HAZARD RATIO (95 % CI) [4]	2.35 (1.19, 4.66)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = EUROPE		
NUMBER OF IMP-TREATED HAE ATTACKS	44	48
EVENTS [1]	35 (79.5)	25 (52.1)
CENSORED [2]	9 (20.5)	23 (47.9)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	1.00 (0.77, 1.35)	1.33 (0.85, 2.04)
MEDIAN	1.81 (1.30, 7.55)	13.02 (1.88, NE)
75TH PERCENTILE	16.01 (3.60, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0229†	
HAZARD RATIO (95 % CI) [4]	1.87 (1.09, 3.21)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	16	13
EVENTS [1]	13 (81.3)	9 (69.2)
CENSORED [2]	3 (18.8)	4 (30.8)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.77 (0.28, 1.31)	1.17 (0.28, 7.22)
MEDIAN	1.70 (0.34, 2.27)	7.76 (0.77, NE)
75TH PERCENTILE	2.27 (1.70, NE)	NE (7.22, NE)
LOG-RANK P-VALUE	0.1295	
HAZARD RATIO (95 % CI) [4]	2.71 (0.98, 7.50)	

2.1.5 Prophylaxe-Status (Variante 1)

- PGI-C=Patient Global Impression of Change; CI=Confidence Interval; NE=Not Evaluable
- Time to beginning of symptom relief within 12 hours is defined as an HAE attack being rated “a little better” or higher on the PGI-C for two time points in a row within 12 hours of the first IMP administration.
- Time to beginning of symptom relief is calculated as Date/time of first rating of “a little better” or higher (i.e. better or much better) which is immediately followed by another rating of “a little better” or higher (without missing values in between) – Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for treatment, subgroup, and subgroup*treatment interaction in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that achieved the described event within 12 hours.
- [2] Attacks are treated as right-censored at 12 hours if they did not achieve beginning of symptom relief defined by PGI-C as at least “a little better” (2 time points in a row) or received conventional attack treatment within 12 hours of the first IMP administration. In the case of discontinuation that prevented event “a little better” or higher HAE attack rating occurrence, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 2 consecutive post-baseline assessments, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to beginning of symptom relief within 12 hours.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment in the model as a fixed effect and patient as a random effect.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 1 HOUR	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.6725	
PROPHYLACTIC TREATMENT STATUS 1 = ON PROPHYLACTIC TREATMENT		
NUMBER OF IMP-TREATED HAE ATTACKS	19	18
EVENTS [1]	3 (15.8)	1 (5.6)
CENSORED [2]	16 (84.2)	17 (94.4)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	NE (0.34, NE)	NE (0.28, NE)
MEDIAN	NE (NE, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.4155	
HAZARD RATIO (95 % CI) [4]	2.50 (0.25, 25.31)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 1 HOUR	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 1 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	8 (11.8)	5 (7.6)
CENSORED [2]	60 (88.2)	61 (92.4)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	NE (0.56, NE)	NE (NE, NE)
MEDIAN	NE (NE, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.5441	
HAZARD RATIO (95 % CI) [4]	1.41 (0.46, 4.34)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOUR	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.7716	
PROPHYLACTIC TREATMENT STATUS 1 = ON PROPHYLACTIC TREATMENT		
NUMBER OF IMP-TREATED HAE ATTACKS	19	18
EVENTS [1]	8 (42.1)	3 (16.7)
CENSORED [2]	11 (57.9)	15 (83.3)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.79 (0.34, 1.30)	NE (0.28, NE)
MEDIAN	NE (0.79, NE)	NE (1.29, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.1622	
HAZARD RATIO (95 % CI) [4]	2.50 (0.66, 9.43)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOUR	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 1 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	34 (50.0)	18 (27.3)
CENSORED [2]	34 (50.0)	48 (72.7)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.78 (0.56, 0.85)	1.32 (0.78, NE)
MEDIAN	1.33 (0.91, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0067†	
HAZARD RATIO (95 % CI) [4]	2.27 (1.26, 4.10)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.9014	
PROPHYLACTIC TREATMENT STATUS 1 = ON PROPHYLACTIC TREATMENT		
NUMBER OF IMP-TREATED HAE ATTACKS	19	18
EVENTS [1]	14 (73.7)	8 (44.4)
CENSORED [2]	5 (26.3)	10 (55.6)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.79 (0.34, 1.77)	2.28 (0.28, 2.99)
MEDIAN	1.85 (0.79, 3.47)	NE (2.28, NE)
75TH PERCENTILE	NE (1.85, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0591	
HAZARD RATIO (95 % CI) [4]	2.27 (0.95, 5.43)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 1 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	44 (64.7)	25 (37.9)
CENSORED [2]	24 (35.3)	41 (62.1)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.78 (0.77, 0.91)	1.31 (0.78, 1.88)
MEDIAN	1.35 (0.91, 1.83)	NE (1.88, NE)
75TH PERCENTILE	NE (1.83, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0015†	
HAZARD RATIO (95 % CI) [4]	2.32 (1.39, 3.86)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.7110	
PROPHYLACTIC TREATMENT STATUS 1 = ON PROPHYLACTIC TREATMENT		
NUMBER OF IMP-TREATED HAE ATTACKS	19	18
EVENTS [1]	14 (73.7)	9 (50.0)
CENSORED [2]	5 (26.3)	9 (50.0)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.79 (0.34, 1.77)	2.28 (0.28, 2.99)
MEDIAN	1.85 (0.79, 3.47)	NE (2.28, NE)
75TH PERCENTILE	NE (1.85, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0876	
HAZARD RATIO (95 % CI) [4]	2.05 (0.88, 4.77)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 1 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	45 (66.2)	25 (37.9)
CENSORED [2]	23 (33.8)	41 (62.1)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.78 (0.77, 0.91)	1.31 (0.78, 1.88)
MEDIAN	1.35 (0.98, 1.83)	NE (1.88, NE)
75TH PERCENTILE	NE (2.27, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0015†	
HAZARD RATIO (95 % CI) [4]	2.32 (1.40, 3.87)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.3935	
PROPHYLACTIC TREATMENT STATUS 1 = ON PROPHYLACTIC TREATMENT		
NUMBER OF IMP-TREATED HAE ATTACKS	19	18
EVENTS [1]	14 (73.7)	12 (66.7)
CENSORED [2]	5 (26.3)	6 (33.3)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.79 (0.34, 1.77)	2.28 (0.28, 2.99)
MEDIAN	1.85 (0.79, 3.47)	4.71 (2.28, NE)
75TH PERCENTILE	NE (1.85, NE)	NE (5.57, NE)
LOG-RANK P-VALUE	0.2514	
HAZARD RATIO (95 % CI) [4]	1.57 (0.72, 3.41)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 1 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	46 (67.6)	28 (42.4)
CENSORED [2]	22 (32.4)	38 (57.6)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.78 (0.77, 0.91)	1.32 (0.78, 1.88)
MEDIAN	1.35 (0.98, 1.83)	NE (1.88, NE)
75TH PERCENTILE	6.54 (2.27, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0018†	
HAZARD RATIO (95 % CI) [4]	2.21 (1.36, 3.60)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.2146	
PROPHYLACTIC TREATMENT STATUS 1 = ON PROPHYLACTIC TREATMENT		
NUMBER OF IMP-TREATED HAE ATTACKS	19	18
EVENTS [1]	14 (73.7)	13 (72.2)
CENSORED [2]	5 (26.3)	5 (27.8)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.79 (0.34, 1.77)	2.28 (0.28, 2.99)
MEDIAN	1.85 (0.79, 3.47)	4.71 (2.28, 8.30)
75TH PERCENTILE	NE (1.85, NE)	NE (5.57, NE)
LOG-RANK P-VALUE	0.3436	
HAZARD RATIO (95 % CI) [4]	1.44 (0.67, 3.08)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 1 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	49 (72.1)	28 (42.4)
CENSORED [2]	19 (27.9)	38 (57.6)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.78 (0.77, 0.91)	1.32 (0.78, 1.88)
MEDIAN	1.35 (0.98, 1.83)	NE (1.88, NE)
75TH PERCENTILE	6.54 (2.27, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0004†	
HAZARD RATIO (95 % CI) [4]	2.44 (1.50, 3.97)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.1935	
PROPHYLACTIC TREATMENT STATUS 1 = ON PROPHYLACTIC TREATMENT		
NUMBER OF IMP-TREATED HAE ATTACKS	19	18
EVENTS [1]	15 (78.9)	13 (72.2)
CENSORED [2]	4 (21.1)	5 (27.8)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.79 (0.34, 1.77)	2.28 (0.28, 2.99)
MEDIAN	1.85 (0.79, 3.47)	4.71 (2.28, 8.30)
75TH PERCENTILE	10.12 (1.85, NE)	NE (5.57, NE)
LOG-RANK P-VALUE	0.2621	
HAZARD RATIO (95 % CI) [4]	1.53 (0.72, 3.23)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 1 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	51 (75.0)	28 (42.4)
CENSORED [2]	17 (25.0)	38 (57.6)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.78 (0.77, 0.91)	1.32 (0.78, 1.88)
MEDIAN	1.35 (0.98, 1.83)	NE (2.04, NE)
75TH PERCENTILE	6.54 (2.27, NE)	NE (NE, NE)
LOG-RANK P-VALUE	<0.0001†	
HAZARD RATIO (95 % CI) [4]	2.62 (1.62, 4.24)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.4134	
PROPHYLACTIC TREATMENT STATUS 1 = ON PROPHYLACTIC TREATMENT		
NUMBER OF IMP-TREATED HAE ATTACKS	19	18
EVENTS [1]	16 (84.2)	13 (72.2)
CENSORED [2]	3 (15.8)	5 (27.8)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.79 (0.34, 1.77)	2.28 (0.28, 2.99)
MEDIAN	1.85 (0.79, 3.47)	4.71 (2.28, 8.30)
75TH PERCENTILE	10.12 (1.85, NE)	NE (5.57, NE)
LOG-RANK P-VALUE	0.1898	
HAZARD RATIO (95 % CI) [4]	1.63 (0.78, 3.40)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 1 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	53 (77.9)	35 (53.0)
CENSORED [2]	15 (22.1)	31 (47.0)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.78 (0.77, 0.98)	1.33 (0.79, 2.04)
MEDIAN	1.61 (1.03, 2.27)	15.87 (2.04, NE)
75TH PERCENTILE	8.51 (2.28, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0008†	
HAZARD RATIO (95 % CI) [4]	2.30 (1.45, 3.64)	

2.1.6 Prophylaxe-Status (Variante 2)

- PGI-C=Patient Global Impression of Change
- Time to beginning of symptom relief within 12 hours is defined as an HAE attack being rated “a little better” or higher on the PGI-C for two time points in a row within 12 hours of the first IMP administration.
- Time to beginning of symptom relief is calculated as Date/time of first rating of “a little better” or higher (i.e. better or much better) which is immediately followed by another rating of “a little better” or higher (without missing values in between) – Date/time of first IMP administration.
- [1] Attacks that achieved the described event within 12 hours.
- [2] Attacks are treated as right-censored at 12 hours if they did not achieve beginning of symptom relief defined by PGI-C as at least “a little better” (2 time points in a row) or received conventional attack treatment within 12 hours of the first IMP administration. In the case of discontinuation that prevented event “a little better” or higher HAE attack rating occurrence, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 2 consecutive post-baseline assessments, attacks will be censored at time 0.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 1 HOUR	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON KALLIKREIN		
NUMBER OF IMP-TREATED HAE ATTACKS	14	14
EVENTS [1]	3 (21.4)	1 (7.1)
CENSORED [2]	11 (78.6)	13 (92.9)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 1 HOUR	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON OTHER		
NUMBER OF IMP-TREATED HAE ATTACKS	5	4
EVENTS [1]	0	0
CENSORED [2]	5 (100)	4 (100)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 1 HOUR	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	8 (11.8)	5 (7.6)
CENSORED [2]	60 (88.2)	61 (92.4)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON KALLIKREIN		
NUMBER OF IMP-TREATED HAE ATTACKS	14	14
EVENTS [1]	4 (28.6)	2 (14.3)
CENSORED [2]	10 (71.4)	12 (85.7)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON OTHER		
NUMBER OF IMP-TREATED HAE ATTACKS	5	4
EVENTS [1]	4 (80.0)	1 (25.0)
CENSORED [2]	1 (20.0)	3 (75.0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	34 (50.0)	18 (27.3)
CENSORED [2]	34 (50.0)	48 (72.7)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON KALLIKREIN		
NUMBER OF IMP-TREATED HAE ATTACKS	14	14
EVENTS [1]	9 (64.3)	6 (42.9)
CENSORED [2]	5 (35.7)	8 (57.1)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON OTHER		
NUMBER OF IMP-TREATED HAE ATTACKS	5	4
EVENTS [1]	5 (100)	2 (50.0)
CENSORED [2]	0	2 (50.0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	44 (64.7)	25 (37.9)
CENSORED [2]	24 (35.3)	41 (62.1)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON KALLIKREIN		
NUMBER OF IMP-TREATED HAE ATTACKS	14	14
EVENTS [1]	9 (64.3)	7 (50.0)
CENSORED [2]	5 (35.7)	7 (50.0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON OTHER		
NUMBER OF IMP-TREATED HAE ATTACKS	5	4
EVENTS [1]	5 (100)	2 (50.0)
CENSORED [2]	0	2 (50.0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	45 (66.2)	25 (37.9)
CENSORED [2]	23 (33.8)	41 (62.1)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON KALLIKREIN		
NUMBER OF IMP-TREATED HAE ATTACKS	14	14
EVENTS [1]	9 (64.3)	10 (71.4)
CENSORED [2]	5 (35.7)	4 (28.6)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON OTHER		
NUMBER OF IMP-TREATED HAE ATTACKS	5	4
EVENTS [1]	5 (100)	2 (50.0)
CENSORED [2]	0	2 (50.0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	46 (67.6)	28 (42.4)
CENSORED [2]	22 (32.4)	38 (57.6)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON KALLIKREIN		
NUMBER OF IMP-TREATED HAE ATTACKS	14	14
EVENTS [1]	9 (64.3)	11 (78.6)
CENSORED [2]	5 (35.7)	3 (21.4)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON OTHER		
NUMBER OF IMP-TREATED HAE ATTACKS	5	4
EVENTS [1]	5 (100)	2 (50.0)
CENSORED [2]	0	2 (50.0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	49 (72.1)	28 (42.4)
CENSORED [2]	19 (27.9)	38 (57.6)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON KALLIKREIN		
NUMBER OF IMP-TREATED HAE ATTACKS	14	14
EVENTS [1]	10 (71.4)	11 (78.6)
CENSORED [2]	4 (28.6)	3 (21.4)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON OTHER		
NUMBER OF IMP-TREATED HAE ATTACKS	5	4
EVENTS [1]	5 (100)	2 (50.0)
CENSORED [2]	0	2 (50.0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	51 (75.0)	28 (42.4)
CENSORED [2]	17 (25.0)	38 (57.6)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON KALLIKREIN		
NUMBER OF IMP-TREATED HAE ATTACKS	14	14
EVENTS [1]	11 (78.6)	11 (78.6)
CENSORED [2]	3 (21.4)	3 (21.4)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON OTHER		
NUMBER OF IMP-TREATED HAE ATTACKS	5	4
EVENTS [1]	5 (100)	2 (50.0)
CENSORED [2]	0	2 (50.0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	53 (77.9)	35 (53.0)
CENSORED [2]	15 (22.1)	31 (47.0)

2.1.7 Attacken-Schwere (PGIS) zu Baseline

- PGI-C=Patient Global Impression of Change; CI=Confidence Interval; NE=Not Evaluable

- Time to beginning of symptom relief within 12 hours is defined as an HAE attack being rated “a little better” or higher on the PGI-C for two time points in a row within 12 hours of the first IMP administration.
- Time to beginning of symptom relief is calculated as Date/time of first rating of “a little better” or higher (i.e. better or much better) which is immediately followed by another rating of “a little better” or higher (without missing values in between) – Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for treatment, subgroup, and subgroup*treatment interaction in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that achieved the described event within 12 hours.
- [2] Attacks are treated as right-censored at 12 hours if they did not achieve beginning of symptom relief defined by PGI-C as at least “a little better” (2 time points in a row) or received conventional attack treatment within 12 hours of the first IMP administration. In the case of discontinuation that prevented event “a little better” or higher HAE attack rating occurrence, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 2 consecutive post-baseline assessments, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to beginning of symptom relief within 12 hours.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment in the model as a fixed effect and patient as a random effect.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 1 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = NONE OR MILD		
NUMBER OF IMP-TREATED HAE ATTACKS	36	38
EVENTS [1]	5 (13.9)	3 (7.9)
CENSORED [2]	31 (86.1)	35 (92.1)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 1 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = MODERATE		
NUMBER OF IMP-TREATED HAE ATTACKS	35	33
EVENTS [1]	4 (11.4)	2 (6.1)
CENSORED [2]	31 (88.6)	31 (93.9)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 1 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = SEVERE OR VERY SEVERE		
NUMBER OF IMP-TREATED HAE ATTACKS	14	13
EVENTS [1]	2 (14.3)	1 (7.7)
CENSORED [2]	12 (85.7)	12 (92.3)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.6078	
ATTACK SEVERITY AT BASELINE PGI-S = NONE OR MILD		
NUMBER OF IMP-TREATED HAE ATTACKS	36	38
EVENTS [1]	17 (47.2)	8 (21.1)
CENSORED [2]	19 (52.8)	30 (78.9)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.77 (0.28, 1.28)	NE (0.33, NE)
MEDIAN	1.35 (0.79, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0172†	
HAZARD RATIO (95 % CI) [4]	2.68 (1.15, 6.22)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = MODERATE		
NUMBER OF IMP-TREATED HAE ATTACKS	35	33
EVENTS [1]	16 (45.7)	10 (30.3)
CENSORED [2]	19 (54.3)	23 (69.7)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.78 (0.34, 1.03)	1.30 (0.30, NE)
MEDIAN	1.33 (0.85, NE)	NE (1.32, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.2381	
HAZARD RATIO (95 % CI) [4]	1.60 (0.73, 3.54)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 2 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = SEVERE OR VERY SEVERE		
NUMBER OF IMP-TREATED HAE ATTACKS	14	13
EVENTS [1]	9 (64.3)	3 (23.1)
CENSORED [2]	5 (35.7)	10 (76.9)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.79 (0.28, 1.30)	NE (0.28, NE)
MEDIAN	1.41 (0.78, NE)	NE (0.77, NE)
75TH PERCENTILE	NE (1.30, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0624	
HAZARD RATIO (95 % CI) [4]	3.11 (0.75, 12.91)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.3733	
ATTACK SEVERITY AT BASELINE PGI-S = NONE OR MILD		
NUMBER OF IMP-TREATED HAE ATTACKS	36	38
EVENTS [1]	25 (69.4)	15 (39.5)
CENSORED [2]	11 (30.6)	23 (60.5)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.78 (0.28, 1.28)	2.04 (0.33, 2.99)
MEDIAN	1.70 (0.84, 2.28)	NE (2.33, NE)
75TH PERCENTILE	3.47 (2.27, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0062†	
HAZARD RATIO (95 % CI) [4]	2.40 (1.26, 4.57)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = MODERATE		
NUMBER OF IMP-TREATED HAE ATTACKS	35	33
EVENTS [1]	22 (62.9)	15 (45.5)
CENSORED [2]	13 (37.1)	18 (54.5)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.78 (0.34, 1.28)	1.30 (0.78, 1.78)
MEDIAN	1.35 (0.85, 2.44)	2.07 (1.32, NE)
75TH PERCENTILE	NE (1.78, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0971	
HAZARD RATIO (95 % CI) [4]	1.80 (0.90, 3.57)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = SEVERE OR VERY SEVERE		
NUMBER OF IMP-TREATED HAE ATTACKS	14	13
EVENTS [1]	11 (78.6)	3 (23.1)
CENSORED [2]	3 (21.4)	10 (76.9)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.79 (0.28, 1.30)	NE (0.28, NE)
MEDIAN	1.41 (0.78, 2.78)	NE (0.77, NE)
75TH PERCENTILE	2.78 (1.30, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0138†	
HAZARD RATIO (95 % CI) [4]	4.39 (1.08, 17.84)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.5113	
ATTACK SEVERITY AT BASELINE PGI-S = NONE OR MILD		
NUMBER OF IMP-TREATED HAE ATTACKS	36	38
EVENTS [1]	25 (69.4)	15 (39.5)
CENSORED [2]	11 (30.6)	23 (60.5)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.78 (0.28, 1.28)	2.04 (0.33, 2.99)
MEDIAN	1.70 (0.84, 2.28)	NE (2.33, NE)
75TH PERCENTILE	3.47 (2.27, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0062†	
HAZARD RATIO (95 % CI) [4]	2.40 (1.26, 4.57)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = MODERATE		
NUMBER OF IMP-TREATED HAE ATTACKS	35	33
EVENTS [1]	23 (65.7)	15 (45.5)
CENSORED [2]	12 (34.3)	18 (54.5)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.78 (0.34, 1.28)	1.30 (0.78, 1.78)
MEDIAN	1.56 (0.85, 3.60)	2.07 (1.32, NE)
75TH PERCENTILE	NE (1.79, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0971	
HAZARD RATIO (95 % CI) [4]	1.77 (0.90, 3.47)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 6 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = SEVERE OR VERY SEVERE		
NUMBER OF IMP-TREATED HAE ATTACKS	14	13
EVENTS [1]	11 (78.6)	4 (30.8)
CENSORED [2]	3 (21.4)	9 (69.2)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.79 (0.28, 1.30)	2.69 (0.28, NE)
MEDIAN	1.41 (0.78, 2.78)	NE (0.77, NE)
75TH PERCENTILE	2.78 (1.30, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0235†	
HAZARD RATIO (95 % CI) [4]	3.66 (0.93, 14.42)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.3853	
ATTACK SEVERITY AT BASELINE PGI-S = NONE OR MILD		
NUMBER OF IMP-TREATED HAE ATTACKS	36	38
EVENTS [1]	25 (69.4)	19 (50.0)
CENSORED [2]	11 (30.6)	19 (50.0)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.78 (0.28, 1.28)	2.04 (0.78, 3.28)
MEDIAN	1.70 (0.84, 2.28)	6.72 (2.33, NE)
75TH PERCENTILE	3.47 (2.27, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0189†	
HAZARD RATIO (95 % CI) [4]	2.03 (1.11, 3.71)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = MODERATE		
NUMBER OF IMP-TREATED HAE ATTACKS	35	33
EVENTS [1]	24 (68.6)	17 (51.5)
CENSORED [2]	11 (31.4)	16 (48.5)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.78 (0.34, 1.28)	1.30 (0.78, 1.78)
MEDIAN	1.56 (0.85, 3.60)	2.07 (1.32, NE)
75TH PERCENTILE	NE (1.79, NE)	NE (5.57, NE)
LOG-RANK P-VALUE	0.1267	
HAZARD RATIO (95 % CI) [4]	1.62 (0.87, 3.01)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = SEVERE OR VERY SEVERE		
NUMBER OF IMP-TREATED HAE ATTACKS	14	13
EVENTS [1]	11 (78.6)	4 (30.8)
CENSORED [2]	3 (21.4)	9 (69.2)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.79 (0.28, 1.30)	2.69 (0.28, NE)
MEDIAN	1.41 (0.78, 2.78)	NE (0.77, NE)
75TH PERCENTILE	2.78 (1.30, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0235†	
HAZARD RATIO (95 % CI) [4]	3.66 (0.93, 14.42)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.4068	
ATTACK SEVERITY AT BASELINE PGI-S = NONE OR MILD		
NUMBER OF IMP-TREATED HAE ATTACKS	36	38
EVENTS [1]	27 (75.0)	20 (52.6)
CENSORED [2]	9 (25.0)	18 (47.4)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.78 (0.28, 1.28)	2.04 (0.78, 3.28)
MEDIAN	1.70 (0.84, 2.28)	6.72 (2.33, NE)
75TH PERCENTILE	3.47 (2.27, NE)	NE (8.30, NE)
LOG-RANK P-VALUE	0.0095†	
HAZARD RATIO (95 % CI) [4]	2.13 (1.19, 3.82)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = MODERATE		
NUMBER OF IMP-TREATED HAE ATTACKS	35	33
EVENTS [1]	25 (71.4)	17 (51.5)
CENSORED [2]	10 (28.6)	16 (48.5)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.78 (0.34, 1.28)	1.30 (0.78, 1.78)
MEDIAN	1.56 (0.85, 3.60)	2.07 (1.32, NE)
75TH PERCENTILE	7.95 (1.79, NE)	NE (5.57, NE)
LOG-RANK P-VALUE	0.0900	
HAZARD RATIO (95 % CI) [4]	1.70 (0.91, 3.14)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 10 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = SEVERE OR VERY SEVERE		
NUMBER OF IMP-TREATED HAE ATTACKS	14	13
EVENTS [1]	11 (78.6)	4 (30.8)
CENSORED [2]	3 (21.4)	9 (69.2)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.79 (0.28, 1.30)	2.69 (0.28, NE)
MEDIAN	1.41 (0.78, 2.78)	NE (0.77, NE)
75TH PERCENTILE	2.78 (1.30, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0235†	
HAZARD RATIO (95 % CI) [4]	3.66 (0.93, 14.42)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.4181	
ATTACK SEVERITY AT BASELINE PGI-S = NONE OR MILD		
NUMBER OF IMP-TREATED HAE ATTACKS	36	38
EVENTS [1]	29 (80.6)	20 (52.6)
CENSORED [2]	7 (19.4)	18 (47.4)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.78 (0.28, 1.28)	2.04 (0.78, 3.28)
MEDIAN	1.70 (0.84, 2.28)	7.22 (2.59, NE)
75TH PERCENTILE	3.47 (2.27, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0018†	
HAZARD RATIO (95 % CI) [4]	2.44 (1.37, 4.34)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = MODERATE		
NUMBER OF IMP-TREATED HAE ATTACKS	35	33
EVENTS [1]	26 (74.3)	17 (51.5)
CENSORED [2]	9 (25.7)	16 (48.5)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.78 (0.34, 1.28)	1.30 (0.78, 1.78)
MEDIAN	1.56 (0.85, 3.60)	2.07 (1.32, NE)
75TH PERCENTILE	7.95 (1.79, NE)	NE (5.57, NE)
LOG-RANK P-VALUE	0.0614	
HAZARD RATIO (95 % CI) [4]	1.78 (0.96, 3.29)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = SEVERE OR VERY SEVERE		
NUMBER OF IMP-TREATED HAE ATTACKS	14	13
EVENTS [1]	11 (78.6)	4 (30.8)
CENSORED [2]	3 (21.4)	9 (69.2)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.79 (0.28, 1.30)	2.69 (0.28, NE)
MEDIAN	1.41 (0.78, 2.78)	NE (0.77, NE)
75TH PERCENTILE	2.78 (1.30, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0235†	
HAZARD RATIO (95 % CI) [4]	3.66 (0.93, 14.42)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.5806	
ATTACK SEVERITY AT BASELINE PGI-S = NONE OR MILD		
NUMBER OF IMP-TREATED HAE ATTACKS	36	38
EVENTS [1]	30 (83.3)	23 (60.5)
CENSORED [2]	6 (16.7)	15 (39.5)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.78 (0.34, 1.28)	2.04 (0.78, 3.28)
MEDIAN	1.85 (0.91, 2.78)	7.22 (2.59, 22.78)
75TH PERCENTILE	7.65 (2.27, NE)	NE (15.04, NE)
LOG-RANK P-VALUE	0.0124†	
HAZARD RATIO (95 % CI) [4]	2.02 (1.16, 3.53)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = MODERATE		
NUMBER OF IMP-TREATED HAE ATTACKS	35	33
EVENTS [1]	27 (77.1)	18 (54.5)
CENSORED [2]	8 (22.9)	15 (45.5)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.79 (0.34, 1.28)	1.30 (0.78, 1.78)
MEDIAN	1.77 (0.98, 3.60)	3.80 (1.33, NE)
75TH PERCENTILE	9.36 (1.83, NE)	NE (17.53, NE)
LOG-RANK P-VALUE	0.0598	
HAZARD RATIO (95 % CI) [4]	1.76 (0.97, 3.21)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = SEVERE OR VERY SEVERE		
NUMBER OF IMP-TREATED HAE ATTACKS	14	13
EVENTS [1]	12 (85.7)	7 (53.8)
CENSORED [2]	2 (14.3)	6 (46.2)
TIME TO BEGINNING OF SYMPTOM RELIEF (95 % CI) [3]		
25TH PERCENTILE	0.79 (0.28, 1.30)	3.85 (0.28, 21.02)
MEDIAN	1.41 (0.78, 2.78)	21.02 (1.54, NE)
75TH PERCENTILE	2.78 (1.30, NE)	NE (16.71, NE)
LOG-RANK P-VALUE	0.0323†	
HAZARD RATIO (95 % CI) [4]	3.30 (0.89, 12.19)	

2.2 Zeit bis zum Beginn der Symptomverbesserung definiert als mindestens „besser“ im PGI-C

2.2.1 Geschlecht

- PGI-C=Patient Global Impression of Change; CI=Confidence Interval; NE=Not Evaluable
- Time to at least “better” on PGI-C is defined as having an HAE attack rating of “better” or higher at two consecutive time points or received conventional attack treatment within considered time of first IMP administration.
- Time to at least better at two time points in a row (hours) = Date/time of first rating of “better” or higher immediately followed by another rating of “better” or higher (with possible missing values in between) – Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for treatment, subgroup, and subgroup*treatment interaction in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if they did not have encountered the event. In the case of discontinuation that prevented the event, patient is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 2 post-baseline assessments, patient will be censored at time 0.
- [3] Kaplan-Meier estimates for time to at least “better” within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment in the model as a fixed effect and patient as a random effect.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.2498	
SEX = MALE		
NUMBER OF IMP-TREATED HAE ATTACKS	33	29
EVENTS [1]	22 (66.7)	5 (17.2)
CENSORED [2]	11 (33.3)	24 (82.8)
TIME TO AT LEAST "BETTER" (95 % CI) [3]		
25TH PERCENTILE	1.60 (0.79, 2.77)	NE (0.56, NE)
MEDIAN	4.54 (2.28, 9.54)	NE (NE, NE)
75TH PERCENTILE	NE (5.65, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0005†	
HAZARD RATIO (95 % CI) [4]	5.08 (1.89, 13.67)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
SEX = FEMALE		
NUMBER OF IMP-TREATED HAE ATTACKS	54	55
EVENTS [1]	31 (57.4)	16 (29.1)
CENSORED [2]	23 (42.6)	39 (70.9)
TIME TO AT LEAST "BETTER" (95 % CI) [3]		
25TH PERCENTILE	1.79 (1.28, 2.82)	5.90 (2.28, NE)
MEDIAN	6.40 (2.80, NE)	NE (NE, NE)
75TH PERCENTILE	NE (10.72, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0016†	
HAZARD RATIO (95 % CI) [4]	2.56 (1.40, 4.68)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.0693	
SEX = MALE		
NUMBER OF IMP-TREATED HAE ATTACKS	33	29
EVENTS [1]	27 (81.8)	10 (34.5)
CENSORED [2]	6 (18.2)	19 (65.5)
TIME TO AT LEAST "BETTER" (95 % CI) [3]		
25TH PERCENTILE	1.60 (0.79, 2.77)	13.12 (0.77, NE)
MEDIAN	4.54 (2.28, 9.54)	NE (13.74, NE)
75TH PERCENTILE	11.53 (5.65, NE)	NE (NE, NE)
LOG-RANK P-VALUE	<0.0001†	
HAZARD RATIO (95 % CI) [4]	5.11 (2.32, 11.25)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
SEX = FEMALE		
NUMBER OF IMP-TREATED HAE ATTACKS	54	55
EVENTS [1]	33 (61.1)	24 (43.6)
CENSORED [2]	21 (38.9)	31 (56.4)
TIME TO AT LEAST "BETTER" (95 % CI) [3]		
25TH PERCENTILE	1.82 (1.28, 2.82)	5.90 (2.28, 13.05)
MEDIAN	7.02 (2.82, 11.73)	NE (13.05, NE)
75TH PERCENTILE	NE (11.73, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0274†	
HAZARD RATIO (95 % CI) [4]	1.92 (1.11, 3.31)	

2.2.2 Alter

- PGI-C=Patient Global Impression of Change; CI=Confidence Interval; NE=Not Evaluable
- Time to at least “better” on PGI-C is defined as having an HAE attack rating of “better” or higher at two consecutive time points or received conventional attack treatment within considered time of first IMP administration.
- Time to at least better at two time points in a row (hours) = Date/time of first rating of “better” or higher immediately followed by another rating of “better” or higher (with possible missing values in between) – Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for treatment, subgroup, and subgroup*treatment interaction in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if they did not have encountered the event. In the case of discontinuation that prevented the event, patient is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 2 post-baseline assessments, patient will be censored at time 0.
- [3] Kaplan-Meier estimates for time to at least “better” within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment in the model as a fixed effect and patient as a random effect.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.4457	
AGE GROUP = <18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	10	9
EVENTS [1]	5 (50.0)	3 (33.3)
CENSORED [2]	5 (50.0)	6 (66.7)
TIME TO AT LEAST "BETTER" (95 % CI) [3]		
25TH PERCENTILE	2.69 (1.28, 8.34)	8.67 (0.56, NE)
MEDIAN	8.34 (1.28, NE)	NE (0.56, NE)
75TH PERCENTILE	NE (3.47, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.3945	
HAZARD RATIO (95 % CI) [4]	1.85 (0.44, 7.82)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
AGE GROUP = >=18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	77	75
EVENTS [1]	48 (62.3)	18 (24.0)
CENSORED [2]	29 (37.7)	57 (76.0)
TIME TO AT LEAST "BETTER" (95 % CI) [3]		
25TH PERCENTILE	1.69 (1.27, 2.77)	7.39 (2.34, NE)
MEDIAN	5.69 (2.80, 9.54)	NE (NE, NE)
75TH PERCENTILE	NE (10.72, NE)	NE (NE, NE)
LOG-RANK P-VALUE	<0.0001†	
HAZARD RATIO (95 % CI) [4]	3.37 (1.96, 5.81)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.3335	
AGE GROUP = <18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	10	9
EVENTS [1]	6 (60.0)	4 (44.4)
CENSORED [2]	4 (40.0)	5 (55.6)
TIME TO AT LEAST "BETTER" (95 % CI) [3]		
25TH PERCENTILE	2.69 (1.28, 11.53)	8.67 (0.56, NE)
MEDIAN	9.93 (1.28, NE)	NE (0.56, NE)
75TH PERCENTILE	NE (8.34, NE)	NE (13.12, NE)
LOG-RANK P-VALUE	0.5000	
HAZARD RATIO (95 % CI) [4]	1.54 (0.43, 5.51)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
AGE GROUP = >=18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	77	75
EVENTS [1]	54 (70.1)	30 (40.0)
CENSORED [2]	23 (29.9)	45 (60.0)
TIME TO AT LEAST "BETTER" (95 % CI) [3]		
25TH PERCENTILE	1.78 (1.27, 2.77)	8.54 (2.72, 14.38)
MEDIAN	5.73 (2.80, 9.54)	NE (17.88, NE)
75TH PERCENTILE	NE (10.12, NE)	NE (NE, NE)
LOG-RANK P-VALUE	<0.0001†	
HAZARD RATIO (95 % CI) [4]	2.97 (1.85, 4.78)	

2.2.3 Region (Variante 1)

- PGI-C=Patient Global Impression of Change; CI=Confidence Interval; NE=Not Evaluable
- Time to at least "better" on PGI-C is defined as having an HAE attack rating of "better" or higher at two consecutive time points or received conventional attack treatment within considered time of first IMP administration.
- Time to at least better at two time points in a row (hours) = Date/time of first rating of "better" or higher immediately followed by another rating of "better" or higher (with possible missing values in between) – Date/time of first IMP administration.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for treatment, subgroup, and subgroup*treatment interaction in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if they did not have encountered the event. In the case of discontinuation that prevented the event, patient is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 2 post-baseline assessments, patient will be censored at time 0.
- [3] Kaplan-Meier estimates for time to at least “better” within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment in the model as a fixed effect and patient as a random effect.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.5168	
REGION 1 = US		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	18 (66.7)	6 (26.1)
CENSORED [2]	9 (33.3)	17 (73.9)
TIME TO AT LEAST "BETTER" (95 % CI) [3]		
25TH PERCENTILE	1.46 (0.77, 2.78)	6.23 (1.27, NE)
MEDIAN	3.13 (1.60, 7.97)	NE (6.23, NE)
75TH PERCENTILE	NE (3.47, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0013†	
HAZARD RATIO (95 % CI) [4]	4.09 (1.61, 10.35)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 1 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	60	61
EVENTS [1]	35 (58.3)	15 (24.6)
CENSORED [2]	25 (41.7)	46 (75.4)
TIME TO AT LEAST "BETTER" (95 % CI) [3]		
25TH PERCENTILE	1.79 (0.98, 2.81)	8.54 (1.81, NE)
MEDIAN	7.52 (2.81, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0005†	
HAZARD RATIO (95 % CI) [4]	3.07 (1.64, 5.76)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.7750	
REGION 1 = US		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	19 (70.4)	11 (47.8)
CENSORED [2]	8 (29.6)	12 (52.2)
TIME TO AT LEAST "BETTER" (95 % CI) [3]		
25TH PERCENTILE	1.46 (0.77, 2.78)	6.23 (1.27, 14.38)
MEDIAN	3.13 (1.60, 7.97)	NE (6.23, NE)
75TH PERCENTILE	10.35 (3.47, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0079†	
HAZARD RATIO (95 % CI) [4]	2.67 (1.26, 5.68)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 1 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	60	61
EVENTS [1]	41 (68.3)	23 (37.7)
CENSORED [2]	19 (31.7)	38 (62.3)
TIME TO AT LEAST "BETTER" (95 % CI) [3]		
25TH PERCENTILE	1.79 (0.98, 3.59)	8.67 (1.81, 20.79)
MEDIAN	7.52 (3.59, 11.53)	NE (20.79, NE)
75TH PERCENTILE	NE (11.73, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0008†	
HAZARD RATIO (95 % CI) [4]	2.71 (1.57, 4.67)	

2.2.4 Region (Variante 2)

- PGI-C=Patient Global Impression of Change; CI=Confidence Interval; NE=Not Evaluable
- Time to at least “better” on PGI-C is defined as having an HAE attack rating of “better” or higher at two consecutive time points or received conventional attack treatment within considered time of first IMP administration.
- Time to at least better at two time points in a row (hours) = Date/time of first rating of “better” or higher immediately followed by another rating of “better” or higher (with possible missing values in between) – Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for treatment, subgroup, and subgroup*treatment interaction in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if they did not have encountered the event. In the case of discontinuation that prevented the event, patient is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 2 post-baseline assessments, patient will be censored at time 0.
- [3] Kaplan-Meier estimates for time to at least “better” within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment in the model as a fixed effect and patient as a random effect.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.2315	
REGION 2 = NORTH AMERICA		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	18 (66.7)	6 (26.1)
CENSORED [2]	9 (33.3)	17 (73.9)
TIME TO AT LEAST "BETTER" (95 % CI) [3]		
25TH PERCENTILE	1.46 (0.77, 2.78)	6.23 (1.27, NE)
MEDIAN	3.13 (1.60, 7.97)	NE (6.23, NE)
75TH PERCENTILE	NE (3.47, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0013†	
HAZARD RATIO (95 % CI) [4]	4.09 (1.61, 10.35)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = EUROPE		
NUMBER OF IMP-TREATED HAE ATTACKS	44	48
EVENTS [1]	23 (52.3)	13 (27.1)
CENSORED [2]	21 (47.7)	35 (72.9)
TIME TO AT LEAST "BETTER" (95 % CI) [3]		
25TH PERCENTILE	2.28 (1.27, 4.54)	3.77 (1.79, NE)
MEDIAN	9.54 (3.59, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0294†	
HAZARD RATIO (95 % CI) [4]	2.31 (1.13, 4.70)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	16	13
EVENTS [1]	12 (75.0)	2 (15.4)
CENSORED [2]	4 (25.0)	11 (84.6)
TIME TO AT LEAST "BETTER" (95 % CI) [3]		
25TH PERCENTILE	0.91 (0.28, 2.69)	NE (0.77, NE)
MEDIAN	5.21 (0.83, 8.34)	NE (1.55, NE)
75TH PERCENTILE	10.72 (5.21, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0027†	
HAZARD RATIO (95 % CI) [4]	8.47 (1.81, 39.66)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.2669	
REGION 2 = NORTH AMERICA		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	19 (70.4)	11 (47.8)
CENSORED [2]	8 (29.6)	12 (52.2)
TIME TO AT LEAST "BETTER" (95 % CI) [3]		
25TH PERCENTILE	1.46 (0.77, 2.78)	6.23 (1.27, 14.38)
MEDIAN	3.13 (1.60, 7.97)	NE (6.23, NE)
75TH PERCENTILE	10.35 (3.47, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0079†	
HAZARD RATIO (95 % CI) [4]	2.67 (1.26, 5.68)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = EUROPE		
NUMBER OF IMP-TREATED HAE ATTACKS	44	48
EVENTS [1]	29 (65.9)	19 (39.6)
CENSORED [2]	15 (34.1)	29 (60.4)
TIME TO AT LEAST "BETTER" (95 % CI) [3]		
25TH PERCENTILE	2.28 (1.27, 5.65)	8.54 (1.81, 16.71)
MEDIAN	9.54 (3.59, 20.79)	NE (14.29, NE)
75TH PERCENTILE	NE (15.10, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0196†	
HAZARD RATIO (95 % CI) [4]	2.23 (1.20, 4.14)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	16	13
EVENTS [1]	12 (75.0)	4 (30.8)
CENSORED [2]	4 (25.0)	9 (69.2)
TIME TO AT LEAST "BETTER" (95 % CI) [3]		
25TH PERCENTILE	0.91 (0.28, 2.69)	17.14 (0.77, NE)
MEDIAN	5.21 (0.83, 8.34)	NE (1.55, NE)
75TH PERCENTILE	10.72 (5.21, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0093†	
HAZARD RATIO (95 % CI) [4]	5.67 (1.62, 19.88)	

2.2.5 Prophylaxe-Status (Variante 1)

- PGI-C=Patient Global Impression of Change; CI=Confidence Interval; NE=Not Evaluable
- Time to at least “better” on PGI-C is defined as having an HAE attack rating of “better” or higher at two consecutive time points or received conventional attack treatment within considered time of first IMP administration.
- Time to at least better at two time points in a row (hours) = Date/time of first rating of “better” or higher immediately followed by another rating of “better” or higher (with possible missing values in between) – Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for treatment, subgroup, and subgroup*treatment interaction in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if they did not have encountered the event. In the case of discontinuation that prevented the event, patient is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 2 post-baseline assessments, patient will be censored at time 0.
- [3] Kaplan-Meier estimates for time to at least “better” within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment in the model as a fixed effect and patient as a random effect.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.0627	
PROPHYLACTIC TREATMENT STATUS 1 = ON PROPHYLACTIC TREATMENT		
NUMBER OF IMP-TREATED HAE ATTACKS	19	18
EVENTS [1]	12 (63.2)	8 (44.4)
CENSORED [2]	7 (36.8)	10 (55.6)
TIME TO AT LEAST "BETTER" (95 % CI) [3]		
25TH PERCENTILE	2.82 (0.34, 6.53)	2.91 (0.77, 6.23)
MEDIAN	7.52 (2.82, NE)	NE (2.91, NE)
75TH PERCENTILE	NE (7.52, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.3954	
HAZARD RATIO (95 % CI) [4]	1.47 (0.60, 3.60)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 1 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	41 (60.3)	13 (19.7)
CENSORED [2]	27 (39.7)	53 (80.3)
TIME TO AT LEAST "BETTER" (95 % CI) [3]		
25TH PERCENTILE	1.60 (1.27, 2.43)	NE (2.07, NE)
MEDIAN	4.88 (2.43, 9.54)	NE (NE, NE)
75TH PERCENTILE	NE (10.72, NE)	NE (NE, NE)
LOG-RANK P-VALUE	<0.0001†	
HAZARD RATIO (95 % CI) [4]	4.35 (2.30, 8.20)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.0120†	
PROPHYLACTIC TREATMENT STATUS 1 = ON PROPHYLACTIC TREATMENT		
NUMBER OF IMP-TREATED HAE ATTACKS	19	18
EVENTS [1]	14 (73.7)	13 (72.2)
CENSORED [2]	5 (26.3)	5 (27.8)
TIME TO AT LEAST "BETTER" (95 % CI) [3]		
25TH PERCENTILE	2.82 (0.34, 6.53)	2.91 (0.77, 6.23)
MEDIAN	7.52 (2.82, 15.10)	11.47 (2.91, 17.88)
75TH PERCENTILE	NE (7.52, NE)	NE (13.05, NE)
LOG-RANK P-VALUE	0.7736	
HAZARD RATIO (95 % CI) [4]	1.12 (0.52, 2.38)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 1 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	46 (67.6)	21 (31.8)
CENSORED [2]	22 (32.4)	45 (68.2)
TIME TO AT LEAST "BETTER" (95 % CI) [3]		
25TH PERCENTILE	1.69 (1.27, 2.43)	13.12 (2.34, NE)
MEDIAN	5.43 (2.69, 9.54)	NE (NE, NE)
75TH PERCENTILE	NE (10.72, NE)	NE (NE, NE)
LOG-RANK P-VALUE	<0.0001†	
HAZARD RATIO (95 % CI) [4]	3.67 (2.13, 6.33)	

2.2.6 Prophylaxe-Status (Variante 2)

- PGI-C=Patient Global Impression of Change
- Time to at least “better” on PGI-C is defined as having an HAE attack rating of “better” or higher at two consecutive time points or received conventional attack treatment within considered time of first IMP administration.
- Time to at least better at two time points in a row (hours) = Date/time of first rating of “better” or higher immediately followed by another rating of “better” or higher (with possible missing values in between) – Date/time of first IMP administration.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if they did not have encountered the event. In the case of discontinuation that prevented the event, patient is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 2 post-baseline assessments, patient will be censored at time 0.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON KALLIKREIN		
NUMBER OF IMP-TREATED HAE ATTACKS	14	14
EVENTS [1]	10 (71.4)	8 (57.1)
CENSORED [2]	4 (28.6)	6 (42.9)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON OTHER		
NUMBER OF IMP-TREATED HAE ATTACKS	5	4
EVENTS [1]	2 (40.0)	0
CENSORED [2]	3 (60.0)	4 (100)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	41 (60.3)	13 (19.7)
CENSORED [2]	27 (39.7)	53 (80.3)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON KALLIKREIN		
NUMBER OF IMP-TREATED HAE ATTACKS	14	14
EVENTS [1]	11 (78.6)	11 (78.6)
CENSORED [2]	3 (21.4)	3 (21.4)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON OTHER		
NUMBER OF IMP-TREATED HAE ATTACKS	5	4
EVENTS [1]	3 (60.0)	2 (50.0)
CENSORED [2]	2 (40.0)	2 (50.0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	46 (67.6)	21 (31.8)
CENSORED [2]	22 (32.4)	45 (68.2)

2.2.7 Attacken-Schwere (PGIS) zu Baseline

- PGI-C=Patient Global Impression of Change; CI=Confidence Interval; NE=Not Evaluable
- Time to at least “better” on PGI-C is defined as having an HAE attack rating of “better” or higher at two consecutive time points or received conventional attack treatment within considered time of first IMP administration.
- Time to at least better at two time points in a row (hours) = Date/time of first rating of “better” or higher immediately followed by another rating of “better” or higher (with possible missing values in between) – Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for treatment, subgroup, and subgroup*treatment interaction in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if they did not have encountered the event. In the case of discontinuation that prevented the event, patient is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 2 post-baseline assessments, patient will be censored at time 0.
- [3] Kaplan-Meier estimates for time to at least “better” within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment in the model as a fixed effect and patient as a random effect.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.3793	
ATTACK SEVERITY AT BASELINE PGI-S = NONE OR MILD		
NUMBER OF IMP-TREATED HAE ATTACKS	36	38
EVENTS [1]	23 (63.9)	9 (23.7)
CENSORED [2]	13 (36.1)	29 (76.3)
TIME TO AT LEAST "BETTER" (95 % CI) [3]		
25TH PERCENTILE	1.37 (0.83, 2.69)	NE (1.55, NE)
MEDIAN	4.49 (1.79, 11.46)	NE (NE, NE)
75TH PERCENTILE	NE (7.97, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0005†	
HAZARD RATIO (95 % CI) [4]	3.62 (1.67, 7.85)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = MODERATE		
NUMBER OF IMP-TREATED HAE ATTACKS	35	33
EVENTS [1]	20 (57.1)	10 (30.3)
CENSORED [2]	15 (42.9)	23 (69.7)
TIME TO AT LEAST "BETTER" (95 % CI) [3]		
25TH PERCENTILE	2.07 (1.29, 3.59)	5.57 (1.79, NE)
MEDIAN	6.31 (2.77, NE)	NE (8.54, NE)
75TH PERCENTILE	NE (10.12, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0371†	
HAZARD RATIO (95 % CI) [4]	2.20 (1.03, 4.71)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = SEVERE OR VERY SEVERE		
NUMBER OF IMP-TREATED HAE ATTACKS	14	13
EVENTS [1]	10 (71.4)	2 (15.4)
CENSORED [2]	4 (28.6)	11 (84.6)
TIME TO AT LEAST "BETTER" (95 % CI) [3]		
25TH PERCENTILE	2.28 (0.77, 4.54)	NE (1.27, NE)
MEDIAN	5.14 (0.81, NE)	NE (3.77, NE)
75TH PERCENTILE	NE (4.54, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0079†	
HAZARD RATIO (95 % CI) [4]	6.71 (1.22, 36.79)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.2491	
ATTACK SEVERITY AT BASELINE PGI-S = NONE OR MILD		
NUMBER OF IMP-TREATED HAE ATTACKS	36	38
EVENTS [1]	26 (72.2)	12 (31.6)
CENSORED [2]	10 (27.8)	26 (68.4)
TIME TO AT LEAST "BETTER" (95 % CI) [3]		
25TH PERCENTILE	1.37 (0.83, 2.69)	9.64 (1.55, NE)
MEDIAN	5.51 (1.79, 10.58)	NE (17.88, NE)
75TH PERCENTILE	NE (8.34, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0004†	
HAZARD RATIO (95 % CI) [4]	3.85 (1.83, 8.13)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = MODERATE		
NUMBER OF IMP-TREATED HAE ATTACKS	35	33
EVENTS [1]	23 (65.7)	16 (48.5)
CENSORED [2]	12 (34.3)	17 (51.5)
TIME TO AT LEAST "BETTER" (95 % CI) [3]		
25TH PERCENTILE	2.28 (1.29, 3.59)	5.57 (1.79, 11.53)
MEDIAN	6.53 (2.82, 11.53)	21.13 (8.67, NE)
75TH PERCENTILE	NE (10.12, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0957	
HAZARD RATIO (95 % CI) [4]	1.87 (0.93, 3.77)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = SEVERE OR VERY SEVERE		
NUMBER OF IMP-TREATED HAE ATTACKS	14	13
EVENTS [1]	11 (78.6)	6 (46.2)
CENSORED [2]	3 (21.4)	7 (53.8)
TIME TO AT LEAST "BETTER" (95 % CI) [3]		
25TH PERCENTILE	2.28 (0.77, 4.54)	14.38 (1.27, NE)
MEDIAN	5.14 (0.81, 15.10)	NE (13.02, NE)
75TH PERCENTILE	15.10 (4.54, NE)	NE (20.79, NE)
LOG-RANK P-VALUE	0.0251†	
HAZARD RATIO (95 % CI) [4]	4.69 (1.12, 19.73)	

2.3 Zeit bis zum ersten Auftreten einer Verschlechterung der Symptome definiert als mindestens „ein wenig schlechter“ im PGI-C oder Verwendung konventioneller Akuttherapien

2.3.1 Geschlecht

- PGI-C=Patient Global Impression of Change; CI=Confidence Interval; NE=Not Evaluable
- Time to HAE attack being rated “a little worse” or lower for 2 time points in a row on the PGI-C (hours) = Date/time of first rating of “a little worse” or lower (i.e. worse or much worse) which is immediately followed by another rating of “a little worse” or lower (with possible missing values in between) – Date/time of first IMP administration.
- Time to conventional attack treatment use (hours) = Date/time of first conventional attack treatment use – Date/time of study drug administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for treatment, subgroup, and subgroup*treatment interaction in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if they did not achieve this endpoint within considered time of the first IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 2 post-baseline assessments, patients will be censored at time 0.
- [3] Kaplan-Meier model estimates for the time to the first incidence of PGI-C being rated ‘a little worse’ or lower for two time points in a row, or use of conventional attack treatment within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment in the model as a fixed effect and patient as a random effect.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.1399	
SEX = MALE		
NUMBER OF IMP-TREATED HAE ATTACKS	33	29
EVENTS [1]	4 (12.1)	11 (37.9)
CENSORED [2]	29 (87.9)	18 (62.1)
TIME TO FIRST INCIDENCE OF PGI-C BEING RATED "A LITTLE WORSE" OR LOWER OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	NE (1.78, NE)	1.52 (0.28, 6.88)
MEDIAN	NE (NE, NE)	NE (2.04, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0098†	
HAZARD RATIO (95 % CI) [4]	0.24 (0.07, 0.76)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
SEX = FEMALE		
NUMBER OF IMP-TREATED HAE ATTACKS	54	55
EVENTS [1]	17 (31.5)	26 (47.3)
CENSORED [2]	37 (68.5)	29 (52.7)
TIME TO FIRST INCIDENCE OF PGI-C BEING RATED "A LITTLE WORSE" OR LOWER OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	8.33 (2.80, NE)	2.56 (1.32, 5.03)
MEDIAN	NE (NE, NE)	NE (5.03, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0644	
HAZARD RATIO (95 % CI) [4]	0.47 (0.24, 0.90)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.1001	
SEX = MALE		
NUMBER OF IMP-TREATED HAE ATTACKS	33	29
EVENTS [1]	5 (15.2)	13 (44.8)
CENSORED [2]	28 (84.8)	16 (55.2)
TIME TO FIRST INCIDENCE OF PGI-C BEING RATED "A LITTLE WORSE" OR LOWER OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	NE (1.78, NE)	1.52 (0.77, 6.88)
MEDIAN	NE (NE, NE)	NE (2.04, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0090†	
HAZARD RATIO (95 % CI) [4]	0.25 (0.09, 0.74)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
SEX = FEMALE		
NUMBER OF IMP-TREATED HAE ATTACKS	54	55
EVENTS [1]	22 (40.7)	27 (49.1)
CENSORED [2]	32 (59.3)	28 (50.9)
TIME TO FIRST INCIDENCE OF PGI-C BEING RATED "A LITTLE WORSE" OR LOWER OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	8.72 (2.80, 16.45)	2.56 (1.32, 5.03)
MEDIAN	NE (16.45, NE)	11.36 (5.03, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.1549	
HAZARD RATIO (95 % CI) [4]	0.57 (0.31, 1.04)	

2.3.2 Alter

- PGI-C=Patient Global Impression of Change; CI=Confidence Interval; NE=Not Evaluable
- Time to HAE attack being rated “a little worse” or lower for 2 time points in a row on the PGI-C (hours) = Date/time of first rating of “a little worse” or lower (i.e. worse or much worse) which is immediately followed by another rating of “a little worse” or lower (with possible missing values in between) – Date/time of first IMP administration.
- Time to conventional attack treatment use (hours) = Date/time of first conventional attack treatment use – Date/time of study drug administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for treatment, subgroup, and subgroup*treatment interaction in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if they did not achieve this endpoint within considered time of the first IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 2 post-baseline assessments, patients will be censored at time 0.
- [3] Kaplan-Meier model estimates for the time to the first incidence of PGI-C being rated ‘a little worse’ or lower for two time points in a row, or use of conventional attack treatment within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment in the model as a fixed effect and patient as a random effect.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.8074	
AGE GROUP = <18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	10	9
EVENTS [1]	3 (30.0)	6 (66.7)
CENSORED [2]	7 (70.0)	3 (33.3)
TIME TO FIRST INCIDENCE OF PGI-C BEING RATED "A LITTLE WORSE" OR LOWER OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	7.12 (0.28, NE)	1.46 (1.28, 5.82)
MEDIAN	NE (0.28, NE)	5.82 (1.28, NE)
75TH PERCENTILE	NE (NE, NE)	NE (5.00, NE)
LOG-RANK P-VALUE	0.2434	
HAZARD RATIO (95 % CI) [4]	0.45 (0.11, 1.88)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
AGE GROUP = >=18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	77	75
EVENTS [1]	18 (23.4)	31 (41.3)
CENSORED [2]	59 (76.6)	44 (58.7)
TIME TO FIRST INCIDENCE OF PGI-C BEING RATED "A LITTLE WORSE" OR LOWER OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	NE (4.63, NE)	2.33 (1.32, 4.52)
MEDIAN	NE (NE, NE)	NE (5.42, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0055†	
HAZARD RATIO (95 % CI) [4]	0.37 (0.20, 0.69)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.6335	
AGE GROUP = <18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	10	9
EVENTS [1]	3 (30.0)	6 (66.7)
CENSORED [2]	7 (70.0)	3 (33.3)
TIME TO FIRST INCIDENCE OF PGI-C BEING RATED "A LITTLE WORSE" OR LOWER OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	7.12 (0.28, NE)	1.46 (1.28, 5.82)
MEDIAN	NE (0.28, NE)	5.82 (1.28, NE)
75TH PERCENTILE	NE (NE, NE)	NE (5.00, NE)
LOG-RANK P-VALUE	0.1715	
HAZARD RATIO (95 % CI) [4]	0.39 (0.09, 1.60)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
AGE GROUP = >=18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	77	75
EVENTS [1]	24 (31.2)	34 (45.3)
CENSORED [2]	53 (68.8)	41 (54.7)
TIME TO FIRST INCIDENCE OF PGI-C BEING RATED "A LITTLE WORSE" OR LOWER OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	15.35 (4.63, NE)	2.34 (1.38, 5.03)
MEDIAN	NE (NE, NE)	NE (6.15, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0220†	
HAZARD RATIO (95 % CI) [4]	0.47 (0.27, 0.82)	

2.3.3 Region (Variante 1)

- PGI-C=Patient Global Impression of Change; CI=Confidence Interval; NE=Not Evaluable
- Time to HAE attack being rated “a little worse” or lower for 2 time points in a row on the PGI-C (hours) = Date/time of first rating of “a little worse” or lower (i.e. worse or much worse) which is immediately followed by another rating of “a little worse” or lower (with possible missing values in between) – Date/time of first IMP administration.
- Time to conventional attack treatment use (hours) = Date/time of first conventional attack treatment use – Date/time of study drug administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for treatment, subgroup, and subgroup*treatment interaction in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if they did not achieve this endpoint within considered time of the first IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 2 post-baseline assessments, patients will be censored at time 0.
- [3] Kaplan-Meier model estimates for the time to the first incidence of PGI-C being rated ‘a little worse’ or lower for two time points in a row, or use of conventional attack treatment within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment in the model as a fixed effect and patient as a random effect.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.6273	
REGION 1 = US		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	5 (18.5)	10 (43.5)
CENSORED [2]	22 (81.5)	13 (56.5)
TIME TO FIRST INCIDENCE OF PGI-C BEING RATED "A LITTLE WORSE" OR LOWER OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	NE (2.34, NE)	2.79 (0.28, 6.75)
MEDIAN	NE (NE, NE)	NE (2.79, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0496†	
HAZARD RATIO (95 % CI) [4]	0.29 (0.10, 0.91)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 1 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	60	61
EVENTS [1]	16 (26.7)	27 (44.3)
CENSORED [2]	44 (73.3)	34 (55.7)
TIME TO FIRST INCIDENCE OF PGI-C BEING RATED "A LITTLE WORSE" OR LOWER OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	12.00 (2.68, NE)	1.78 (1.29, 4.52)
MEDIAN	NE (NE, NE)	NE (4.52, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0174†	
HAZARD RATIO (95 % CI) [4]	0.43 (0.22, 0.83)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.7484	
REGION 1 = US		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	8 (29.6)	10 (43.5)
CENSORED [2]	19 (70.4)	13 (56.5)
TIME TO FIRST INCIDENCE OF PGI-C BEING RATED "A LITTLE WORSE" OR LOWER OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	12.87 (2.34, NE)	2.79 (0.28, 6.75)
MEDIAN	NE (15.35, NE)	NE (2.79, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.2231	
HAZARD RATIO (95 % CI) [4]	0.50 (0.19, 1.32)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 1 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	60	61
EVENTS [1]	19 (31.7)	30 (49.2)
CENSORED [2]	41 (68.3)	31 (50.8)
TIME TO FIRST INCIDENCE OF PGI-C BEING RATED "A LITTLE WORSE" OR LOWER OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	14.00 (2.68, NE)	2.04 (1.29, 5.03)
MEDIAN	NE (NE, NE)	16.37 (5.03, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0168†	
HAZARD RATIO (95 % CI) [4]	0.44 (0.24, 0.82)	

2.3.4 Region (Variante 2)

- PGI-C=Patient Global Impression of Change; CI=Confidence Interval; NE=Not Evaluable
- Time to HAE attack being rated “a little worse” or lower for 2 time points in a row on the PGI-C (hours) = Date/time of first rating of “a little worse” or lower (i.e. worse or much worse) which is immediately followed by another rating of “a little worse” or lower (with possible missing values in between) – Date/time of first IMP administration.
- Time to conventional attack treatment use (hours) = Date/time of first conventional attack treatment use – Date/time of study drug administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for treatment, subgroup, and subgroup*treatment interaction in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if they did not achieve this endpoint within considered time of the first IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 2 post-baseline assessments, patients will be censored at time 0.
- [3] Kaplan-Meier model estimates for the time to the first incidence of PGI-C being rated ‘a little worse’ or lower for two time points in a row, or use of conventional attack treatment within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment in the model as a fixed effect and patient as a random effect.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.7149	
REGION 2 = NORTH AMERICA		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	5 (18.5)	10 (43.5)
CENSORED [2]	22 (81.5)	13 (56.5)
TIME TO FIRST INCIDENCE OF PGI-C BEING RATED "A LITTLE WORSE" OR LOWER OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	NE (2.34, NE)	2.79 (0.28, 6.75)
MEDIAN	NE (NE, NE)	NE (2.79, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0496†	
HAZARD RATIO (95 % CI) [4]	0.29 (0.10, 0.91)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = EUROPE		
NUMBER OF IMP-TREATED HAE ATTACKS	44	48
EVENTS [1]	13 (29.5)	21 (43.8)
CENSORED [2]	31 (70.5)	27 (56.3)
TIME TO FIRST INCIDENCE OF PGI-C BEING RATED "A LITTLE WORSE" OR LOWER OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	10.55 (1.28, NE)	1.46 (0.95, 4.20)
MEDIAN	NE (NE, NE)	NE (3.82, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0749	
HAZARD RATIO (95 % CI) [4]	0.51 (0.24, 1.06)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	16	13
EVENTS [1]	3 (18.8)	6 (46.2)
CENSORED [2]	13 (81.3)	7 (53.8)
TIME TO FIRST INCIDENCE OF PGI-C BEING RATED "A LITTLE WORSE" OR LOWER OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	NE (2.54, NE)	5.23 (1.29, 11.20)
MEDIAN	NE (6.53, NE)	NE (2.04, NE)
75TH PERCENTILE	NE (NE, NE)	NE (11.20, NE)
LOG-RANK P-VALUE	0.1149	
HAZARD RATIO (95 % CI) [4]	0.29 (0.07, 1.20)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.9082	
REGION 2 = NORTH AMERICA		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	8 (29.6)	10 (43.5)
CENSORED [2]	19 (70.4)	13 (56.5)
TIME TO FIRST INCIDENCE OF PGI-C BEING RATED "A LITTLE WORSE" OR LOWER OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	12.87 (2.34, NE)	2.79 (0.28, 6.75)
MEDIAN	NE (15.35, NE)	NE (2.79, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.2231	
HAZARD RATIO (95 % CI) [4]	0.50 (0.19, 1.32)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = EUROPE		
NUMBER OF IMP-TREATED HAE ATTACKS	44	48
EVENTS [1]	15 (34.1)	24 (50.0)
CENSORED [2]	29 (65.9)	24 (50.0)
TIME TO FIRST INCIDENCE OF PGI-C BEING RATED "A LITTLE WORSE" OR LOWER OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	12.28 (1.28, NE)	1.52 (1.28, 4.20)
MEDIAN	NE (24.00, NE)	16.37 (4.00, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0504	
HAZARD RATIO (95 % CI) [4]	0.49 (0.25, 0.98)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	16	13
EVENTS [1]	4 (25.0)	6 (46.2)
CENSORED [2]	12 (75.0)	7 (53.8)
TIME TO FIRST INCIDENCE OF PGI-C BEING RATED "A LITTLE WORSE" OR LOWER OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	16.45 (2.54, NE)	5.23 (1.29, 11.20)
MEDIAN	NE (6.53, NE)	NE (2.04, NE)
75TH PERCENTILE	NE (NE, NE)	NE (11.20, NE)
LOG-RANK P-VALUE	0.1984	
HAZARD RATIO (95 % CI) [4]	0.34 (0.09, 1.30)	

2.3.5 Prophylaxe-Status (Variante 1)

- PGI-C=Patient Global Impression of Change; CI=Confidence Interval; NE=Not Evaluable
- Time to HAE attack being rated “a little worse” or lower for 2 time points in a row on the PGI-C (hours) = Date/time of first rating of “a little worse” or lower (i.e. worse or much worse) which is immediately followed by another rating of “a little worse” or lower (with possible missing values in between) – Date/time of first IMP administration.
- Time to conventional attack treatment use (hours) = Date/time of first conventional attack treatment use – Date/time of study drug administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for treatment, subgroup, and subgroup*treatment interaction in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if they did not achieve this endpoint within considered time of the first IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 2 post-baseline assessments, patients will be censored at time 0.
- [3] Kaplan-Meier model estimates for the time to the first incidence of PGI-C being rated ‘a little worse’ or lower for two time points in a row, or use of conventional attack treatment within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment in the model as a fixed effect and patient as a random effect.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.2833	
PROPHYLACTIC TREATMENT STATUS 1 = ON PROPHYLACTIC TREATMENT		
NUMBER OF IMP-TREATED HAE ATTACKS	19	18
EVENTS [1]	6 (31.6)	6 (33.3)
CENSORED [2]	13 (68.4)	12 (66.7)
TIME TO FIRST INCIDENCE OF PGI-C BEING RATED "A LITTLE WORSE" OR LOWER OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	8.33 (2.34, NE)	2.79 (0.95, NE)
MEDIAN	NE (8.33, NE)	NE (2.79, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.7075	
HAZARD RATIO (95 % CI) [4]	0.60 (0.18, 2.02)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 1 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	15 (22.1)	31 (47.0)
CENSORED [2]	53 (77.9)	35 (53.0)
TIME TO FIRST INCIDENCE OF PGI-C BEING RATED "A LITTLE WORSE" OR LOWER OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	NE (2.80, NE)	2.04 (1.29, 4.52)
MEDIAN	NE (NE, NE)	9.21 (4.52, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0012†	
HAZARD RATIO (95 % CI) [4]	0.34 (0.18, 0.65)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.2430	
PROPHYLACTIC TREATMENT STATUS 1 = ON PROPHYLACTIC TREATMENT		
NUMBER OF IMP-TREATED HAE ATTACKS	19	18
EVENTS [1]	7 (36.8)	6 (33.3)
CENSORED [2]	12 (63.2)	12 (66.7)
TIME TO FIRST INCIDENCE OF PGI-C BEING RATED "A LITTLE WORSE" OR LOWER OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	8.33 (2.34, NE)	2.79 (0.95, NE)
MEDIAN	NE (8.33, NE)	NE (2.79, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.9263	
HAZARD RATIO (95 % CI) [4]	0.77 (0.24, 2.44)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 1 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	20 (29.4)	34 (51.5)
CENSORED [2]	48 (70.6)	32 (48.5)
TIME TO FIRST INCIDENCE OF PGI-C BEING RATED "A LITTLE WORSE" OR LOWER OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	15.23 (2.80, NE)	2.27 (1.29, 4.52)
MEDIAN	NE (NE, NE)	11.20 (5.03, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0032†	
HAZARD RATIO (95 % CI) [4]	0.40 (0.22, 0.72)	

2.3.6 Prophylaxe-Status (Variante 2)

- PGI-C=Patient Global Impression of Change
- Time to HAE attack being rated “a little worse” or lower for 2 time points in a row on the PGI-C (hours) = Date/time of first rating of “a little worse” or lower (i.e. worse or much worse) which is immediately followed by another rating of “a little worse” or lower (with possible missing values in between) – Date/time of first IMP administration.
- Time to conventional attack treatment use (hours) = Date/time of first conventional attack treatment use – Date/time of study drug administration.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if they did not achieve this endpoint within considered time of the first IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 2 post-baseline assessments, patients will be censored at time 0.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON KALLIKREIN		
NUMBER OF IMP-TREATED HAE ATTACKS	14	14
EVENTS [1]	4 (28.6)	4 (28.6)
CENSORED [2]	10 (71.4)	10 (71.4)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON OTHER		
NUMBER OF IMP-TREATED HAE ATTACKS	5	4
EVENTS [1]	2 (40.0)	2 (50.0)
CENSORED [2]	3 (60.0)	2 (50.0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	15 (22.1)	31 (47.0)
CENSORED [2]	53 (77.9)	35 (53.0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON KALLIKREIN		
NUMBER OF IMP-TREATED HAE ATTACKS	14	14
EVENTS [1]	5 (35.7)	4 (28.6)
CENSORED [2]	9 (64.3)	10 (71.4)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON OTHER		
NUMBER OF IMP-TREATED HAE ATTACKS	5	4
EVENTS [1]	2 (40.0)	2 (50.0)
CENSORED [2]	3 (60.0)	2 (50.0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	20 (29.4)	34 (51.5)
CENSORED [2]	48 (70.6)	32 (48.5)

2.3.7 Attacken-Schwere (PGIS) zu Baseline

- PGI-C=Patient Global Impression of Change; CI=Confidence Interval; NE=Not Evaluable
- Time to HAE attack being rated “a little worse” or lower for 2 time points in a row on the PGI-C (hours) = Date/time of first rating of “a little worse” or lower (i.e. worse or much worse) which is immediately followed by another rating of “a little worse” or lower (with possible missing values in between) – Date/time of first IMP administration.
- Time to conventional attack treatment use (hours) = Date/time of first conventional attack treatment use – Date/time of study drug administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for treatment, subgroup, and subgroup*treatment interaction in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if they did not achieve this endpoint within considered time of the first IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 2 post-baseline assessments, patients will be censored at time 0.
- [3] Kaplan-Meier model estimates for the time to the first incidence of PGI-C being rated ‘a little worse’ or lower for two time points in a row, or use of conventional attack treatment within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment in the model as a fixed effect and patient as a random effect.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.6332	
ATTACK SEVERITY AT BASELINE PGI-S = NONE OR MILD		
NUMBER OF IMP-TREATED HAE ATTACKS	36	38
EVENTS [1]	8 (22.2)	19 (50.0)
CENSORED [2]	28 (77.8)	19 (50.0)
TIME TO FIRST INCIDENCE OF PGI-C BEING RATED "A LITTLE WORSE" OR LOWER OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	NE (2.54, NE)	2.16 (1.38, 5.00)
MEDIAN	NE (NE, NE)	9.04 (3.29, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0119†	
HAZARD RATIO (95 % CI) [4]	0.30 (0.12, 0.75)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = MODERATE		
NUMBER OF IMP-TREATED HAE ATTACKS	35	33
EVENTS [1]	10 (28.6)	12 (36.4)
CENSORED [2]	25 (71.4)	21 (63.6)
TIME TO FIRST INCIDENCE OF PGI-C BEING RATED "A LITTLE WORSE" OR LOWER OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	9.44 (2.34, NE)	1.29 (0.28, 9.21)
MEDIAN	NE (12.00, NE)	NE (2.79, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.2851	
HAZARD RATIO (95 % CI) [4]	0.63 (0.27, 1.47)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = SEVERE OR VERY SEVERE		
NUMBER OF IMP-TREATED HAE ATTACKS	14	13
EVENTS [1]	2 (14.3)	6 (46.2)
CENSORED [2]	12 (85.7)	7 (53.8)
TIME TO FIRST INCIDENCE OF PGI-C BEING RATED "A LITTLE WORSE" OR LOWER OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	NE (0.26, NE)	4.36 (1.32, 6.15)
MEDIAN	NE (NE, NE)	NE (2.34, NE)
75TH PERCENTILE	NE (NE, NE)	NE (6.15, NE)
LOG-RANK P-VALUE	0.0724	
HAZARD RATIO (95 % CI) [4]	0.27 (0.05, 1.46)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.5398	
ATTACK SEVERITY AT BASELINE PGI-S = NONE OR MILD		
NUMBER OF IMP-TREATED HAE ATTACKS	36	38
EVENTS [1]	11 (30.6)	21 (55.3)
CENSORED [2]	25 (69.4)	17 (44.7)
TIME TO FIRST INCIDENCE OF PGI-C BEING RATED "A LITTLE WORSE" OR LOWER OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	14.00 (2.54, NE)	2.16 (1.38, 5.00)
MEDIAN	NE (NE, NE)	9.04 (3.29, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.0146†	
HAZARD RATIO (95 % CI) [4]	0.33 (0.14, 0.77)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = MODERATE		
NUMBER OF IMP-TREATED HAE ATTACKS	35	33
EVENTS [1]	11 (31.4)	13 (39.4)
CENSORED [2]	24 (68.6)	20 (60.6)
TIME TO FIRST INCIDENCE OF PGI-C BEING RATED "A LITTLE WORSE" OR LOWER OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	10.55 (2.34, NE)	1.29 (0.28, 9.21)
MEDIAN	NE (24.00, NE)	NE (4.00, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
LOG-RANK P-VALUE	0.2917	
HAZARD RATIO (95 % CI) [4]	0.65 (0.29, 1.45)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = SEVERE OR VERY SEVERE		
NUMBER OF IMP-TREATED HAE ATTACKS	14	13
EVENTS [1]	4 (28.6)	6 (46.2)
CENSORED [2]	10 (71.4)	7 (53.8)
TIME TO FIRST INCIDENCE OF PGI-C BEING RATED "A LITTLE WORSE" OR LOWER OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	15.35 (0.26, NE)	4.52 (1.32, NE)
MEDIAN	NE (10.39, NE)	NE (4.20, NE)
75TH PERCENTILE	NE (NE, NE)	NE (6.15, NE)
LOG-RANK P-VALUE	0.3185	
HAZARD RATIO (95 % CI) [4]	0.52 (0.12, 2.31)	

2.4 Zeit bis zum ersten Auftreten einer Verringerung der Attacken-Schwere von mindestens einem Punkt oder mehr im PGI-S

2.4.1 Geschlecht

- PGI-S=Patient Global Impression of Severity; CI=Confidence Interval; NE=Not Evaluable
- Time to First Incidence of Decrease from Baseline for two time points in a row (hours) = Date/time of first incidence of decrease of symptom intensity from baseline for two time points in a row (with possible missing values in between) – Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for visit, treatment, subgroup, subgroup*treatment interaction, and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if they did not have a decrease in PGI-S score from baseline for two time points in a row or received conventional attack treatment within considered time of the first IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 2 post-baseline assessments, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to first incidence of decrease on PGI-S within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as a fixed effect and patient as a random effect.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- [5] Stratified log-rank test controlling for the baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.9983	
SEX = MALE		
NUMBER OF IMP-TREATED HAE ATTACKS	33	29
EVENTS [1]	18 (54.5)	8 (27.6)
CENSORED [2]	15 (45.5)	21 (72.4)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	1.27 (0.34, 2.76)	1.76 (0.30, NE)
MEDIAN	5.21 (1.35, NE)	NE (4.57, NE)
75TH PERCENTILE	NE (9.36, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.1492	
HAZARD RATIO (95 % CI) [4]	1.93 (0.77, 4.80)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
SEX = FEMALE		
NUMBER OF IMP-TREATED HAE ATTACKS	54	55
EVENTS [1]	26 (48.1)	18 (32.7)
CENSORED [2]	28 (51.9)	37 (67.3)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	1.81 (0.81, 4.76)	7.13 (2.07, NE)
MEDIAN	10.42 (4.08, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0289†	
HAZARD RATIO (95 % CI) [4]	2.15 (1.15, 4.03)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.8113	
SEX = MALE		
NUMBER OF IMP-TREATED HAE ATTACKS	33	29
EVENTS [1]	20 (60.6)	11 (37.9)
CENSORED [2]	13 (39.4)	18 (62.1)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	1.27 (0.34, 2.76)	1.54 (0.56, 16.71)
MEDIAN	5.21 (1.35, NE)	NE (1.76, NE)
75TH PERCENTILE	NE (9.36, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0566	
HAZARD RATIO (95 % CI) [4]	2.00 (0.88, 4.59)	

 Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
SEX = FEMALE		
NUMBER OF IMP-TREATED HAE ATTACKS	54	55
EVENTS [1]	33 (61.1)	25 (45.5)
CENSORED [2]	21 (38.9)	30 (54.5)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	2.04 (0.81, 4.76)	7.13 (2.07, 9.90)
MEDIAN	10.57 (4.76, 21.03)	NE (9.90, NE)
75TH PERCENTILE	NE (21.03, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0413†	
HAZARD RATIO (95 % CI) [4]	1.95 (1.12, 3.38)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.8620	
SEX = MALE		
NUMBER OF IMP-TREATED HAE ATTACKS	33	29
EVENTS [1]	20 (60.6)	12 (41.4)
CENSORED [2]	13 (39.4)	17 (58.6)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	1.27 (0.34, 2.76)	1.54 (0.56, 16.71)
MEDIAN	5.21 (1.35, NE)	NE (1.76, NE)
75TH PERCENTILE	NE (9.36, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0699	
HAZARD RATIO (95 % CI) [4]	1.94 (0.86, 4.40)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
SEX = FEMALE		
NUMBER OF IMP-TREATED HAE ATTACKS	54	55
EVENTS [1]	34 (63.0)	26 (47.3)
CENSORED [2]	20 (37.0)	29 (52.7)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	2.04 (0.81, 4.76)	7.13 (2.07, 9.90)
MEDIAN	10.57 (4.76, 21.03)	NE (9.90, NE)
75TH PERCENTILE	NE (21.03, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0403†	
HAZARD RATIO (95 % CI) [4]	1.89 (1.10, 3.25)	

2.4.2 Alter

- PGI-S=Patient Global Impression of Severity; CI=Confidence Interval; NE=Not Evaluable
- Time to First Incidence of Decrease from Baseline for two time points in a row (hours) = Date/time of first incidence of decrease of symptom intensity from baseline for two time points in a row (with possible missing values in between) – Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for visit, treatment, subgroup, subgroup*treatment interaction, and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if they did not have a decrease in PGI-S score from baseline for two time points in a row or received conventional attack treatment within considered time of the first IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 2 post-baseline assessments, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to first incidence of decrease on PGI-S within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as a fixed effect and patient as a random effect.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- [5] Stratified log-rank test controlling for the baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.2286	
AGE GROUP = <18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	10	9
EVENTS [1]	4 (40.0)	4 (44.4)
CENSORED [2]	6 (60.0)	5 (55.6)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	4.08 (0.28, NE)	1.55 (0.56, NE)
MEDIAN	NE (0.28, NE)	NE (0.56, NE)
75TH PERCENTILE	NE (9.36, NE)	NE (7.56, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.4915	
HAZARD RATIO (95 % CI) [4]	2.82 (0.40, 19.96)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
AGE GROUP = >=18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	77	75
EVENTS [1]	40 (51.9)	22 (29.3)
CENSORED [2]	37 (48.1)	53 (70.7)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	1.34 (0.81, 2.76)	6.52 (1.81, NE)
MEDIAN	8.04 (3.30, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0024†	
HAZARD RATIO (95 % CI) [4]	2.52 (1.45, 4.38)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.0946	
AGE GROUP = <18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	10	9
EVENTS [1]	6 (60.0)	5 (55.6)
CENSORED [2]	4 (40.0)	4 (44.4)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	4.08 (0.28, 20.56)	1.55 (0.56, 13.12)
MEDIAN	16.79 (0.28, NE)	13.12 (0.56, NE)
75TH PERCENTILE	NE (13.02, NE)	NE (7.56, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.8025	
HAZARD RATIO (95 % CI) [4]	1.09 (0.23, 5.11)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
AGE GROUP = >=18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	77	75
EVENTS [1]	47 (61.0)	31 (41.3)
CENSORED [2]	30 (39.0)	44 (58.7)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	1.35 (0.81, 2.76)	6.23 (1.81, 11.53)
MEDIAN	8.54 (3.30, 15.86)	NE (15.10, NE)
75TH PERCENTILE	NE (21.03, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0027†	
HAZARD RATIO (95 % CI) [4]	2.45 (1.49, 4.04)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.1145	
AGE GROUP = <18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	10	9
EVENTS [1]	6 (60.0)	5 (55.6)
CENSORED [2]	4 (40.0)	4 (44.4)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	4.08 (0.28, 20.56)	1.55 (0.56, 13.12)
MEDIAN	16.79 (0.28, NE)	13.12 (0.56, NE)
75TH PERCENTILE	NE (13.02, NE)	NE (7.56, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.8025	
HAZARD RATIO (95 % CI) [4]	1.09 (0.23, 5.11)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
AGE GROUP = >=18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	77	75
EVENTS [1]	48 (62.3)	33 (44.0)
CENSORED [2]	29 (37.7)	42 (56.0)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	1.35 (0.81, 2.76)	6.23 (1.81, 11.53)
MEDIAN	8.54 (3.30, 15.86)	NE (15.10, NE)
75TH PERCENTILE	NE (21.03, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0037†	
HAZARD RATIO (95 % CI) [4]	2.35 (1.44, 3.83)	

2.4.3 Region (Variante 1)

- PGI-S=Patient Global Impression of Severity; CI=Confidence Interval; NE=Not Evaluable
- Time to First Incidence of Decrease from Baseline for two time points in a row (hours) = Date/time of first incidence of decrease of symptom intensity from baseline for two time points in a row (with possible missing values in between) – Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for visit, treatment, subgroup, subgroup*treatment interaction, and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if they did not have a decrease in PGI-S score from baseline for two time points in a row or received conventional attack treatment within considered time of the first IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 2 post-baseline assessments, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to first incidence of decrease on PGI-S within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as a fixed effect and patient as a random effect.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- [5] Stratified log-rank test controlling for the baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.8417	
REGION 1 = US		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	12 (44.4)	7 (30.4)
CENSORED [2]	15 (55.6)	16 (69.6)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	1.09 (0.27, 3.30)	7.46 (1.27, NE)
MEDIAN	NE (1.33, NE)	NE (7.46, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.1607	
HAZARD RATIO (95 % CI) [4]	2.10 (0.79, 5.54)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 1 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	60	61
EVENTS [1]	32 (53.3)	19 (31.1)
CENSORED [2]	28 (46.7)	42 (68.9)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	1.78 (0.98, 4.08)	3.08 (1.33, NE)
MEDIAN	8.54 (4.08, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0080†	
HAZARD RATIO (95 % CI) [4]	2.37 (1.29, 4.35)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.7900	
REGION 1 = US		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	17 (63.0)	10 (43.5)
CENSORED [2]	10 (37.0)	13 (56.5)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	1.09 (0.27, 3.30)	7.46 (1.27, 17.88)
MEDIAN	10.34 (1.33, 21.03)	NE (7.46, NE)
75TH PERCENTILE	NE (10.58, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0892	
HAZARD RATIO (95 % CI) [4]	2.31 (1.00, 5.35)	

 Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 1 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	60	61
EVENTS [1]	36 (60.0)	26 (42.6)
CENSORED [2]	24 (40.0)	35 (57.4)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	1.78 (0.98, 4.76)	3.08 (1.33, 13.12)
MEDIAN	9.27 (4.76, NE)	NE (13.12, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0127†	
HAZARD RATIO (95 % CI) [4]	2.08 (1.19, 3.63)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.7263	
REGION 1 = US		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	17 (63.0)	10 (43.5)
CENSORED [2]	10 (37.0)	13 (56.5)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	1.09 (0.27, 3.30)	7.46 (1.27, 17.88)
MEDIAN	10.34 (1.33, 21.03)	NE (7.46, NE)
75TH PERCENTILE	NE (10.58, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0892	
HAZARD RATIO (95 % CI) [4]	2.31 (1.00, 5.35)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 1 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	60	61
EVENTS [1]	37 (61.7)	28 (45.9)
CENSORED [2]	23 (38.3)	33 (54.1)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	1.78 (0.98, 4.76)	3.08 (1.33, 13.12)
MEDIAN	9.27 (4.76, 24.95)	NE (13.12, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0136†	
HAZARD RATIO (95 % CI) [4]	2.01 (1.16, 3.46)	

2.4.4 Region (Variante 2)

- PGI-S=Patient Global Impression of Severity; CI=Confidence Interval; NE=Not Evaluable
- Time to First Incidence of Decrease from Baseline for two time points in a row (hours) = Date/time of first incidence of decrease of symptom intensity from baseline for two time points in a row (with possible missing values in between) – Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for visit, treatment, subgroup, subgroup*treatment interaction, and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if they did not have a decrease in PGI-S score from baseline for two time points in a row or received conventional attack treatment within considered time of the first IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 2 post-baseline assessments, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to first incidence of decrease on PGI-S within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as a fixed effect and patient as a random effect.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- [5] Stratified log-rank test controlling for the baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.9676	
REGION 2 = NORTH AMERICA		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	12 (44.4)	7 (30.4)
CENSORED [2]	15 (55.6)	16 (69.6)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	1.09 (0.27, 3.30)	7.46 (1.27, NE)
MEDIAN	NE (1.33, NE)	NE (7.46, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.1607	
HAZARD RATIO (95 % CI) [4]	2.10 (0.79, 5.54)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = EUROPE		
NUMBER OF IMP-TREATED HAE ATTACKS	44	48
EVENTS [1]	22 (50.0)	14 (29.2)
CENSORED [2]	22 (50.0)	34 (70.8)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	1.78 (0.81, 4.76)	6.81 (0.85, NE)
MEDIAN	8.45 (2.76, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0367†	
HAZARD RATIO (95 % CI) [4]	2.46 (1.17, 5.18)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	16	13
EVENTS [1]	10 (62.5)	5 (38.5)
CENSORED [2]	6 (37.5)	8 (61.5)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	1.31 (0.34, 5.21)	1.66 (0.76, NE)
MEDIAN	8.54 (1.27, NE)	NE (0.78, NE)
75TH PERCENTILE	NE (8.54, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.2560	
HAZARD RATIO (95 % CI) [4]	2.09 (0.65, 6.75)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.9660	
REGION 2 = NORTH AMERICA		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	17 (63.0)	10 (43.5)
CENSORED [2]	10 (37.0)	13 (56.5)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	1.09 (0.27, 3.30)	7.46 (1.27, 17.88)
MEDIAN	10.34 (1.33, 21.03)	NE (7.46, NE)
75TH PERCENTILE	NE (10.58, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0892	
HAZARD RATIO (95 % CI) [4]	2.31 (1.00, 5.35)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = EUROPE		
NUMBER OF IMP-TREATED HAE ATTACKS	44	48
EVENTS [1]	26 (59.1)	19 (39.6)
CENSORED [2]	18 (40.9)	29 (60.4)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	1.78 (0.81, 4.78)	6.81 (1.33, 15.03)
MEDIAN	11.19 (2.76, NE)	NE (13.12, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0325†	
HAZARD RATIO (95 % CI) [4]	2.22 (1.13, 4.36)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	16	13
EVENTS [1]	10 (62.5)	7 (53.8)
CENSORED [2]	6 (37.5)	6 (46.2)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	1.31 (0.34, 5.21)	1.66 (0.76, 15.10)
MEDIAN	8.54 (1.27, NE)	18.16 (0.78, NE)
75TH PERCENTILE	NE (8.54, NE)	NE (15.10, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.4053	
HAZARD RATIO (95 % CI) [4]	1.57 (0.56, 4.45)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.9370	
REGION 2 = NORTH AMERICA		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	17 (63.0)	10 (43.5)
CENSORED [2]	10 (37.0)	13 (56.5)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	1.09 (0.27, 3.30)	7.46 (1.27, 17.88)
MEDIAN	10.34 (1.33, 21.03)	NE (7.46, NE)
75TH PERCENTILE	NE (10.58, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0892	
HAZARD RATIO (95 % CI) [4]	2.31 (1.00, 5.35)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = EUROPE		
NUMBER OF IMP-TREATED HAE ATTACKS	44	48
EVENTS [1]	27 (61.4)	21 (43.8)
CENSORED [2]	17 (38.6)	27 (56.3)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	1.78 (0.81, 4.78)	6.81 (1.33, 15.03)
MEDIAN	11.19 (2.76, NE)	NE (13.12, NE)
75TH PERCENTILE	NE (24.95, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0353†	
HAZARD RATIO (95 % CI) [4]	2.14 (1.11, 4.10)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	16	13
EVENTS [1]	10 (62.5)	7 (53.8)
CENSORED [2]	6 (37.5)	6 (46.2)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	1.31 (0.34, 5.21)	1.66 (0.76, 15.10)
MEDIAN	8.54 (1.27, NE)	18.16 (0.78, NE)
75TH PERCENTILE	NE (8.54, NE)	NE (15.10, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.4053	
HAZARD RATIO (95 % CI) [4]	1.57 (0.56, 4.45)	

2.4.5 Prophylaxe-Status (Variante 1)

- PGI-S=Patient Global Impression of Severity; CI=Confidence Interval; NE=Not Evaluable
- Time to First Incidence of Decrease from Baseline for two time points in a row (hours) = Date/time of first incidence of decrease of symptom intensity from baseline for two time points in a row (with possible missing values in between) – Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for visit, treatment, subgroup, subgroup*treatment interaction, and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if they did not have a decrease in PGI-S score from baseline for two time points in a row or received conventional attack treatment within considered time of the first IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 2 post-baseline assessments, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to first incidence of decrease on PGI-S within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as a fixed effect and patient as a random effect.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- [5] Stratified log-rank test controlling for the baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.4467	
PROPHYLACTIC TREATMENT STATUS 1 = ON PROPHYLACTIC TREATMENT		
NUMBER OF IMP-TREATED HAE ATTACKS	19	18
EVENTS [1]	11 (57.9)	8 (44.4)
CENSORED [2]	8 (42.1)	10 (55.6)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	1.79 (0.34, 8.54)	5.57 (1.27, 9.79)
MEDIAN	9.27 (1.79, NE)	NE (5.57, NE)
75TH PERCENTILE	NE (9.27, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.2105	
HAZARD RATIO (95 % CI) [4]	1.78 (0.71, 4.49)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 1 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	33 (48.5)	18 (27.3)
CENSORED [2]	35 (51.5)	48 (72.7)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	1.35 (0.80, 3.40)	6.81 (1.33, NE)
MEDIAN	8.45 (3.40, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0060†	
HAZARD RATIO (95 % CI) [4]	2.52 (1.36, 4.67)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.2178	
PROPHYLACTIC TREATMENT STATUS 1 = ON PROPHYLACTIC TREATMENT		
NUMBER OF IMP-TREATED HAE ATTACKS	19	18
EVENTS [1]	13 (68.4)	12 (66.7)
CENSORED [2]	6 (31.6)	6 (33.3)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	1.79 (0.34, 8.54)	5.57 (1.27, 9.79)
MEDIAN	9.27 (1.79, NE)	12.47 (5.57, NE)
75TH PERCENTILE	NE (9.27, NE)	NE (15.03, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.3795	
HAZARD RATIO (95 % CI) [4]	1.55 (0.65, 3.66)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 1 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	40 (58.8)	24 (36.4)
CENSORED [2]	28 (41.2)	42 (63.6)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	1.44 (0.80, 3.40)	6.81 (1.50, 16.71)
MEDIAN	10.04 (4.08, 21.03)	NE (21.12, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0022†	
HAZARD RATIO (95 % CI) [4]	2.51 (1.44, 4.37)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.2501	
PROPHYLACTIC TREATMENT STATUS 1 = ON PROPHYLACTIC TREATMENT		
NUMBER OF IMP-TREATED HAE ATTACKS	19	18
EVENTS [1]	13 (68.4)	12 (66.7)
CENSORED [2]	6 (31.6)	6 (33.3)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	1.79 (0.34, 8.54)	5.57 (1.27, 9.79)
MEDIAN	9.27 (1.79, NE)	12.47 (5.57, NE)
75TH PERCENTILE	NE (9.27, NE)	NE (15.03, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.3795	
HAZARD RATIO (95 % CI) [4]	1.55 (0.65, 3.66)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 1 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	41 (60.3)	26 (39.4)
CENSORED [2]	27 (39.7)	40 (60.6)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	1.44 (0.80, 3.40)	6.81 (1.50, 16.71)
MEDIAN	10.04 (4.08, 21.03)	NE (21.12, NE)
75TH PERCENTILE	NE (24.95, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0026†	
HAZARD RATIO (95 % CI) [4]	2.40 (1.40, 4.11)	

2.4.6 Prophylaxe-Status (Variante 2)

- PGI-S=Patient Global Impression of Severity; CI=Confidence Interval; NE=Not Evaluable
- Time to First Incidence of Decrease from Baseline for two time points in a row (hours) = Date/time of first incidence of decrease of symptom intensity from baseline for two time points in a row (with possible missing values in between) – Date/time of first IMP administration.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if they did not have a decrease in PGI-S score from baseline for two time points in a row or received conventional attack treatment within considered time of the first IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 2 post-baseline assessments, attacks will be censored at time 0.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON KALLIKREIN		
NUMBER OF IMP-TREATED HAE ATTACKS	14	14
EVENTS [1]	8 (57.1)	8 (57.1)
CENSORED [2]	6 (42.9)	6 (42.9)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON OTHER		
NUMBER OF IMP-TREATED HAE ATTACKS	5	4
EVENTS [1]	3 (60.0)	0
CENSORED [2]	2 (40.0)	4 (100)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	33 (48.5)	18 (27.3)
CENSORED [2]	35 (51.5)	48 (72.7)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON KALLIKREIN		
NUMBER OF IMP-TREATED HAE ATTACKS	14	14
EVENTS [1]	10 (71.4)	10 (71.4)
CENSORED [2]	4 (28.6)	4 (28.6)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON OTHER		
NUMBER OF IMP-TREATED HAE ATTACKS	5	4
EVENTS [1]	3 (60.0)	2 (50.0)
CENSORED [2]	2 (40.0)	2 (50.0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	40 (58.8)	24 (36.4)
CENSORED [2]	28 (41.2)	42 (63.6)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON KALLIKREIN		
NUMBER OF IMP-TREATED HAE ATTACKS	14	14
EVENTS [1]	10 (71.4)	10 (71.4)
CENSORED [2]	4 (28.6)	4 (28.6)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON OTHER		
NUMBER OF IMP-TREATED HAE ATTACKS	5	4
EVENTS [1]	3 (60.0)	2 (50.0)
CENSORED [2]	2 (40.0)	2 (50.0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	41 (60.3)	26 (39.4)
CENSORED [2]	27 (39.7)	40 (60.6)

2.4.7 Attacken-Schwere (PGIS) zu Baseline

- PGI-S=Patient Global Impression of Severity; CI=Confidence Interval; NE=Not Evaluable
- Time to First Incidence of Decrease from Baseline for two time points in a row (hours) = Date/time of first incidence of decrease of symptom intensity from baseline for two time points in a row (with possible missing values in between) – Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for visit, treatment, subgroup, and subgroup*treatment interaction in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if they did not have a decrease in PGI-S score from baseline for two time points in a row or received conventional attack treatment within considered time of the first IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 2 post-baseline assessments, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to first incidence of decrease on PGI-S within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as a fixed effect and patient as a random effect.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment in the model as a fixed effect and patient as a random effect.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.9519	
ATTACK SEVERITY AT BASELINE PGI-S = NONE OR MILD		
NUMBER OF IMP-TREATED HAE ATTACKS	36	38
EVENTS [1]	10 (27.8)	6 (15.8)
CENSORED [2]	26 (72.2)	32 (84.2)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	8.54 (3.28, NE)	NE (6.23, NE)
MEDIAN	NE (NE, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
UNSTRATIFIED LOG-RANK P-VALUE	0.2044	
HAZARD RATIO (95 % CI) [4]	2.15 (0.73, 6.29)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = MODERATE		
NUMBER OF IMP-TREATED HAE ATTACKS	35	33
EVENTS [1]	23 (65.7)	13 (39.4)
CENSORED [2]	12 (34.3)	20 (60.6)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	1.14 (0.77, 2.27)	2.77 (0.78, 7.58)
MEDIAN	4.98 (1.33, 10.12)	NE (4.57, NE)
75TH PERCENTILE	NE (6.09, NE)	NE (NE, NE)
UNSTRATIFIED LOG-RANK P-VALUE	0.0370†	
HAZARD RATIO (95 % CI) [4]	2.18 (1.05, 4.53)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = SEVERE OR VERY SEVERE		
NUMBER OF IMP-TREATED HAE ATTACKS	14	13
EVENTS [1]	11 (78.6)	7 (53.8)
CENSORED [2]	3 (21.4)	6 (46.2)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	0.79 (0.27, 1.28)	1.16 (0.30, 5.53)
MEDIAN	1.31 (0.31, 2.78)	6.17 (0.36, NE)
75TH PERCENTILE	2.78 (1.28, NE)	NE (5.53, NE)
UNSTRATIFIED LOG-RANK P-VALUE	0.1438	
HAZARD RATIO (95 % CI) [4]	2.65 (0.67, 10.53)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.7766	
ATTACK SEVERITY AT BASELINE PGI-S = NONE OR MILD		
NUMBER OF IMP-TREATED HAE ATTACKS	36	38
EVENTS [1]	15 (41.7)	8 (21.1)
CENSORED [2]	21 (58.3)	30 (78.9)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	8.54 (3.28, 16.91)	NE (6.23, NE)
MEDIAN	NE (10.58, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
UNSTRATIFIED LOG-RANK P-VALUE	0.0680	
HAZARD RATIO (95 % CI) [4]	2.61 (1.02, 6.73)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = MODERATE		
NUMBER OF IMP-TREATED HAE ATTACKS	35	33
EVENTS [1]	26 (74.3)	19 (57.6)
CENSORED [2]	9 (25.7)	14 (42.4)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	1.31 (0.77, 2.27)	2.77 (0.78, 7.58)
MEDIAN	5.21 (1.78, 10.12)	12.33 (5.57, NE)
75TH PERCENTILE	15.86 (7.53, NE)	NE (21.12, NE)
UNSTRATIFIED LOG-RANK P-VALUE	0.0919	
HAZARD RATIO (95 % CI) [4]	1.76 (0.92, 3.37)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = SEVERE OR VERY SEVERE		
NUMBER OF IMP-TREATED HAE ATTACKS	14	13
EVENTS [1]	12 (85.7)	9 (69.2)
CENSORED [2]	2 (14.3)	4 (30.8)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	0.79 (0.27, 1.28)	1.50 (0.30, 5.53)
MEDIAN	1.31 (0.31, 2.78)	5.53 (0.78, NE)
75TH PERCENTILE	2.78 (1.28, NE)	NE (3.08, NE)
UNSTRATIFIED LOG-RANK P-VALUE	0.1445	
HAZARD RATIO (95 % CI) [4]	2.79 (0.70, 11.18)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.8030	
ATTACK SEVERITY AT BASELINE PGI-S = NONE OR MILD		
NUMBER OF IMP-TREATED HAE ATTACKS	36	38
EVENTS [1]	15 (41.7)	9 (23.7)
CENSORED [2]	21 (58.3)	29 (76.3)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	8.54 (3.28, 16.91)	NE (6.23, NE)
MEDIAN	NE (10.58, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
UNSTRATIFIED LOG-RANK P-VALUE	0.1059	
HAZARD RATIO (95 % CI) [4]	2.24 (0.91, 5.52)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = MODERATE		
NUMBER OF IMP-TREATED HAE ATTACKS	35	33
EVENTS [1]	27 (77.1)	20 (60.6)
CENSORED [2]	8 (22.9)	13 (39.4)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	1.31 (0.77, 2.27)	2.77 (0.78, 7.58)
MEDIAN	5.21 (1.78, 10.12)	12.33 (5.57, NE)
75TH PERCENTILE	15.86 (7.53, NE)	NE (21.12, NE)
UNSTRATIFIED LOG-RANK P-VALUE	0.0842	
HAZARD RATIO (95 % CI) [4]	1.76 (0.94, 3.32)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = SEVERE OR VERY SEVERE		
NUMBER OF IMP-TREATED HAE ATTACKS	14	13
EVENTS [1]	12 (85.7)	9 (69.2)
CENSORED [2]	2 (14.3)	4 (30.8)
TIME TO FIRST INCIDENCE OF DECREASE ON PGI-S (95 % CI) [3]		
25TH PERCENTILE	0.79 (0.27, 1.28)	1.50 (0.30, 5.53)
MEDIAN	1.31 (0.31, 2.78)	5.53 (0.78, NE)
75TH PERCENTILE	2.78 (1.28, NE)	NE (3.08, NE)
UNSTRATIFIED LOG-RANK P-VALUE	0.1445	
HAZARD RATIO (95 % CI) [4]	2.79 (0.70, 11.18)	

2.5 Zeit bis zum ersten Auftreten einer Steigerung der Attacken-Schwere von mindestens einem Punkt im PGI-S, oder Verwendung konventioneller Akuttherapien

2.5.1 Geschlecht

- PGI-S=Patient Global Impression of Severity; CI=Confidence Interval; NE=Not Evaluable
- Time to first incidence of worsening in attack severity by one level or more from baseline on the PGI-S for two time points in a row (hours) = Date/time of first incidence of increase from baseline on the PGI-S for two time points in a row (with possible missing values in between) – Date/time of first IMP administration.
- Time to conventional attack treatment use (hours) = Date/time of first conventional attack treatment use – Date/time of study drug administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for visit, treatment, subgroup, subgroup*treatment interaction, and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if they did not achieve this endpoint within considered time of the first IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 2 post-baseline assessments, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to either (1) first incidence of worsening in attack severity on the PGI-S by one level or more from baseline for two time points in a row, or (2) use of conventional attack treatment, whichever comes first within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- [5] Stratified log-rank test controlling for the baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.5067	
SEX = MALE		
NUMBER OF IMP-TREATED HAE ATTACKS	33	29
EVENTS [1]	4 (12.1)	9 (31.0)
CENSORED [2]	29 (87.9)	20 (69.0)
TIME TO FIRST INCIDENCE OF WORSENING IN ATTACK SEVERITY ON THE PGI-S OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	NE (2.93, NE)	4.20 (0.29, NE)
MEDIAN	NE (NE, NE)	NE (6.98, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0642	
HAZARD RATIO (95 % CI) [4]	0.34 (0.11, 1.13)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
SEX = FEMALE		
NUMBER OF IMP-TREATED HAE ATTACKS	54	55
EVENTS [1]	17 (31.5)	27 (49.1)
CENSORED [2]	37 (68.5)	28 (50.9)
TIME TO FIRST INCIDENCE OF WORSENING IN ATTACK SEVERITY ON THE PGI-S OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	8.33 (2.68, NE)	2.79 (1.35, 4.52)
MEDIAN	NE (NE, NE)	6.71 (4.52, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0490†	
HAZARD RATIO (95 % CI) [4]	0.46 (0.24, 0.89)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.6044	
SEX = MALE		
NUMBER OF IMP-TREATED HAE ATTACKS	33	29
EVENTS [1]	6 (18.2)	11 (37.9)
CENSORED [2]	27 (81.8)	18 (62.1)
TIME TO FIRST INCIDENCE OF WORSENING IN ATTACK SEVERITY ON THE PGI-S OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	NE (2.93, NE)	4.20 (0.95, 22.43)
MEDIAN	NE (NE, NE)	NE (6.98, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0702	
HAZARD RATIO (95 % CI) [4]	0.41 (0.15, 1.15)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
SEX = FEMALE		
NUMBER OF IMP-TREATED HAE ATTACKS	54	55
EVENTS [1]	21 (38.9)	28 (50.9)
CENSORED [2]	33 (61.1)	27 (49.1)
TIME TO FIRST INCIDENCE OF WORSENING IN ATTACK SEVERITY ON THE PGI-S OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	8.37 (2.68, 16.45)	2.79 (1.35, 4.52)
MEDIAN	NE (16.45, NE)	6.71 (4.52, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0864	
HAZARD RATIO (95 % CI) [4]	0.52 (0.28, 0.97)	

2.5.2 Alter

- PGI-S=Patient Global Impression of Severity; CI=Confidence Interval; NE=Not Evaluable
- Time to first incidence of worsening in attack severity by one level or more from baseline on the PGI-S for two time points in a row (hours) = Date/time of first incidence of increase from baseline on the PGI-S for two time points in a row (with possible missing values in between) – Date/time of first IMP administration.
- Time to conventional attack treatment use (hours) = Date/time of first conventional attack treatment use – Date/time of study drug administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for visit, treatment, subgroup, subgroup*treatment interaction, and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if they did not achieve this endpoint within considered time of the first IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 2 post-baseline assessments, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to either (1) first incidence of worsening in attack severity on the PGI-S by one level or more from baseline for two time points in a row, or (2) use of conventional attack treatment, whichever comes first within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- [5] Stratified log-rank test controlling for the baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.9925	
AGE GROUP = <18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	10	9
EVENTS [1]	2 (20.0)	4 (44.4)
CENSORED [2]	8 (80.0)	5 (55.6)
TIME TO FIRST INCIDENCE OF WORSENING IN ATTACK SEVERITY ON THE PGI-S OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	NE (1.28, NE)	5.00 (1.63, NE)
MEDIAN	NE (1.28, NE)	NE (1.63, NE)
75TH PERCENTILE	NE (NE, NE)	NE (5.82, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.3380	
HAZARD RATIO (95 % CI) [4]	0.26 (0.03, 2.25)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
AGE GROUP = >=18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	77	75
EVENTS [1]	19 (24.7)	32 (42.7)
CENSORED [2]	58 (75.3)	43 (57.3)
TIME TO FIRST INCIDENCE OF WORSENING IN ATTACK SEVERITY ON THE PGI-S OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	12.00 (3.80, NE)	2.79 (1.32, 4.52)
MEDIAN	NE (NE, NE)	NE (5.42, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0102†	
HAZARD RATIO (95 % CI) [4]	0.43 (0.23, 0.78)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.6397	
AGE GROUP = <18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	10	9
EVENTS [1]	2 (20.0)	4 (44.4)
CENSORED [2]	8 (80.0)	5 (55.6)
TIME TO FIRST INCIDENCE OF WORSENING IN ATTACK SEVERITY ON THE PGI-S OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	NE (1.28, NE)	5.00 (1.63, NE)
MEDIAN	NE (1.28, NE)	NE (1.63, NE)
75TH PERCENTILE	NE (NE, NE)	NE (5.82, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.2733	
HAZARD RATIO (95 % CI) [4]	0.21 (0.03, 1.67)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
AGE GROUP = >=18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	77	75
EVENTS [1]	25 (32.5)	35 (46.7)
CENSORED [2]	52 (67.5)	40 (53.3)
TIME TO FIRST INCIDENCE OF WORSENING IN ATTACK SEVERITY ON THE PGI-S OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	15.35 (3.80, NE)	2.79 (1.35, 5.03)
MEDIAN	NE (NE, NE)	NE (6.15, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0324†	
HAZARD RATIO (95 % CI) [4]	0.51 (0.29, 0.89)	

2.5.3 Region (Variante 1)

- PGI-S=Patient Global Impression of Severity; CI=Confidence Interval; NE=Not Evaluable
- Time to first incidence of worsening in attack severity by one level or more from baseline on the PGI-S for two time points in a row (hours) = Date/time of first incidence of increase from baseline on the PGI-S for two time points in a row (with possible missing values in between) – Date/time of first IMP administration.
- Time to conventional attack treatment use (hours) = Date/time of first conventional attack treatment use – Date/time of study drug administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for visit, treatment, subgroup, subgroup*treatment interaction, and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if they did not achieve this endpoint within considered time of the first IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 2 post-baseline assessments, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to either (1) first incidence of worsening in attack severity on the PGI-S by one level or more from baseline for two time points in a row, or (2) use of conventional attack treatment, whichever comes first within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- [5] Stratified log-rank test controlling for the baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.5762	
REGION 1 = US		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	5 (18.5)	8 (34.8)
CENSORED [2]	22 (81.5)	15 (65.2)
TIME TO FIRST INCIDENCE OF WORSENING IN ATTACK SEVERITY ON THE PGI-S OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	NE (0.30, NE)	6.50 (0.28, NE)
MEDIAN	NE (NE, NE)	NE (6.50, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.1680	
HAZARD RATIO (95 % CI) [4]	0.32 (0.09, 1.18)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 1 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	60	61
EVENTS [1]	16 (26.7)	28 (45.9)
CENSORED [2]	44 (73.3)	33 (54.1)
TIME TO FIRST INCIDENCE OF WORSENING IN ATTACK SEVERITY ON THE PGI-S OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	12.00 (2.68, NE)	1.78 (1.32, 4.00)
MEDIAN	NE (NE, NE)	7.97 (4.00, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0066†	
HAZARD RATIO (95 % CI) [4]	0.40 (0.21, 0.77)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.2782	
REGION 1 = US		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	7 (25.9)	8 (34.8)
CENSORED [2]	20 (74.1)	15 (65.2)
TIME TO FIRST INCIDENCE OF WORSENING IN ATTACK SEVERITY ON THE PGI-S OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	16.43 (0.30, NE)	6.50 (0.28, NE)
MEDIAN	NE (17.52, NE)	NE (6.50, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.3858	
HAZARD RATIO (95 % CI) [4]	0.53 (0.17, 1.64)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 1 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	60	61
EVENTS [1]	20 (33.3)	31 (50.8)
CENSORED [2]	40 (66.7)	30 (49.2)
TIME TO FIRST INCIDENCE OF WORSENING IN ATTACK SEVERITY ON THE PGI-S OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	14.00 (2.68, NE)	2.04 (1.32, 4.20)
MEDIAN	NE (NE, NE)	11.53 (4.20, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0077†	
HAZARD RATIO (95 % CI) [4]	0.41 (0.22, 0.77)	

2.5.4 Region (Variante 2)

- PGI-S=Patient Global Impression of Severity; CI=Confidence Interval; NE=Not Evaluable
- Time to first incidence of worsening in attack severity by one level or more from baseline on the PGI-S for two time points in a row (hours) = Date/time of first incidence of increase from baseline on the PGI-S for two time points in a row (with possible missing values in between) – Date/time of first IMP administration.
- Time to conventional attack treatment use (hours) = Date/time of first conventional attack treatment use – Date/time of study drug administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for visit, treatment, subgroup, subgroup*treatment interaction, and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if they did not achieve this endpoint within considered time of the first IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 2 post-baseline assessments, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to either (1) first incidence of worsening in attack severity on the PGI-S by one level or more from baseline for two time points in a row, or (2) use of conventional attack treatment, whichever comes first within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- [5] Stratified log-rank test controlling for the baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.5682	
REGION 2 = NORTH AMERICA		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	5 (18.5)	8 (34.8)
CENSORED [2]	22 (81.5)	15 (65.2)
TIME TO FIRST INCIDENCE OF WORSENING IN ATTACK SEVERITY ON THE PGI-S OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	NE (0.30, NE)	6.50 (0.28, NE)
MEDIAN	NE (NE, NE)	NE (6.50, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.1680	
HAZARD RATIO (95 % CI) [4]	0.32 (0.09, 1.18)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = EUROPE		
NUMBER OF IMP-TREATED HAE ATTACKS	44	48
EVENTS [1]	13 (29.5)	22 (45.8)
CENSORED [2]	31 (70.5)	26 (54.2)
TIME TO FIRST INCIDENCE OF WORSENING IN ATTACK SEVERITY ON THE PGI-S OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	9.10 (1.28, NE)	1.78 (1.28, 4.20)
MEDIAN	NE (NE, NE)	7.97 (3.82, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0611	
HAZARD RATIO (95 % CI) [4]	0.49 (0.24, 1.02)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	16	13
EVENTS [1]	3 (18.8)	6 (46.2)
CENSORED [2]	13 (81.3)	7 (53.8)
TIME TO FIRST INCIDENCE OF WORSENING IN ATTACK SEVERITY ON THE PGI-S OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	NE (2.54, NE)	1.84 (0.77, 5.42)
MEDIAN	NE (8.40, NE)	NE (1.29, NE)
75TH PERCENTILE	NE (NE, NE)	NE (5.42, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.1263	
HAZARD RATIO (95 % CI) [4]	0.18 (0.04, 0.90)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.4471	
REGION 2 = NORTH AMERICA		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	7 (25.9)	8 (34.8)
CENSORED [2]	20 (74.1)	15 (65.2)
TIME TO FIRST INCIDENCE OF WORSENING IN ATTACK SEVERITY ON THE PGI-S OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	16.43 (0.30, NE)	6.50 (0.28, NE)
MEDIAN	NE (17.52, NE)	NE (6.50, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.3858	
HAZARD RATIO (95 % CI) [4]	0.53 (0.17, 1.64)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = EUROPE		
NUMBER OF IMP-TREATED HAE ATTACKS	44	48
EVENTS [1]	16 (36.4)	25 (52.1)
CENSORED [2]	28 (63.6)	23 (47.9)
TIME TO FIRST INCIDENCE OF WORSENING IN ATTACK SEVERITY ON THE PGI-S OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	11.55 (1.28, NE)	2.78 (1.32, 4.20)
MEDIAN	NE (24.00, NE)	11.53 (4.00, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0357†	
HAZARD RATIO (95 % CI) [4]	0.48 (0.24, 0.95)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	16	13
EVENTS [1]	4 (25.0)	6 (46.2)
CENSORED [2]	12 (75.0)	7 (53.8)
TIME TO FIRST INCIDENCE OF WORSENING IN ATTACK SEVERITY ON THE PGI-S OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	16.45 (2.54, NE)	1.84 (0.77, 5.42)
MEDIAN	NE (8.40, NE)	NE (1.29, NE)
75TH PERCENTILE	NE (NE, NE)	NE (5.42, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.2466	
HAZARD RATIO (95 % CI) [4]	0.21 (0.05, 0.97)	

2.5.5 Prophylaxe-Status (Variante 1)

- PGI-S=Patient Global Impression of Severity; CI=Confidence Interval; NE=Not Evaluable
- Time to first incidence of worsening in attack severity by one level or more from baseline on the PGI-S for two time points in a row (hours) = Date/time of first incidence of increase from baseline on the PGI-S for two time points in a row (with possible missing values in between) – Date/time of first IMP administration.
- Time to conventional attack treatment use (hours) = Date/time of first conventional attack treatment use – Date/time of study drug administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for visit, treatment, subgroup, subgroup*treatment interaction, and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if they did not achieve this endpoint within considered time of the first IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 2 post-baseline assessments, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to either (1) first incidence of worsening in attack severity on the PGI-S by one level or more from baseline for two time points in a row, or (2) use of conventional attack treatment, whichever comes first within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- [5] Stratified log-rank test controlling for the baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.3279	
PROPHYLACTIC TREATMENT STATUS 1 = ON PROPHYLACTIC TREATMENT		
NUMBER OF IMP-TREATED HAE ATTACKS	19	18
EVENTS [1]	5 (26.3)	5 (27.8)
CENSORED [2]	14 (73.7)	13 (72.2)
TIME TO FIRST INCIDENCE OF WORSENING IN ATTACK SEVERITY ON THE PGI-S OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	12.00 (0.30, NE)	5.00 (0.95, NE)
MEDIAN	NE (12.00, NE)	NE (5.00, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.5673	
HAZARD RATIO (95 % CI) [4]	0.55 (0.13, 2.45)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 1 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	16 (23.5)	31 (47.0)
CENSORED [2]	52 (76.5)	35 (53.0)
TIME TO FIRST INCIDENCE OF WORSENING IN ATTACK SEVERITY ON THE PGI-S OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	12.00 (2.79, NE)	2.04 (1.32, 4.52)
MEDIAN	NE (NE, NE)	6.98 (4.52, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0031†	
HAZARD RATIO (95 % CI) [4]	0.38 (0.20, 0.71)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.2080	
PROPHYLACTIC TREATMENT STATUS 1 = ON PROPHYLACTIC TREATMENT		
NUMBER OF IMP-TREATED HAE ATTACKS	19	18
EVENTS [1]	6 (31.6)	5 (27.8)
CENSORED [2]	13 (68.4)	13 (72.2)
TIME TO FIRST INCIDENCE OF WORSENING IN ATTACK SEVERITY ON THE PGI-S OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	15.35 (0.30, NE)	5.00 (0.95, NE)
MEDIAN	NE (15.35, NE)	NE (5.00, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.6990	
HAZARD RATIO (95 % CI) [4]	0.72 (0.18, 2.86)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 1 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	21 (30.9)	34 (51.5)
CENSORED [2]	47 (69.1)	32 (48.5)
TIME TO FIRST INCIDENCE OF WORSENING IN ATTACK SEVERITY ON THE PGI-S OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	14.99 (2.79, NE)	2.78 (1.32, 4.52)
MEDIAN	NE (NE, NE)	7.97 (5.03, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0048†	
HAZARD RATIO (95 % CI) [4]	0.41 (0.23, 0.74)	

2.5.6 Prophylaxe-Status (Variante 2)

- PGI-S=Patient Global Impression of Severity; CI=Confidence Interval; NE=Not Evaluable
- Time to first incidence of worsening in attack severity by one level or more from baseline on the PGI-S for two time points in a row (hours) = Date/time of first incidence of increase from baseline on the PGI-S for two time points in a row (with possible missing values in between) – Date/time of first IMP administration.
- Time to conventional attack treatment use (hours) = Date/time of first conventional attack treatment use – Date/time of study drug administration.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if they did not achieve this endpoint within considered time of the first IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 2 post-baseline assessments, attacks will be censored at time 0.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON KALLIKREIN		
NUMBER OF IMP-TREATED HAE ATTACKS	14	14
EVENTS [1]	3 (21.4)	3 (21.4)
CENSORED [2]	11 (78.6)	11 (78.6)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON OTHER		
NUMBER OF IMP-TREATED HAE ATTACKS	5	4
EVENTS [1]	2 (40.0)	2 (50.0)
CENSORED [2]	3 (60.0)	2 (50.0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	16 (23.5)	31 (47.0)
CENSORED [2]	52 (76.5)	35 (53.0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON KALLIKREIN		
NUMBER OF IMP-TREATED HAE ATTACKS	14	14
EVENTS [1]	4 (28.6)	3 (21.4)
CENSORED [2]	10 (71.4)	11 (78.6)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON OTHER		
NUMBER OF IMP-TREATED HAE ATTACKS	5	4
EVENTS [1]	2 (40.0)	2 (50.0)
CENSORED [2]	3 (60.0)	2 (50.0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	21 (30.9)	34 (51.5)
CENSORED [2]	47 (69.1)	32 (48.5)

2.5.7 Attacken-Schwere (PGIS) zu Baseline

- PGI-S=Patient Global Impression of Severity; CI=Confidence Interval; NE=Not Evaluable
- Time to first incidence of worsening in attack severity by one level or more from baseline on the PGI-S for two time points in a row (hours) = Date/time of first incidence of increase from baseline on the PGI-S for two time points in a row (with possible missing values in between) – Date/time of first IMP administration.
- Time to conventional attack treatment use (hours) = Date/time of first conventional attack treatment use – Date/time of study drug administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for visit, treatment, subgroup, and subgroup*treatment interaction in the model as fixed effects and patient as a random effect.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if they did not achieve this endpoint within considered time of the first IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 2 post-baseline assessments, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to either (1) first incidence of worsening in attack severity on the PGI-S by one level or more from baseline for two time points in a row, or (2) use of conventional attack treatment, whichever comes first within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment in the model as a fixed effect and patient as a random effect.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.7331	
ATTACK SEVERITY AT BASELINE PGI-S = NONE OR MILD		
NUMBER OF IMP-TREATED HAE ATTACKS	36	38
EVENTS [1]	11 (30.6)	19 (50.0)
CENSORED [2]	25 (69.4)	19 (50.0)
TIME TO FIRST INCIDENCE OF WORSENING IN ATTACK SEVERITY ON THE PGI-S OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	7.12 (0.96, NE)	2.41 (1.35, 5.03)
MEDIAN	NE (9.10, NE)	7.48 (3.82, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
UNSTRATIFIED LOG-RANK P-VALUE	0.0943	
HAZARD RATIO (95 % CI) [4]	0.51 (0.23, 1.11)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = MODERATE		
NUMBER OF IMP-TREATED HAE ATTACKS	35	33
EVENTS [1]	7 (20.0)	11 (33.3)
CENSORED [2]	28 (80.0)	22 (66.7)
TIME TO FIRST INCIDENCE OF WORSENING IN ATTACK SEVERITY ON THE PGI-S OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	NE (2.93, NE)	2.79 (0.77, NE)
MEDIAN	NE (NE, NE)	NE (3.61, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
UNSTRATIFIED LOG-RANK P-VALUE	0.1210	
HAZARD RATIO (95 % CI) [4]	0.39 (0.13, 1.17)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = SEVERE OR VERY SEVERE		
NUMBER OF IMP-TREATED HAE ATTACKS	14	13
EVENTS [1]	2 (14.3)	6 (46.2)
CENSORED [2]	12 (85.7)	7 (53.8)
TIME TO FIRST INCIDENCE OF WORSENING IN ATTACK SEVERITY ON THE PGI-S OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	NE (1.97, NE)	4.36 (1.32, 6.15)
MEDIAN	NE (NE, NE)	NE (2.93, NE)
75TH PERCENTILE	NE (NE, NE)	NE (6.15, NE)
UNSTRATIFIED LOG-RANK P-VALUE	0.0728	
HAZARD RATIO (95 % CI) [4]	0.27 (0.05, 1.48)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.9530	
ATTACK SEVERITY AT BASELINE PGI-S = NONE OR MILD		
NUMBER OF IMP-TREATED HAE ATTACKS	36	38
EVENTS [1]	14 (38.9)	21 (55.3)
CENSORED [2]	22 (61.1)	17 (44.7)
TIME TO FIRST INCIDENCE OF WORSENING IN ATTACK SEVERITY ON THE PGI-S OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	7.12 (0.96, 21.66)	2.41 (1.35, 5.03)
MEDIAN	NE (14.00, NE)	7.48 (3.82, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
UNSTRATIFIED LOG-RANK P-VALUE	0.1026	
HAZARD RATIO (95 % CI) [4]	0.54 (0.26, 1.10)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = MODERATE		
NUMBER OF IMP-TREATED HAE ATTACKS	35	33
EVENTS [1]	9 (25.7)	12 (36.4)
CENSORED [2]	26 (74.3)	21 (63.6)
TIME TO FIRST INCIDENCE OF WORSENING IN ATTACK SEVERITY ON THE PGI-S OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	24.00 (2.93, NE)	2.79 (0.77, 22.43)
MEDIAN	NE (NE, NE)	NE (4.00, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
UNSTRATIFIED LOG-RANK P-VALUE	0.1959	
HAZARD RATIO (95 % CI) [4]	0.44 (0.16, 1.21)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = SEVERE OR VERY SEVERE		
NUMBER OF IMP-TREATED HAE ATTACKS	14	13
EVENTS [1]	3 (21.4)	6 (46.2)
CENSORED [2]	11 (78.6)	7 (53.8)
TIME TO FIRST INCIDENCE OF WORSENING IN ATTACK SEVERITY ON THE PGI-S OR USE OF CONVENTIONAL ATTACK TREATMENT (95% CI) [3]		
25TH PERCENTILE	NE (1.97, NE)	4.52 (1.32, NE)
MEDIAN	NE (15.35, NE)	NE (4.20, NE)
75TH PERCENTILE	NE (NE, NE)	NE (6.15, NE)
UNSTRATIFIED LOG-RANK P-VALUE	0.1905	
HAZARD RATIO (95 % CI) [4]	0.42 (0.09, 2.01)	

2.6 Zeit bis zur Auflösung der Attacke definiert als „keine“ (PGI-S = 0)

2.6.1 Geschlecht

- PGI-S=Patient Global Impression of Severity; CI=Confidence Interval; NE=Not Evaluable
- Time to HAE attack resolution (hours) = Date/time of first rating of “None”– Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for visit, treatment, subgroup, subgroup*treatment interaction, and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks treated as right-censored at considered time if they did not have a HAE attack resolution or received conventional attack treatment within considered time of IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 1 post-baseline assessment, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to HAE attack resolution within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- [5] Stratified log-rank test controlling for the baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.4941	
SEX = MALE		
NUMBER OF IMP-TREATED HAE ATTACKS	33	29
EVENTS [1]	13 (39.4)	5 (17.2)
CENSORED [2]	20 (60.6)	24 (82.8)
TIME TO HAE ATTACK RESOLUTION (95% CI) [3]		
25TH PERCENTILE	9.57 (2.46, 24.00)	NE (3.78, NE)
MEDIAN	NE (14.98, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0921	
HAZARD RATIO (95 % CI) [4]	3.06 (0.98, 9.54)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
SEX = FEMALE		
NUMBER OF IMP-TREATED HAE ATTACKS	54	55
EVENTS [1]	24 (44.4)	18 (32.7)
CENSORED [2]	30 (55.6)	37 (67.3)
TIME TO HAE ATTACK RESOLUTION (95% CI) [3]		
25TH PERCENTILE	7.07 (3.28, 11.53)	15.10 (6.61, NE)
MEDIAN	NE (11.53, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0960	
HAZARD RATIO (95 % CI) [4]	1.92 (1.00, 3.67)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.6909	
SEX = MALE		
NUMBER OF IMP-TREATED HAE ATTACKS	33	29
EVENTS [1]	16 (48.5)	10 (34.5)
CENSORED [2]	17 (51.5)	19 (65.5)
TIME TO HAE ATTACK RESOLUTION (95% CI) [3]		
25TH PERCENTILE	9.57 (2.46, 24.47)	33.17 (3.78, NE)
MEDIAN	NE (14.98, NE)	NE (36.41, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.2883	
HAZARD RATIO (95 % CI) [4]	2.20 (0.87, 5.56)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
SEX = FEMALE		
NUMBER OF IMP-TREATED HAE ATTACKS	54	55
EVENTS [1]	25 (46.3)	24 (43.6)
CENSORED [2]	29 (53.7)	31 (56.4)
TIME TO HAE ATTACK RESOLUTION (95% CI) [3]		
25TH PERCENTILE	7.07 (3.28, 11.53)	15.10 (6.61, 36.71)
MEDIAN	NE (11.53, NE)	NE (36.71, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.3972	
HAZARD RATIO (95 % CI) [4]	1.55 (0.84, 2.84)	

2.6.2 Alter

- PGI-S=Patient Global Impression of Severity; CI=Confidence Interval; NE=Not Evaluable
- Time to HAE attack resolution (hours) = Date/time of first rating of “None”– Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for visit, treatment, subgroup, subgroup*treatment interaction, and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks treated as right-censored at considered time if they did not have a HAE attack resolution or received conventional attack treatment within considered time of IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 1 post-baseline assessment, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to HAE attack resolution within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- [5] Stratified log-rank test controlling for the baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.4552	
AGE GROUP = <18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	10	9
EVENTS [1]	4 (40.0)	3 (33.3)
CENSORED [2]	6 (60.0)	6 (66.7)
TIME TO HAE ATTACK RESOLUTION (95% CI) [3]		
25TH PERCENTILE	8.62 (3.28, NE)	21.31 (1.55, NE)
MEDIAN	NE (3.28, NE)	NE (1.55, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.8567	
HAZARD RATIO (95 % CI) [4]	1.11 (0.19, 6.40)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
AGE GROUP = >=18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	77	75
EVENTS [1]	33 (42.9)	20 (26.7)
CENSORED [2]	44 (57.1)	55 (73.3)
TIME TO HAE ATTACK RESOLUTION (95% CI) [3]		
25TH PERCENTILE	8.54 (3.78, 13.33)	22.92 (8.28, NE)
MEDIAN	NE (16.60, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0232†	
HAZARD RATIO (95 % CI) [4]	2.21 (1.22, 3.99)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.5082	
AGE GROUP = <18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	10	9
EVENTS [1]	5 (50.0)	5 (55.6)
CENSORED [2]	5 (50.0)	4 (44.4)
TIME TO HAE ATTACK RESOLUTION (95% CI) [3]		
25TH PERCENTILE	8.62 (3.28, NE)	21.31 (1.55, 48.00)
MEDIAN	NE (3.28, NE)	48.00 (1.55, NE)
75TH PERCENTILE	NE (47.26, NE)	NE (45.53, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.6502	
HAZARD RATIO (95 % CI) [4]	0.76 (0.13, 4.34)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
AGE GROUP = >=18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	77	75
EVENTS [1]	36 (46.8)	29 (38.7)
CENSORED [2]	41 (53.2)	46 (61.3)
TIME TO HAE ATTACK RESOLUTION (95% CI) [3]		
25TH PERCENTILE	8.54 (3.78, 13.33)	22.92 (8.28, 38.77)
MEDIAN	NE (16.60, NE)	NE (45.09, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.1776	
HAZARD RATIO (95 % CI) [4]	1.70 (1.00, 2.89)	

2.6.3 Region (Variante 1)

- PGI-S=Patient Global Impression of Severity; CI=Confidence Interval; NE=Not Evaluable
- Time to HAE attack resolution (hours) = Date/time of first rating of “None”– Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for visit, treatment, subgroup, subgroup*treatment interaction, and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks treated as right-censored at considered time if they did not have a HAE attack resolution or received conventional attack treatment within considered time of IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 1 post-baseline assessment, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to HAE attack resolution within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- [5] Stratified log-rank test controlling for the baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.7157	
REGION 1 = US		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	12 (44.4)	8 (34.8)
CENSORED [2]	15 (55.6)	15 (65.2)
TIME TO HAE ATTACK RESOLUTION (95% CI) [3]		
25TH PERCENTILE	10.53 (1.20, 13.13)	14.38 (1.27, NE)
MEDIAN	NE (10.55, NE)	NE (14.38, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.2297	
HAZARD RATIO (95 % CI) [4]	1.89 (0.72, 4.97)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 1 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	60	61
EVENTS [1]	25 (41.7)	15 (24.6)
CENSORED [2]	35 (58.3)	46 (75.4)
TIME TO HAE ATTACK RESOLUTION (95% CI) [3]		
25TH PERCENTILE	7.07 (4.08, 16.60)	23.44 (6.61, NE)
MEDIAN	NE (16.60, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0492†	
HAZARD RATIO (95 % CI) [4]	2.29 (1.14, 4.60)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.5120	
REGION 1 = US		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	12 (44.4)	11 (47.8)
CENSORED [2]	15 (55.6)	12 (52.2)
TIME TO HAE ATTACK RESOLUTION (95% CI) [3]		
25TH PERCENTILE	10.53 (1.20, 13.13)	14.38 (1.27, 45.07)
MEDIAN	NE (10.55, NE)	NE (14.38, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.6473	
HAZARD RATIO (95 % CI) [4]	1.37 (0.55, 3.44)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 1 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	60	61
EVENTS [1]	29 (48.3)	23 (37.7)
CENSORED [2]	31 (51.7)	38 (62.3)
TIME TO HAE ATTACK RESOLUTION (95% CI) [3]		
25TH PERCENTILE	7.07 (4.08, 16.60)	23.44 (6.61, 45.53)
MEDIAN	NE (16.60, NE)	NE (45.53, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.1647	
HAZARD RATIO (95 % CI) [4]	1.85 (1.01, 3.42)	

2.6.4 Region (Variante 2)

- PGI-S=Patient Global Impression of Severity; CI=Confidence Interval; NE=Not Evaluable
- Time to HAE attack resolution (hours) = Date/time of first rating of “None”– Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for visit, treatment, subgroup, subgroup*treatment interaction, and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks treated as right-censored at considered time if they did not have a HAE attack resolution or received conventional attack treatment within considered time of IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 1 post-baseline assessment, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to HAE attack resolution within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- [5] Stratified log-rank test controlling for the baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.4136	
REGION 2 = NORTH AMERICA		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	12 (44.4)	8 (34.8)
CENSORED [2]	15 (55.6)	15 (65.2)
TIME TO HAE ATTACK RESOLUTION (95% CI) [3]		
25TH PERCENTILE	10.53 (1.20, 13.13)	14.38 (1.27, NE)
MEDIAN	NE (10.55, NE)	NE (14.38, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.2297	
HAZARD RATIO (95 % CI) [4]	1.89 (0.72, 4.97)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = EUROPE		
NUMBER OF IMP-TREATED HAE ATTACKS	44	48
EVENTS [1]	16 (36.4)	12 (25.0)
CENSORED [2]	28 (63.6)	36 (75.0)
TIME TO HAE ATTACK RESOLUTION (95% CI) [3]		
25TH PERCENTILE	14.32 (2.74, NE)	23.44 (6.61, NE)
MEDIAN	NE (22.90, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.2384	
HAZARD RATIO (95 % CI) [4]	1.86 (0.83, 4.18)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	16	13
EVENTS [1]	9 (56.3)	3 (23.1)
CENSORED [2]	7 (43.8)	10 (76.9)
TIME TO HAE ATTACK RESOLUTION (95% CI) [3]		
25TH PERCENTILE	4.31 (0.34, 8.62)	NE (1.55, NE)
MEDIAN	8.94 (4.08, NE)	NE (15.10, NE)
75TH PERCENTILE	NE (8.62, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.1510	
HAZARD RATIO (95 % CI) [4]	4.14 (0.97, 17.73)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.5713	
REGION 2 = NORTH AMERICA		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	12 (44.4)	11 (47.8)
CENSORED [2]	15 (55.6)	12 (52.2)
TIME TO HAE ATTACK RESOLUTION (95% CI) [3]		
25TH PERCENTILE	10.53 (1.20, 13.13)	14.38 (1.27, 45.07)
MEDIAN	NE (10.55, NE)	NE (14.38, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.6473	
HAZARD RATIO (95 % CI) [4]	1.37 (0.55, 3.44)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = EUROPE		
NUMBER OF IMP-TREATED HAE ATTACKS	44	48
EVENTS [1]	20 (45.5)	17 (35.4)
CENSORED [2]	24 (54.5)	31 (64.6)
TIME TO HAE ATTACK RESOLUTION (95% CI) [3]		
25TH PERCENTILE	14.32 (2.74, 33.03)	23.44 (6.61, NE)
MEDIAN	NE (22.90, NE)	NE (45.34, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.3004	
HAZARD RATIO (95 % CI) [4]	1.62 (0.80, 3.30)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	16	13
EVENTS [1]	9 (56.3)	6 (46.2)
CENSORED [2]	7 (43.8)	7 (53.8)
TIME TO HAE ATTACK RESOLUTION (95% CI) [3]		
25TH PERCENTILE	4.31 (0.34, 8.62)	33.17 (1.55, NE)
MEDIAN	8.94 (4.08, NE)	NE (15.10, NE)
75TH PERCENTILE	NE (8.62, NE)	NE (48.00, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.5208	
HAZARD RATIO (95 % CI) [4]	2.28 (0.68, 7.70)	

2.6.5 Prophylaxe-Status (Variante 1)

- PGI-S=Patient Global Impression of Severity; CI=Confidence Interval; NE=Not Evaluable
- Time to HAE attack resolution (hours) = Date/time of first rating of “None”– Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for visit, treatment, subgroup, subgroup*treatment interaction, and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks treated as right-censored at considered time if they did not have a HAE attack resolution or received conventional attack treatment within considered time of IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 1 post-baseline assessment, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to HAE attack resolution within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- [5] Stratified log-rank test controlling for the baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.0781	
PROPHYLACTIC TREATMENT STATUS 1 = ON PROPHYLACTIC TREATMENT		
NUMBER OF IMP-TREATED HAE ATTACKS	19	18
EVENTS [1]	12 (63.2)	11 (61.1)
CENSORED [2]	7 (36.8)	7 (38.9)
TIME TO HAE ATTACK RESOLUTION (95% CI) [3]		
25TH PERCENTILE	10.55 (0.34, 16.60)	7.46 (1.27, 14.38)
MEDIAN	17.05 (10.55, NE)	16.49 (7.46, NE)
75TH PERCENTILE	NE (17.05, NE)	NE (17.88, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.8082	
HAZARD RATIO (95 % CI) [4]	1.22 (0.50, 3.02)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 1 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	25 (36.8)	12 (18.2)
CENSORED [2]	43 (63.2)	54 (81.8)
TIME TO HAE ATTACK RESOLUTION (95% CI) [3]		
25TH PERCENTILE	5.60 (3.78, 13.67)	NE (14.86, NE)
MEDIAN	NE (22.90, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0115†	
HAZARD RATIO (95 % CI) [4]	2.82 (1.37, 5.84)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.1241	
PROPHYLACTIC TREATMENT STATUS 1 = ON PROPHYLACTIC TREATMENT		
NUMBER OF IMP-TREATED HAE ATTACKS	19	18
EVENTS [1]	12 (63.2)	13 (72.2)
CENSORED [2]	7 (36.8)	5 (27.8)
TIME TO HAE ATTACK RESOLUTION (95% CI) [3]		
25TH PERCENTILE	10.55 (0.34, 16.60)	7.46 (1.27, 14.38)
MEDIAN	17.05 (10.55, NE)	16.49 (7.46, 45.34)
75TH PERCENTILE	NE (17.05, NE)	NE (17.88, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.8845	
HAZARD RATIO (95 % CI) [4]	1.06 (0.44, 2.60)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 1 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	29 (42.6)	21 (31.8)
CENSORED [2]	39 (57.4)	45 (68.2)
TIME TO HAE ATTACK RESOLUTION (95% CI) [3]		
25TH PERCENTILE	5.60 (3.78, 13.67)	36.41 (14.86, NE)
MEDIAN	NE (22.90, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.1253	
HAZARD RATIO (95 % CI) [4]	1.99 (1.08, 3.66)	

2.6.6 Prophylaxe-Status (Variante 2)

- PGI-S=Patient Global Impression of Severity; CI=Confidence Interval; NE=Not Evaluable
- Time to HAE attack resolution (hours) = Date/time of first rating of “None”– Date/time of first IMP administration.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks treated as right-censored at considered time if they did not have a HAE attack resolution or received conventional attack treatment within considered time of IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 1 post-baseline assessment, attacks will be censored at time 0.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON KALLIKREIN		
NUMBER OF IMP-TREATED HAE ATTACKS	14	14
EVENTS [1]	9 (64.3)	10 (71.4)
CENSORED [2]	5 (35.7)	4 (28.6)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON OTHER		
NUMBER OF IMP-TREATED HAE ATTACKS	5	4
EVENTS [1]	3 (60.0)	1 (25.0)
CENSORED [2]	2 (40.0)	3 (75.0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	25 (36.8)	12 (18.2)
CENSORED [2]	43 (63.2)	54 (81.8)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON KALLIKREIN		
NUMBER OF IMP-TREATED HAE ATTACKS	14	14
EVENTS [1]	9 (64.3)	11 (78.6)
CENSORED [2]	5 (35.7)	3 (21.4)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON OTHER		
NUMBER OF IMP-TREATED HAE ATTACKS	5	4
EVENTS [1]	3 (60.0)	2 (50.0)
CENSORED [2]	2 (40.0)	2 (50.0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	29 (42.6)	21 (31.8)
CENSORED [2]	39 (57.4)	45 (68.2)

2.6.7 Attacken-Schwere (PGIS) zu Baseline

- PGI-S=Patient Global Impression of Severity; CI=Confidence Interval; NE=Not Evaluable
- Time to HAE attack resolution (hours) = Date/time of first rating of “None”– Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for visit, treatment, subgroup, and subgroup*treatment interaction in the model as fixed effects and patient as a random effect.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks treated as right-censored at considered time if they did not have a HAE attack resolution or received conventional attack treatment within considered time of IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 1 post-baseline assessment, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to HAE attack resolution within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment in the model as a fixed effect and patient as a random effect.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.5968	
ATTACK SEVERITY AT BASELINE PGI-S = NONE OR MILD		
NUMBER OF IMP-TREATED HAE ATTACKS	36	38
EVENTS [1]	18 (50.0)	11 (28.9)
CENSORED [2]	18 (50.0)	27 (71.1)
TIME TO HAE ATTACK RESOLUTION (95% CI) [3]		
25TH PERCENTILE	5.15 (1.81, 9.54)	17.88 (1.76, NE)
MEDIAN	NE (8.62, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
UNSTRATIFIED LOG-RANK P-VALUE	0.0735	
HAZARD RATIO (95 % CI) [4]	2.19 (0.97, 4.94)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = MODERATE		
NUMBER OF IMP-TREATED HAE ATTACKS	35	33
EVENTS [1]	14 (40.0)	8 (24.2)
CENSORED [2]	21 (60.0)	25 (75.8)
TIME TO HAE ATTACK RESOLUTION (95% CI) [3]		
25TH PERCENTILE	13.13 (2.74, 16.60)	23.06 (8.28, NE)
MEDIAN	NE (13.67, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
UNSTRATIFIED LOG-RANK P-VALUE	0.1272	
HAZARD RATIO (95 % CI) [4]	1.94 (0.81, 4.64)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = SEVERE OR VERY SEVERE		
NUMBER OF IMP-TREATED HAE ATTACKS	14	13
EVENTS [1]	5 (35.7)	4 (30.8)
CENSORED [2]	9 (64.3)	9 (69.2)
TIME TO HAE ATTACK RESOLUTION (95% CI) [3]		
25TH PERCENTILE	17.05 (2.27, NE)	14.38 (3.78, NE)
MEDIAN	NE (4.69, NE)	NE (13.02, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
UNSTRATIFIED LOG-RANK P-VALUE	0.7777	
HAZARD RATIO (95 % CI) [4]	1.16 (0.26, 5.24)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.3120	
ATTACK SEVERITY AT BASELINE PGI-S = NONE OR MILD		
NUMBER OF IMP-TREATED HAE ATTACKS	36	38
EVENTS [1]	18 (50.0)	13 (34.2)
CENSORED [2]	18 (50.0)	25 (65.8)
TIME TO HAE ATTACK RESOLUTION (95% CI) [3]		
25TH PERCENTILE	5.15 (1.81, 9.54)	17.88 (1.76, NE)
MEDIAN	NE (8.62, NE)	NE (48.00, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
UNSTRATIFIED LOG-RANK P-VALUE	0.1519	
HAZARD RATIO (95 % CI) [4]	2.02 (0.90, 4.54)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = MODERATE		
NUMBER OF IMP-TREATED HAE ATTACKS	35	33
EVENTS [1]	15 (42.9)	17 (51.5)
CENSORED [2]	20 (57.1)	16 (48.5)
TIME TO HAE ATTACK RESOLUTION (95% CI) [3]		
25TH PERCENTILE	13.13 (2.74, 16.60)	23.06 (8.28, 36.71)
MEDIAN	NE (13.67, NE)	45.34 (33.04, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
UNSTRATIFIED LOG-RANK P-VALUE	0.8682	
HAZARD RATIO (95 % CI) [4]	0.99 (0.47, 2.09)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = SEVERE OR VERY SEVERE		
NUMBER OF IMP-TREATED HAE ATTACKS	14	13
EVENTS [1]	8 (57.1)	4 (30.8)
CENSORED [2]	6 (42.9)	9 (69.2)
TIME TO HAE ATTACK RESOLUTION (95% CI) [3]		
25TH PERCENTILE	17.05 (2.27, 33.09)	14.38 (3.78, NE)
MEDIAN	40.18 (4.69, NE)	NE (13.02, NE)
75TH PERCENTILE	NE (33.09, NE)	NE (NE, NE)
UNSTRATIFIED LOG-RANK P-VALUE	0.2439	
HAZARD RATIO (95 % CI) [4]	1.84 (0.43, 7.84)	

2.7 Zeit bis zur Verbesserung des GA-NRS um mindestens 15 % der Gesamtskala (entspricht 2 Punkten)

2.7.1 Geschlecht

- GA-NRS=General Anxiety Numeric Rating Scale; CI=Confidence Interval; NE=Not Evaluable
- Time to at least 2 points reduction (hours) = Date/time of first ≥ 2 points reduction in GA-NRS score – Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for visit, treatment, subgroup, subgroup*treatment interaction, and baseline GA-NRS category (not at all anxious (0), mildly anxious (1-3), moderately anxious (4-6), extremely anxious (7-10)) in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that had a baseline GA-NRS score below a cutoff point will be excluded from the corresponding analysis.
- [2] Attacks are treated as right-censored at considered time if a ≥ 2 points reduction in GA-NRS score did not occur or received conventional attack treatment within considered time of IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 1 post-baseline assessment, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to at least 2 points reduction on GA-NRS from baseline within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline GA-NRS category (not at all anxious (0), mildly anxious (1-3), moderately anxious (4-6), extremely anxious (7-10)) in the model as fixed effects and patient as a random effect.
- [5] Stratified log-rank test controlling for the baseline GA-NRS category (not at all anxious, mildly anxious, moderately anxious, extremely anxious).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.3000	
SEX = MALE		
NUMBER OF IMP-TREATED HAE ATTACKS	33	29
EVENTS [1]	13 (39.4)	6 (20.7)
CENSORED [2]	20 (60.6)	23 (79.3)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	1.28 (0.77, 2.81)	NE (1.27, NE)
MEDIAN	NE (1.79, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0410†	
HAZARD RATIO (95 % CI) [4]	3.82 (1.21, 12.09)	

 Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
SEX = FEMALE		
NUMBER OF IMP-TREATED HAE ATTACKS	54	55
EVENTS [1]	22 (40.7)	18 (32.7)
CENSORED [2]	32 (59.3)	37 (67.3)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	1.08 (0.77, 2.27)	1.58 (0.79, NE)
MEDIAN	4.21 (1.82, NE)	NE (NE, NE)
75TH PERCENTILE	4.21 (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.3514	
HAZARD RATIO (95 % CI) [4]	1.56 (0.81, 3.03)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.1397	
SEX = MALE		
NUMBER OF IMP-TREATED HAE ATTACKS	33	29
EVENTS [1]	15 (45.5)	6 (20.7)
CENSORED [2]	18 (54.5)	23 (79.3)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	1.28 (0.77, 2.81)	NE (1.27, NE)
MEDIAN	NE (1.79, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0147†	
HAZARD RATIO (95 % CI) [4]	4.70 (1.50, 14.74)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
SEX = FEMALE		
NUMBER OF IMP-TREATED HAE ATTACKS	54	55
EVENTS [1]	23 (42.6)	22 (40.0)
CENSORED [2]	31 (57.4)	33 (60.0)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	1.08 (0.77, 2.27)	1.81 (0.79, 6.23)
MEDIAN	NE (1.82, NE)	NE (5.57, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.4274	
HAZARD RATIO (95 % CI) [4]	1.39 (0.75, 2.55)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.0756	
SEX = MALE		
NUMBER OF IMP-TREATED HAE ATTACKS	33	29
EVENTS [1]	16 (48.5)	6 (20.7)
CENSORED [2]	17 (51.5)	23 (79.3)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	1.28 (0.77, 2.81)	NE (1.27, NE)
MEDIAN	NE (1.79, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0080†	
HAZARD RATIO (95 % CI) [4]	5.09 (1.65, 15.71)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
SEX = FEMALE		
NUMBER OF IMP-TREATED HAE ATTACKS	54	55
EVENTS [1]	24 (44.4)	24 (43.6)
CENSORED [2]	30 (55.6)	31 (56.4)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	1.10 (0.77, 2.27)	1.81 (0.79, 6.23)
MEDIAN	NE (2.27, NE)	NE (6.23, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.5263	
HAZARD RATIO (95 % CI) [4]	1.29 (0.71, 2.33)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.0257†	
SEX = MALE		
NUMBER OF IMP-TREATED HAE ATTACKS	33	29
EVENTS [1]	17 (51.5)	7 (24.1)
CENSORED [2]	16 (48.5)	22 (75.9)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	1.28 (0.77, 2.81)	16.71 (1.27, NE)
MEDIAN	12.70 (1.79, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0066†	
HAZARD RATIO (95 % CI) [4]	5.88 (1.90, 18.17)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
SEX = FEMALE		
NUMBER OF IMP-TREATED HAE ATTACKS	54	55
EVENTS [1]	24 (44.4)	29 (52.7)
CENSORED [2]	30 (55.6)	26 (47.3)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	1.10 (0.77, 2.27)	1.81 (0.79, 6.23)
MEDIAN	NE (2.27, NE)	19.07 (6.23, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.9826	
HAZARD RATIO (95 % CI) [4]	1.09 (0.61, 1.92)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.0230†	
SEX = MALE		
NUMBER OF IMP-TREATED HAE ATTACKS	33	29
EVENTS [1]	17 (51.5)	8 (27.6)
CENSORED [2]	16 (48.5)	21 (72.4)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	1.28 (0.77, 2.81)	16.71 (1.27, NE)
MEDIAN	12.70 (1.79, NE)	NE (45.05, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0113†	
HAZARD RATIO (95 % CI) [4]	5.74 (1.90, 17.35)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
SEX = FEMALE		
NUMBER OF IMP-TREATED HAE ATTACKS	54	55
EVENTS [1]	24 (44.4)	31 (56.4)
CENSORED [2]	30 (55.6)	24 (43.6)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	1.10 (0.77, 2.27)	1.81 (0.79, 6.23)
MEDIAN	NE (2.27, NE)	19.07 (6.23, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.7717	
HAZARD RATIO (95 % CI) [4]	1.03 (0.58, 1.82)	

2.7.2 Alter

- GA-NRS=General Anxiety Numeric Rating Scale; CI=Confidence Interval; NE=Not Evaluable
- Time to at least 2 points reduction (hours) = Date/time of first ≥ 2 points reduction in GA-NRS score – Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for visit, treatment, subgroup, subgroup*treatment interaction, and baseline GA-NRS category (not at all anxious (0), mildly anxious (1-3), moderately anxious (4-6), extremely anxious (7-10)) in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that had a baseline GA-NRS score below a cutoff point will be excluded from the corresponding analysis.
- [2] Attacks are treated as right-censored at considered time if a ≥ 2 points reduction in GA-NRS score did not occur or received conventional attack treatment within considered time of IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 1 post-baseline assessment, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to at least 2 points reduction on GA-NRS from baseline within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline GA-NRS category (not at all anxious (0), mildly anxious (1-3), moderately anxious (4-6), extremely anxious (7-10)) in the model as fixed effects and patient as a random effect.
- [5] Stratified log-rank test controlling for the baseline GA-NRS category (not at all anxious, mildly anxious, moderately anxious, extremely anxious).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.0077†	
AGE GROUP = <18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	10	9
EVENTS [1]	1 (10.0)	5 (55.6)
CENSORED [2]	9 (90.0)	4 (44.4)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	NE (0.77, NE)	0.82 (0.31, 2.95)
MEDIAN	NE (0.77, NE)	2.95 (0.31, NE)
75TH PERCENTILE	NE (NE, NE)	NE (2.89, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.1366	
HAZARD RATIO (95 % CI) [4]	0.03 (0.00, 1.05)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
AGE GROUP = >=18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	77	75
EVENTS [1]	34 (44.2)	19 (25.3)
CENSORED [2]	43 (55.8)	56 (74.7)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	1.08 (0.78, 1.79)	2.87 (1.33, NE)
MEDIAN	4.21 (2.27, NE)	NE (NE, NE)
75TH PERCENTILE	4.21 (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0107†	
HAZARD RATIO (95 % CI) [4]	3.08 (1.65, 5.76)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.0093†	
AGE GROUP = <18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	10	9
EVENTS [1]	2 (20.0)	5 (55.6)
CENSORED [2]	8 (80.0)	4 (44.4)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	NE (0.77, NE)	0.82 (0.31, 2.95)
MEDIAN	NE (0.77, NE)	2.95 (0.31, NE)
75TH PERCENTILE	NE (NE, NE)	NE (2.89, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.1366	
HAZARD RATIO (95 % CI) [4]	0.05 (0.00, 0.90)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
AGE GROUP = >=18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	77	75
EVENTS [1]	36 (46.8)	23 (30.7)
CENSORED [2]	41 (53.2)	52 (69.3)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	1.08 (0.78, 1.79)	2.87 (1.33, NE)
MEDIAN	NE (2.27, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0103†	
HAZARD RATIO (95 % CI) [4]	2.72 (1.53, 4.85)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.0059†	
AGE GROUP = <18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	10	9
EVENTS [1]	2 (20.0)	6 (66.7)
CENSORED [2]	8 (80.0)	3 (33.3)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	NE (0.77, NE)	0.82 (0.31, 2.95)
MEDIAN	NE (0.77, NE)	2.95 (0.31, NE)
75TH PERCENTILE	NE (NE, NE)	NE (2.89, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0650	
HAZARD RATIO (95 % CI) [4]	0.04 (0.00, 0.71)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
AGE GROUP = >=18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	77	75
EVENTS [1]	38 (49.4)	24 (32.0)
CENSORED [2]	39 (50.6)	51 (68.0)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	1.08 (0.78, 1.79)	3.10 (1.33, NE)
MEDIAN	9.83 (2.27, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0080†	
HAZARD RATIO (95 % CI) [4]	2.61 (1.49, 4.57)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.0020†	
AGE GROUP = <18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	10	9
EVENTS [1]	2 (20.0)	7 (77.8)
CENSORED [2]	8 (80.0)	2 (22.2)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	NE (0.77, NE)	0.82 (0.31, 2.95)
MEDIAN	NE (0.77, NE)	2.95 (0.31, NE)
75TH PERCENTILE	NE (NE, NE)	15.03 (2.89, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0212†	
HAZARD RATIO (95 % CI) [4]	0.03 (0.00, 0.48)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
AGE GROUP = >=18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	77	75
EVENTS [1]	39 (50.6)	29 (38.7)
CENSORED [2]	38 (49.4)	46 (61.3)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	1.08 (0.78, 1.79)	3.10 (1.33, 15.09)
MEDIAN	9.83 (2.27, NE)	NE (23.06, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0258†	
HAZARD RATIO (95 % CI) [4]	2.54 (1.47, 4.39)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.0018†	
AGE GROUP = <18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	10	9
EVENTS [1]	2 (20.0)	7 (77.8)
CENSORED [2]	8 (80.0)	2 (22.2)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	NE (0.77, NE)	0.82 (0.31, 2.95)
MEDIAN	NE (0.77, NE)	2.95 (0.31, NE)
75TH PERCENTILE	NE (NE, NE)	15.03 (2.89, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0212†	
HAZARD RATIO (95 % CI) [4]	0.03 (0.00, 0.48)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
AGE GROUP = >=18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	77	75
EVENTS [1]	39 (50.6)	32 (42.7)
CENSORED [2]	38 (49.4)	43 (57.3)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	1.08 (0.78, 1.79)	3.10 (1.33, 15.09)
MEDIAN	9.83 (2.27, NE)	NE (23.06, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0548	
HAZARD RATIO (95 % CI) [4]	2.46 (1.43, 4.24)	

2.7.3 Region (Variante 1)

- GA-NRS=General Anxiety Numeric Rating Scale; CI=Confidence Interval; NE=Not Evaluable
- Time to at least 2 points reduction (hours) = Date/time of first ≥ 2 points reduction in GA-NRS score – Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for visit, treatment, subgroup, subgroup*treatment interaction, and baseline GA-NRS category (not at all anxious (0), mildly anxious (1-3), moderately anxious (4-6), extremely anxious (7-10)) in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that had a baseline GA-NRS score below a cutoff point will be excluded from the corresponding analysis.
- [2] Attacks are treated as right-censored at considered time if a ≥ 2 points reduction in GA-NRS score did not occur or received conventional attack treatment within considered time of IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 1 post-baseline assessment, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to at least 2 points reduction on GA-NRS from baseline within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline GA-NRS category (not at all anxious (0), mildly anxious (1-3), moderately anxious (4-6), extremely anxious (7-10)) in the model as fixed effects and patient as a random effect.
- [5] Stratified log-rank test controlling for the baseline GA-NRS category (not at all anxious, mildly anxious, moderately anxious, extremely anxious).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.1756	
REGION 1 = US		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	8 (29.6)	5 (21.7)
CENSORED [2]	19 (70.4)	18 (78.3)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	2.05 (0.30, NE)	NE (0.47, NE)
MEDIAN	4.21 (2.27, NE)	NE (NE, NE)
75TH PERCENTILE	4.21 (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.9122	
HAZARD RATIO (95 % CI) [4]	0.92 (0.27, 3.17)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 1 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	60	61
EVENTS [1]	27 (45.0)	19 (31.1)
CENSORED [2]	33 (55.0)	42 (68.9)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	0.92 (0.77, 1.63)	1.81 (1.27, NE)
MEDIAN	NE (1.79, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0223†	
HAZARD RATIO (95 % CI) [4]	2.60 (1.37, 4.93)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.1080	
REGION 1 = US		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	8 (29.6)	7 (30.4)
CENSORED [2]	19 (70.4)	16 (69.6)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	2.05 (0.30, NE)	5.57 (0.47, NE)
MEDIAN	NE (2.27, NE)	NE (5.57, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.7455	
HAZARD RATIO (95 % CI) [4]	0.85 (0.29, 2.48)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 1 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	60	61
EVENTS [1]	30 (50.0)	21 (34.4)
CENSORED [2]	30 (50.0)	40 (65.6)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	0.92 (0.77, 1.63)	1.81 (1.27, 7.22)
MEDIAN	5.47 (1.79, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0123†	
HAZARD RATIO (95 % CI) [4]	2.72 (1.47, 5.03)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.0668	
REGION 1 = US		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	9 (33.3)	8 (34.8)
CENSORED [2]	18 (66.7)	15 (65.2)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	2.05 (0.30, NE)	5.57 (0.47, NE)
MEDIAN	NE (2.27, NE)	NE (5.57, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.6640	
HAZARD RATIO (95 % CI) [4]	0.79 (0.29, 2.17)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 1 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	60	61
EVENTS [1]	31 (51.7)	22 (36.1)
CENSORED [2]	29 (48.3)	39 (63.9)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	1.00 (0.77, 1.79)	1.81 (1.27, 8.67)
MEDIAN	7.63 (1.79, NE)	NE (8.67, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0132†	
HAZARD RATIO (95 % CI) [4]	2.72 (1.49, 4.97)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.0594	
REGION 1 = US		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	9 (33.3)	9 (39.1)
CENSORED [2]	18 (66.7)	14 (60.9)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	2.05 (0.30, NE)	5.57 (0.47, NE)
MEDIAN	NE (2.27, NE)	NE (5.57, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.5021	
HAZARD RATIO (95 % CI) [4]	0.73 (0.27, 1.92)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 1 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	60	61
EVENTS [1]	32 (53.3)	27 (44.3)
CENSORED [2]	28 (46.7)	34 (55.7)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	1.00 (0.77, 1.79)	1.81 (1.27, 8.67)
MEDIAN	7.63 (1.79, NE)	NE (8.67, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0377†	
HAZARD RATIO (95 % CI) [4]	2.45 (1.37, 4.36)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.0366†	
REGION 1 = US		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	9 (33.3)	10 (43.5)
CENSORED [2]	18 (66.7)	13 (56.5)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	2.05 (0.30, NE)	5.57 (0.47, 45.04)
MEDIAN	NE (2.27, NE)	NE (5.57, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.3568	
HAZARD RATIO (95 % CI) [4]	0.61 (0.22, 1.71)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 1 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	60	61
EVENTS [1]	32 (53.3)	29 (47.5)
CENSORED [2]	28 (46.7)	32 (52.5)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	1.00 (0.77, 1.79)	1.81 (1.27, 8.67)
MEDIAN	7.63 (1.79, NE)	NE (8.67, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0636	
HAZARD RATIO (95 % CI) [4]	2.37 (1.34, 4.20)	

2.7.4 Region (Variante 2)

- GA-NRS=General Anxiety Numeric Rating Scale; CI=Confidence Interval; NE=Not Evaluable
- Time to at least 2 points reduction (hours) = Date/time of first ≥ 2 points reduction in GA-NRS score – Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for visit, treatment, subgroup, subgroup*treatment interaction, and baseline GA-NRS category (not at all anxious (0), mildly anxious (1-3), moderately anxious (4-6), extremely anxious (7-10)) in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that had a baseline GA-NRS score below a cutoff point will be excluded from the corresponding analysis.
- [2] Attacks are treated as right-censored at considered time if a ≥ 2 points reduction in GA-NRS score did not occur or received conventional attack treatment within considered time of IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 1 post-baseline assessment, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to at least 2 points reduction on GA-NRS from baseline within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline GA-NRS category (not at all anxious (0), mildly anxious (1-3), moderately anxious (4-6), extremely anxious (7-10)) in the model as fixed effects and patient as a random effect.
- [5] Stratified log-rank test controlling for the baseline GA-NRS category (not at all anxious, mildly anxious, moderately anxious, extremely anxious).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.2194	
REGION 2 = NORTH AMERICA		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	8 (29.6)	5 (21.7)
CENSORED [2]	19 (70.4)	18 (78.3)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	2.05 (0.30, NE)	NE (0.47, NE)
MEDIAN	4.21 (2.27, NE)	NE (NE, NE)
75TH PERCENTILE	4.21 (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.9122	
HAZARD RATIO (95 % CI) [4]	0.92 (0.27, 3.17)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = EUROPE		
NUMBER OF IMP-TREATED HAE ATTACKS	44	48
EVENTS [1]	20 (45.5)	17 (35.4)
CENSORED [2]	24 (54.5)	31 (64.6)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	1.08 (0.77, 1.79)	1.50 (0.82, 2.89)
MEDIAN	NE (1.63, NE)	NE (2.78, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0968	
HAZARD RATIO (95 % CI) [4]	2.45 (1.19, 5.04)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	16	13
EVENTS [1]	7 (43.8)	2 (15.4)
CENSORED [2]	9 (56.3)	11 (84.6)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	0.87 (0.34, NE)	NE (0.31, NE)
MEDIAN	NE (0.83, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0614	
HAZARD RATIO (95 % CI) [4]	6.69 (1.08, 41.26)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.1103	
REGION 2 = NORTH AMERICA		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	8 (29.6)	7 (30.4)
CENSORED [2]	19 (70.4)	16 (69.6)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	2.05 (0.30, NE)	5.57 (0.47, NE)
MEDIAN	NE (2.27, NE)	NE (5.57, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.7455	
HAZARD RATIO (95 % CI) [4]	0.85 (0.29, 2.48)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = EUROPE		
NUMBER OF IMP-TREATED HAE ATTACKS	44	48
EVENTS [1]	22 (50.0)	19 (39.6)
CENSORED [2]	22 (50.0)	29 (60.4)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	1.08 (0.77, 1.79)	1.50 (0.82, 2.89)
MEDIAN	5.21 (1.63, NE)	NE (2.78, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0818	
HAZARD RATIO (95 % CI) [4]	2.43 (1.22, 4.86)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	16	13
EVENTS [1]	8 (50.0)	2 (15.4)
CENSORED [2]	8 (50.0)	11 (84.6)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	0.87 (0.34, 5.21)	NE (0.31, NE)
MEDIAN	NE (0.83, NE)	NE (NE, NE)
75TH PERCENTILE	NE (5.21, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0263†	
HAZARD RATIO (95 % CI) [4]	8.47 (1.42, 50.46)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.0709	
REGION 2 = NORTH AMERICA		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	9 (33.3)	8 (34.8)
CENSORED [2]	18 (66.7)	15 (65.2)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	2.05 (0.30, NE)	5.57 (0.47, NE)
MEDIAN	NE (2.27, NE)	NE (5.57, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.6640	
HAZARD RATIO (95 % CI) [4]	0.79 (0.29, 2.17)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = EUROPE		
NUMBER OF IMP-TREATED HAE ATTACKS	44	48
EVENTS [1]	23 (52.3)	20 (41.7)
CENSORED [2]	21 (47.7)	28 (58.3)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	1.10 (0.77, 2.31)	1.50 (0.82, 6.81)
MEDIAN	7.63 (1.63, NE)	NE (2.78, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0817	
HAZARD RATIO (95 % CI) [4]	2.46 (1.25, 4.84)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	16	13
EVENTS [1]	8 (50.0)	2 (15.4)
CENSORED [2]	8 (50.0)	11 (84.6)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	0.87 (0.34, 5.21)	NE (0.31, NE)
MEDIAN	NE (0.83, NE)	NE (NE, NE)
75TH PERCENTILE	NE (5.21, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0263†	
HAZARD RATIO (95 % CI) [4]	8.47 (1.42, 50.46)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.1038	
REGION 2 = NORTH AMERICA		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	9 (33.3)	9 (39.1)
CENSORED [2]	18 (66.7)	14 (60.9)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	2.05 (0.30, NE)	5.57 (0.47, NE)
MEDIAN	NE (2.27, NE)	NE (5.57, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.5021	
HAZARD RATIO (95 % CI) [4]	0.73 (0.27, 1.92)	

 Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = EUROPE		
NUMBER OF IMP-TREATED HAE ATTACKS	44	48
EVENTS [1]	24 (54.5)	23 (47.9)
CENSORED [2]	20 (45.5)	25 (52.1)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	1.10 (0.77, 2.31)	1.50 (0.82, 6.81)
MEDIAN	7.63 (1.63, NE)	NE (2.78, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.1129	
HAZARD RATIO (95 % CI) [4]	2.48 (1.27, 4.85)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	16	13
EVENTS [1]	8 (50.0)	4 (30.8)
CENSORED [2]	8 (50.0)	9 (69.2)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	0.87 (0.34, 5.21)	15.09 (0.31, NE)
MEDIAN	NE (0.83, NE)	NE (15.03, NE)
75TH PERCENTILE	NE (5.21, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0913	
HAZARD RATIO (95 % CI) [4]	4.09 (1.05, 15.99)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.0752	
REGION 2 = NORTH AMERICA		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	9 (33.3)	10 (43.5)
CENSORED [2]	18 (66.7)	13 (56.5)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	2.05 (0.30, NE)	5.57 (0.47, 45.04)
MEDIAN	NE (2.27, NE)	NE (5.57, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.3568	
HAZARD RATIO (95 % CI) [4]	0.61 (0.22, 1.71)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = EUROPE		
NUMBER OF IMP-TREATED HAE ATTACKS	44	48
EVENTS [1]	24 (54.5)	24 (50.0)
CENSORED [2]	20 (45.5)	24 (50.0)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	1.10 (0.77, 2.31)	1.50 (0.82, 6.81)
MEDIAN	7.63 (1.63, NE)	34.25 (2.78, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.1438	
HAZARD RATIO (95 % CI) [4]	2.45 (1.26, 4.76)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	16	13
EVENTS [1]	8 (50.0)	5 (38.5)
CENSORED [2]	8 (50.0)	8 (61.5)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	0.87 (0.34, 5.21)	15.09 (0.31, NE)
MEDIAN	NE (0.83, NE)	NE (15.03, NE)
75TH PERCENTILE	NE (5.21, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.1544	
HAZARD RATIO (95 % CI) [4]	3.63 (0.99, 13.31)	

2.7.5 Prophylaxe-Status (Variante 1)

- GA-NRS=General Anxiety Numeric Rating Scale; CI=Confidence Interval; NE=Not Evaluable
- Time to at least 2 points reduction (hours) = Date/time of first ≥ 2 points reduction in GA-NRS score – Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for visit, treatment, subgroup, subgroup*treatment interaction, and baseline GA-NRS category (not at all anxious (0), mildly anxious (1-3), moderately anxious (4-6), extremely anxious (7-10)) in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that had a baseline GA-NRS score below a cutoff point will be excluded from the corresponding analysis.
- [2] Attacks are treated as right-censored at considered time if a ≥ 2 points reduction in GA-NRS score did not occur or received conventional attack treatment within considered time of IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 1 post-baseline assessment, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to at least 2 points reduction on GA-NRS from baseline within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline GA-NRS category (not at all anxious (0), mildly anxious (1-3), moderately anxious (4-6), extremely anxious (7-10)) in the model as fixed effects and patient as a random effect.
- [5] Stratified log-rank test controlling for the baseline GA-NRS category (not at all anxious, mildly anxious, moderately anxious, extremely anxious).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.5979	
PROPHYLACTIC TREATMENT STATUS 1 = ON PROPHYLACTIC TREATMENT		
NUMBER OF IMP-TREATED HAE ATTACKS	19	18
EVENTS [1]	9 (47.4)	5 (27.8)
CENSORED [2]	10 (52.6)	13 (72.2)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	0.81 (0.27, NE)	3.33 (0.29, NE)
MEDIAN	4.21 (0.81, NE)	NE (3.33, NE)
75TH PERCENTILE	4.21 (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.7016	
HAZARD RATIO (95 % CI) [4]	1.48 (0.43, 5.04)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 1 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	26 (38.2)	19 (28.8)
CENSORED [2]	42 (61.8)	47 (71.2)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	1.11 (0.78, 2.31)	2.07 (1.30, NE)
MEDIAN	NE (2.78, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0605	
HAZARD RATIO (95 % CI) [4]	2.30 (1.21, 4.38)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.3143	
PROPHYLACTIC TREATMENT STATUS 1 = ON PROPHYLACTIC TREATMENT		
NUMBER OF IMP-TREATED HAE ATTACKS	19	18
EVENTS [1]	9 (47.4)	7 (38.9)
CENSORED [2]	10 (52.6)	11 (61.1)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	0.81 (0.27, 4.21)	3.33 (0.29, NE)
MEDIAN	NE (0.81, NE)	NE (3.33, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.9804	
HAZARD RATIO (95 % CI) [4]	1.09 (0.36, 3.35)	

 Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 1 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	29 (42.6)	21 (31.8)
CENSORED [2]	39 (57.4)	45 (68.2)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	1.11 (0.78, 2.31)	2.07 (1.30, NE)
MEDIAN	NE (2.78, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0303†	
HAZARD RATIO (95 % CI) [4]	2.48 (1.33, 4.60)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.2258	
PROPHYLACTIC TREATMENT STATUS 1 = ON PROPHYLACTIC TREATMENT		
NUMBER OF IMP-TREATED HAE ATTACKS	19	18
EVENTS [1]	10 (52.6)	8 (44.4)
CENSORED [2]	9 (47.4)	10 (55.6)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	0.81 (0.27, 4.21)	3.33 (0.29, 9.90)
MEDIAN	10.12 (0.81, NE)	NE (3.33, NE)
75TH PERCENTILE	NE (10.12, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.8935	
HAZARD RATIO (95 % CI) [4]	0.97 (0.33, 2.85)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 1 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	30 (44.1)	22 (33.3)
CENSORED [2]	38 (55.9)	44 (66.7)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	1.27 (0.79, 2.31)	2.07 (1.30, NE)
MEDIAN	NE (2.81, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0311†	
HAZARD RATIO (95 % CI) [4]	2.48 (1.35, 4.55)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.2288	
PROPHYLACTIC TREATMENT STATUS 1 = ON PROPHYLACTIC TREATMENT		
NUMBER OF IMP-TREATED HAE ATTACKS	19	18
EVENTS [1]	10 (52.6)	9 (50.0)
CENSORED [2]	9 (47.4)	9 (50.0)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	0.81 (0.27, 4.21)	3.33 (0.29, 9.90)
MEDIAN	10.12 (0.81, NE)	NE (3.33, NE)
75TH PERCENTILE	NE (10.12, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.6930	
HAZARD RATIO (95 % CI) [4]	0.86 (0.30, 2.44)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 1 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	31 (45.6)	27 (40.9)
CENSORED [2]	37 (54.4)	39 (59.1)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	1.27 (0.79, 2.31)	2.07 (1.30, 15.03)
MEDIAN	NE (2.81, NE)	NE (15.09, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0912	
HAZARD RATIO (95 % CI) [4]	2.22 (1.24, 3.98)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.2106	
PROPHYLACTIC TREATMENT STATUS 1 = ON PROPHYLACTIC TREATMENT		
NUMBER OF IMP-TREATED HAE ATTACKS	19	18
EVENTS [1]	10 (52.6)	10 (55.6)
CENSORED [2]	9 (47.4)	8 (44.4)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	0.81 (0.27, 4.21)	3.33 (0.29, 9.90)
MEDIAN	10.12 (0.81, NE)	30.92 (3.33, NE)
75TH PERCENTILE	NE (10.12, NE)	NE (47.46, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.5790	
HAZARD RATIO (95 % CI) [4]	0.76 (0.27, 2.10)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 1 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	31 (45.6)	29 (43.9)
CENSORED [2]	37 (54.4)	37 (56.1)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	1.27 (0.79, 2.31)	2.07 (1.30, 15.03)
MEDIAN	NE (2.81, NE)	NE (15.09, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.1522	
HAZARD RATIO (95 % CI) [4]	2.14 (1.20, 3.80)	

2.7.6 Prophylaxe-Status (Variante 2)

- GA-NRS=General Anxiety Numeric Rating Scale; CI=Confidence Interval; NE=Not Evaluable
- Time to at least 2 points reduction (hours) = Date/time of first ≥ 2 points reduction in GA-NRS score – Date/time of first IMP administration.
- [1] Attacks that had a baseline GA-NRS score below a cutoff point will be excluded from the corresponding analysis.
- [2] Attacks are treated as right-censored at considered time if a ≥ 2 points reduction in GA-NRS score did not occur or received conventional attack treatment within considered time of IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 1 post-baseline assessment, attacks will be censored at time 0.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON KALLIKREIN		
NUMBER OF IMP-TREATED HAE ATTACKS	14	14
EVENTS [1]	5 (35.7)	3 (21.4)
CENSORED [2]	9 (64.3)	11 (78.6)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON OTHER		
NUMBER OF IMP-TREATED HAE ATTACKS	5	4
EVENTS [1]	4 (80.0)	2 (50.0)
CENSORED [2]	1 (20.0)	2 (50.0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	26 (38.2)	19 (28.8)
CENSORED [2]	42 (61.8)	47 (71.2)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON KALLIKREIN		
NUMBER OF IMP-TREATED HAE ATTACKS	14	14
EVENTS [1]	5 (35.7)	5 (35.7)
CENSORED [2]	9 (64.3)	9 (64.3)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON OTHER		
NUMBER OF IMP-TREATED HAE ATTACKS	5	4
EVENTS [1]	4 (80.0)	2 (50.0)
CENSORED [2]	1 (20.0)	2 (50.0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	29 (42.6)	21 (31.8)
CENSORED [2]	39 (57.4)	45 (68.2)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON KALLIKREIN		
NUMBER OF IMP-TREATED HAE ATTACKS	14	14
EVENTS [1]	6 (42.9)	6 (42.9)
CENSORED [2]	8 (57.1)	8 (57.1)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON OTHER		
NUMBER OF IMP-TREATED HAE ATTACKS	5	4
EVENTS [1]	4 (80.0)	2 (50.0)
CENSORED [2]	1 (20.0)	2 (50.0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	30 (44.1)	22 (33.3)
CENSORED [2]	38 (55.9)	44 (66.7)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHOUT 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON KALLIKREIN		
NUMBER OF IMP-TREATED HAE ATTACKS	14	14
EVENTS [1]	6 (42.9)	7 (50.0)
CENSORED [2]	8 (57.1)	7 (50.0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON OTHER		
NUMBER OF IMP-TREATED HAE ATTACKS	5	4
EVENTS [1]	4 (80.0)	2 (50.0)
CENSORED [2]	1 (20.0)	2 (50.0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	31 (45.6)	27 (40.9)
CENSORED [2]	37 (54.4)	39 (59.1)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON KALLIKREIN		
NUMBER OF IMP-TREATED HAE ATTACKS	14	14
EVENTS [1]	6 (42.9)	8 (57.1)
CENSORED [2]	8 (57.1)	6 (42.9)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON OTHER		
NUMBER OF IMP-TREATED HAE ATTACKS	5	4
EVENTS [1]	4 (80.0)	2 (50.0)
CENSORED [2]	1 (20.0)	2 (50.0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	31 (45.6)	29 (43.9)
CENSORED [2]	37 (54.4)	37 (56.1)

2.7.7 Attacken-Schwere (PGIS) zu Baseline

- GA-NRS=General Anxiety Numeric Rating Scale; CI=Confidence Interval; NE=Not Evaluable
- Time to at least 2 points reduction (hours) = Date/time of first ≥ 2 points reduction in GA-NRS score – Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for visit, treatment, subgroup, subgroup*treatment interaction, and baseline GA-NRS category (not at all anxious (0), mildly anxious (1-3), moderately anxious (4-6), extremely anxious (7-10)) in the model as fixed effects and patient as a random effect.
- [1] Attacks that had a baseline GA-NRS score below a cutoff point will be excluded from the corresponding analysis.
- [2] Attacks are treated as right-censored at considered time if a ≥ 2 points reduction in GA-NRS score did not occur or received conventional attack treatment within considered time of IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 1 post-baseline assessment, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to at least 2 points reduction on GA-NRS from baseline within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline GA-NRS category (not at all anxious (0), mildly anxious (1-3), moderately anxious (4-6), extremely anxious (7-10)) in the model as fixed effects and patient as a random effect.
- [5] Stratified log-rank test controlling for the baseline GA-NRS category (not at all anxious, mildly anxious, moderately anxious, extremely anxious).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.5631	
ATTACK SEVERITY AT BASELINE PGI-S = NONE OR MILD		
NUMBER OF IMP-TREATED HAE ATTACKS	36	38
EVENTS [1]	11 (30.6)	8 (21.1)
CENSORED [2]	25 (69.4)	30 (78.9)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	2.31 (0.81, NE)	NE (0.80, NE)
MEDIAN	NE (NE, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.4736	
HAZARD RATIO (95 % CI) [4]	1.76 (0.61, 5.09)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = MODERATE		
NUMBER OF IMP-TREATED HAE ATTACKS	35	33
EVENTS [1]	15 (42.9)	12 (36.4)
CENSORED [2]	20 (57.1)	21 (63.6)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	0.94 (0.30, 1.29)	1.81 (0.79, 2.89)
MEDIAN	NE (1.11, NE)	NE (2.78, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.3015	
HAZARD RATIO (95 % CI) [4]	1.85 (0.73, 4.72)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 4 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = SEVERE OR VERY SEVERE		
NUMBER OF IMP-TREATED HAE ATTACKS	14	13
EVENTS [1]	9 (64.3)	4 (30.8)
CENSORED [2]	5 (35.7)	9 (69.2)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	0.79 (0.77, 1.79)	1.54 (0.30, NE)
MEDIAN	2.30 (0.79, NE)	NE (1.50, NE)
75TH PERCENTILE	4.21 (1.79, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.1216	
HAZARD RATIO (95 % CI) [4]	3.67 (0.57, 23.74)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.5163	
ATTACK SEVERITY AT BASELINE PGI-S = NONE OR MILD		
NUMBER OF IMP-TREATED HAE ATTACKS	36	38
EVENTS [1]	11 (30.6)	10 (26.3)
CENSORED [2]	25 (69.4)	28 (73.7)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	2.31 (0.81, NE)	7.22 (0.80, NE)
MEDIAN	NE (NE, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.6230	
HAZARD RATIO (95 % CI) [4]	1.58 (0.57, 4.33)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = MODERATE		
NUMBER OF IMP-TREATED HAE ATTACKS	35	33
EVENTS [1]	18 (51.4)	13 (39.4)
CENSORED [2]	17 (48.6)	20 (60.6)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	0.94 (0.30, 1.29)	1.81 (0.79, 2.89)
MEDIAN	4.96 (1.11, NE)	NE (2.78, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.1863	
HAZARD RATIO (95 % CI) [4]	1.95 (0.82, 4.65)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 8 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = SEVERE OR VERY SEVERE		
NUMBER OF IMP-TREATED HAE ATTACKS	14	13
EVENTS [1]	9 (64.3)	5 (38.5)
CENSORED [2]	5 (35.7)	8 (61.5)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	0.79 (0.77, 1.79)	1.54 (0.30, NE)
MEDIAN	2.30 (0.79, NE)	NE (1.50, NE)
75TH PERCENTILE	NE (1.79, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.1216	
HAZARD RATIO (95 % CI) [4]	3.81 (0.60, 24.21)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.5341	
ATTACK SEVERITY AT BASELINE PGI-S = NONE OR MILD		
NUMBER OF IMP-TREATED HAE ATTACKS	36	38
EVENTS [1]	12 (33.3)	10 (26.3)
CENSORED [2]	24 (66.7)	28 (73.7)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	2.55 (0.81, NE)	7.22 (0.80, NE)
MEDIAN	NE (9.54, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.5542	
HAZARD RATIO (95 % CI) [4]	1.68 (0.63, 4.48)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = MODERATE		
NUMBER OF IMP-TREATED HAE ATTACKS	35	33
EVENTS [1]	19 (54.3)	15 (45.5)
CENSORED [2]	16 (45.7)	18 (54.5)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	1.08 (0.30, 1.29)	1.81 (0.79, 5.57)
MEDIAN	5.21 (1.28, NE)	NE (2.78, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.1869	
HAZARD RATIO (95 % CI) [4]	1.90 (0.81, 4.44)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = SEVERE OR VERY SEVERE		
NUMBER OF IMP-TREATED HAE ATTACKS	14	13
EVENTS [1]	9 (64.3)	5 (38.5)
CENSORED [2]	5 (35.7)	8 (61.5)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	0.79 (0.77, 1.79)	1.54 (0.30, NE)
MEDIAN	2.30 (0.79, NE)	NE (1.50, NE)
75TH PERCENTILE	NE (1.79, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.1216	
HAZARD RATIO (95 % CI) [4]	3.81 (0.60, 24.21)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.6056	
ATTACK SEVERITY AT BASELINE PGI-S = NONE OR MILD		
NUMBER OF IMP-TREATED HAE ATTACKS	36	38
EVENTS [1]	12 (33.3)	12 (31.6)
CENSORED [2]	24 (66.7)	26 (68.4)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	2.55 (0.81, NE)	7.22 (0.80, NE)
MEDIAN	NE (9.54, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.8334	
HAZARD RATIO (95 % CI) [4]	1.39 (0.54, 3.54)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = MODERATE		
NUMBER OF IMP-TREATED HAE ATTACKS	35	33
EVENTS [1]	20 (57.1)	17 (51.5)
CENSORED [2]	15 (42.9)	16 (48.5)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	1.08 (0.30, 1.29)	1.81 (0.79, 5.57)
MEDIAN	5.21 (1.28, NE)	15.09 (2.78, NE)
75TH PERCENTILE	NE (15.86, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.2101	
HAZARD RATIO (95 % CI) [4]	1.80 (0.78, 4.14)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = SEVERE OR VERY SEVERE		
NUMBER OF IMP-TREATED HAE ATTACKS	14	13
EVENTS [1]	9 (64.3)	7 (53.8)
CENSORED [2]	5 (35.7)	6 (46.2)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	0.79 (0.77, 1.79)	1.54 (0.30, 16.71)
MEDIAN	2.30 (0.79, NE)	16.71 (1.50, NE)
75TH PERCENTILE	NE (1.79, NE)	NE (14.38, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.1216	
HAZARD RATIO (95 % CI) [4]	3.10 (0.55, 17.63)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHOUT 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.6677	
ATTACK SEVERITY AT BASELINE PGI-S = NONE OR MILD		
NUMBER OF IMP-TREATED HAE ATTACKS	36	38
EVENTS [1]	12 (33.3)	13 (34.2)
CENSORED [2]	24 (66.7)	25 (65.8)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	2.55 (0.81, NE)	7.22 (0.80, NE)
MEDIAN	NE (9.54, NE)	NE (47.46, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.9870	
HAZARD RATIO (95 % CI) [4]	1.29 (0.51, 3.24)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = MODERATE		
NUMBER OF IMP-TREATED HAE ATTACKS	35	33
EVENTS [1]	20 (57.1)	18 (54.5)
CENSORED [2]	15 (42.9)	15 (45.5)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	1.08 (0.30, 1.29)	1.81 (0.79, 5.57)
MEDIAN	5.21 (1.28, NE)	15.09 (2.78, NE)
75TH PERCENTILE	NE (15.86, NE)	NE (45.04, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.2511	
HAZARD RATIO (95 % CI) [4]	1.73 (0.74, 4.04)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 48 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = SEVERE OR VERY SEVERE		
NUMBER OF IMP-TREATED HAE ATTACKS	14	13
EVENTS [1]	9 (64.3)	8 (61.5)
CENSORED [2]	5 (35.7)	5 (38.5)
TIME TO AT LEAST 2 POINTS REDUCTION ON GA-NRS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	0.79 (0.77, 1.79)	1.54 (0.30, 16.71)
MEDIAN	2.30 (0.79, NE)	16.71 (1.50, NE)
75TH PERCENTILE	NE (1.79, NE)	NE (14.38, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.2812	
HAZARD RATIO (95 % CI) [4]	3.05 (0.50, 18.54)	

2.8 Zeit bis zu einer Verringerung der VAS von mindestens 50 % zur Baseline

2.8.1 Geschlecht

- VAS=Visual Analogic Scale; CI=Confidence Interval; NE=Not Evaluable
- Composite VAS score is defined as the mean score across all 3 symptom scores.
- Time to at least 50% decrease (hours) = Date/time of first $\geq 50\%$ decrease in composite VAS score for 3 consecutive time points (with possible missing values in between) – Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for visit, treatment, subgroup, subgroup*treatment interaction, and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if a $\geq 50\%$ reduction in composite VAS score for 3 consecutive time points did not occur or received conventional attack treatment within considered time of IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 3 post-baseline assessments, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to at least 50% decrease on Composite VAS from baseline within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- [5] Stratified log-rank test controlling for the baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.3048	
SEX = MALE		
NUMBER OF IMP-TREATED HAE ATTACKS	33	29
EVENTS [1]	20 (60.6)	6 (20.7)
CENSORED [2]	13 (39.4)	23 (79.3)
TIME TO AT LEAST 50% DECREASE ON COMPOSITE VAS FROM BASELINE (95 % CI) [3]		
25TH PERCENTILE	2.32 (0.98, 3.80)	NE (0.77, NE)
MEDIAN	4.55 (2.40, NE)	NE (NE, NE)
75TH PERCENTILE	NE (6.58, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0064†	
HAZARD RATIO (95 % CI) [4]	4.08 (1.49, 11.17)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
SEX = FEMALE		
NUMBER OF IMP-TREATED HAE ATTACKS	54	55
EVENTS [1]	24 (44.4)	16 (29.1)
CENSORED [2]	30 (55.6)	39 (70.9)
 TIME TO AT LEAST 50% DECREASE ON COMPOSITE VAS FROM BASELINE (95 % CI) [3]		
25TH PERCENTILE	2.79 (1.33, 4.76)	6.23 (2.28, NE)
MEDIAN	NE (3.84, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0614	
HAZARD RATIO (95 % CI) [4]	1.96 (1.01, 3.80)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.2394	
SEX = MALE		
NUMBER OF IMP-TREATED HAE ATTACKS	33	29
EVENTS [1]	22 (66.7)	9 (31.0)
CENSORED [2]	11 (33.3)	20 (69.0)
TIME TO AT LEAST 50% DECREASE ON COMPOSITE VAS FROM BASELINE (95 % CI) [3]		
25TH PERCENTILE	2.32 (0.98, 3.80)	13.02 (1.27, NE)
MEDIAN	4.55 (2.40, 11.53)	NE (13.12, NE)
75TH PERCENTILE	NE (6.58, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0033†	
HAZARD RATIO (95 % CI) [4]	4.06 (1.68, 9.82)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
SEX = FEMALE		
NUMBER OF IMP-TREATED HAE ATTACKS	54	55
EVENTS [1]	29 (53.7)	20 (36.4)
CENSORED [2]	25 (46.3)	35 (63.6)
TIME TO AT LEAST 50% DECREASE ON COMPOSITE VAS FROM BASELINE (95 % CI) [3]		
25TH PERCENTILE	2.79 (1.78, 4.76)	6.23 (2.28, 11.53)
MEDIAN	10.12 (3.84, NE)	NE (10.69, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0661	
HAZARD RATIO (95 % CI) [4]	1.93 (1.05, 3.55)	

2.8.2 Alter

- VAS=Visual Analogic Scale; CI=Confidence Interval; NE=Not Evaluable
- Composite VAS score is defined as the mean score across all 3 symptom scores.
- Time to at least 50% decrease (hours) = Date/time of first $\geq 50\%$ decrease in composite VAS score for 3 consecutive time points (with possible missing values in between) – Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for visit, treatment, subgroup, subgroup*treatment interaction, and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if a $\geq 50\%$ reduction in composite VAS score for 3 consecutive time points did not occur or received conventional attack treatment within considered time of IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 3 post-baseline assessments, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to at least 50% decrease on Composite VAS from baseline within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- [5] Stratified log-rank test controlling for the baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.7210	
AGE GROUP = <18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	10	9
EVENTS [1]	4 (40.0)	1 (11.1)
CENSORED [2]	6 (60.0)	8 (88.9)
TIME TO AT LEAST 50% DECREASE ON COMPOSITE VAS FROM BASELINE (95 % CI) [3]		
25TH PERCENTILE	3.37 (1.87, NE)	NE (0.31, NE)
MEDIAN	NE (1.87, NE)	NE (0.31, NE)
75TH PERCENTILE	NE (4.55, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.2424	
HAZARD RATIO (95 % CI) [4]	3.72 (0.33, 41.54)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
AGE GROUP = >=18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	77	75
EVENTS [1]	40 (51.9)	21 (28.0)
CENSORED [2]	37 (48.1)	54 (72.0)
TIME TO AT LEAST 50% DECREASE ON COMPOSITE VAS FROM BASELINE (95 % CI) [3]		
25TH PERCENTILE	2.34 (1.78, 3.77)	5.56 (2.93, NE)
MEDIAN	6.58 (3.80, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0023†	
HAZARD RATIO (95 % CI) [4]	2.49 (1.43, 4.35)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHOUT 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.9416	
AGE GROUP = <18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	10	9
EVENTS [1]	5 (50.0)	2 (22.2)
CENSORED [2]	5 (50.0)	7 (77.8)
TIME TO AT LEAST 50% DECREASE ON COMPOSITE VAS FROM BASELINE (95 % CI) [3]		
25TH PERCENTILE	3.37 (1.87, NE)	NE (0.31, NE)
MEDIAN	NE (1.87, NE)	NE (0.31, NE)
75TH PERCENTILE	NE (11.53, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.1654	
HAZARD RATIO (95 % CI) [4]	2.87 (0.45, 18.46)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
AGE GROUP = >=18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	77	75
EVENTS [1]	46 (59.7)	27 (36.0)
CENSORED [2]	31 (40.3)	48 (64.0)
TIME TO AT LEAST 50% DECREASE ON COMPOSITE VAS FROM BASELINE (95 % CI) [3]		
25TH PERCENTILE	2.37 (1.78, 3.80)	5.90 (2.93, 11.53)
MEDIAN	6.81 (3.84, 13.33)	NE (14.38, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0019†	
HAZARD RATIO (95 % CI) [4]	2.47 (1.48, 4.12)	

2.8.3 Region (Variante 1)

- VAS=Visual Analogic Scale; CI=Confidence Interval; NE=Not Evaluable
- Composite VAS score is defined as the mean score across all 3 symptom scores.
- Time to at least 50% decrease (hours) = Date/time of first $\geq 50\%$ decrease in composite VAS score for 3 consecutive time points (with possible missing values in between) – Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for visit, treatment, subgroup, subgroup*treatment interaction, and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if a $\geq 50\%$ reduction in composite VAS score for 3 consecutive time points did not occur or received conventional attack treatment within considered time of IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 3 post-baseline assessments, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to at least 50% decrease on Composite VAS from baseline within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- [5] Stratified log-rank test controlling for the baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.7997	
REGION 1 = US		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	12 (44.4)	7 (30.4)
CENSORED [2]	15 (55.6)	16 (69.6)
TIME TO AT LEAST 50% DECREASE ON COMPOSITE VAS FROM BASELINE (95 % CI) [3]		
25TH PERCENTILE	2.27 (0.77, 3.77)	6.35 (1.27, NE)
MEDIAN	5.73 (2.32, NE)	NE (6.35, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0378†	
HAZARD RATIO (95 % CI) [4]	3.14 (1.13, 8.71)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 1 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	60	61
EVENTS [1]	32 (53.3)	15 (24.6)
CENSORED [2]	28 (46.7)	46 (75.4)
TIME TO AT LEAST 50% DECREASE ON COMPOSITE VAS FROM BASELINE (95 % CI) [3]		
25TH PERCENTILE	2.79 (1.87, 3.84)	3.77 (1.79, NE)
MEDIAN	7.03 (3.84, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0062†	
HAZARD RATIO (95 % CI) [4]	2.52 (1.31, 4.86)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.6899	
REGION 1 = US		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	14 (51.9)	10 (43.5)
CENSORED [2]	13 (48.1)	13 (56.5)
TIME TO AT LEAST 50% DECREASE ON COMPOSITE VAS FROM BASELINE (95 % CI) [3]		
25TH PERCENTILE	2.27 (0.77, 3.77)	6.35 (1.27, 11.53)
MEDIAN	5.73 (2.32, NE)	NE (6.35, NE)
75TH PERCENTILE	NE (10.12, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.1139	
HAZARD RATIO (95 % CI) [4]	2.42 (0.97, 6.04)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 1 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	60	61
EVENTS [1]	37 (61.7)	19 (31.1)
CENSORED [2]	23 (38.3)	42 (68.9)
TIME TO AT LEAST 50% DECREASE ON COMPOSITE VAS FROM BASELINE (95 % CI) [3]		
25TH PERCENTILE	2.79 (1.87, 3.95)	5.66 (2.07, NE)
MEDIAN	7.52 (3.95, 19.10)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0028†	
HAZARD RATIO (95 % CI) [4]	2.72 (1.48, 4.98)	

2.8.4 Region (Variante 2)

- VAS=Visual Analogic Scale; CI=Confidence Interval; NE=Not Evaluable
- Composite VAS score is defined as the mean score across all 3 symptom scores.
- Time to at least 50% decrease (hours) = Date/time of first $\geq 50\%$ decrease in composite VAS score for 3 consecutive time points (with possible missing values in between) – Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for visit, treatment, subgroup, subgroup*treatment interaction, and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if a $\geq 50\%$ reduction in composite VAS score for 3 consecutive time points did not occur or received conventional attack treatment within considered time of IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 3 post-baseline assessments, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to at least 50% decrease on Composite VAS from baseline within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- [5] Stratified log-rank test controlling for the baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.8331	
REGION 2 = NORTH AMERICA		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	12 (44.4)	7 (30.4)
CENSORED [2]	15 (55.6)	16 (69.6)
TIME TO AT LEAST 50% DECREASE ON COMPOSITE VAS FROM BASELINE (95 % CI) [3]		
25TH PERCENTILE	2.27 (0.77, 3.77)	6.35 (1.27, NE)
MEDIAN	5.73 (2.32, NE)	NE (6.35, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0378†	
HAZARD RATIO (95 % CI) [4]	3.14 (1.13, 8.71)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = EUROPE		
NUMBER OF IMP-TREATED HAE ATTACKS	44	48
EVENTS [1]	22 (50.0)	11 (22.9)
CENSORED [2]	22 (50.0)	37 (77.1)
TIME TO AT LEAST 50% DECREASE ON COMPOSITE VAS FROM BASELINE (95 % CI) [3]		
25TH PERCENTILE	2.34 (1.78, 3.96)	7.54 (2.95, NE)
MEDIAN	9.28 (3.95, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0170†	
HAZARD RATIO (95 % CI) [4]	2.95 (1.33, 6.55)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	16	13
EVENTS [1]	10 (62.5)	4 (30.8)
CENSORED [2]	6 (37.5)	9 (69.2)
TIME TO AT LEAST 50% DECREASE ON COMPOSITE VAS FROM BASELINE (95 % CI) [3]		
25TH PERCENTILE	2.79 (0.34, 3.84)	1.27 (0.31, NE)
MEDIAN	4.55 (2.40, NE)	NE (0.77, NE)
75TH PERCENTILE	NE (4.55, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.4030	
HAZARD RATIO (95 % CI) [4]	1.67 (0.52, 5.38)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.9015	
REGION 2 = NORTH AMERICA		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	14 (51.9)	10 (43.5)
CENSORED [2]	13 (48.1)	13 (56.5)
TIME TO AT LEAST 50% DECREASE ON COMPOSITE VAS FROM BASELINE (95 % CI) [3]		
25TH PERCENTILE	2.27 (0.77, 3.77)	6.35 (1.27, 11.53)
MEDIAN	5.73 (2.32, NE)	NE (6.35, NE)
75TH PERCENTILE	NE (10.12, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.1139	
HAZARD RATIO (95 % CI) [4]	2.42 (0.97, 6.04)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = EUROPE		
NUMBER OF IMP-TREATED HAE ATTACKS	44	48
EVENTS [1]	27 (61.4)	15 (31.3)
CENSORED [2]	17 (38.6)	33 (68.8)
TIME TO AT LEAST 50% DECREASE ON COMPOSITE VAS FROM BASELINE (95 % CI) [3]		
25TH PERCENTILE	2.83 (1.78, 4.76)	9.12 (2.95, NE)
MEDIAN	9.80 (3.95, NE)	NE (16.71, NE)
75TH PERCENTILE	NE (19.10, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0072†	
HAZARD RATIO (95 % CI) [4]	3.25 (1.59, 6.62)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	16	13
EVENTS [1]	10 (62.5)	4 (30.8)
CENSORED [2]	6 (37.5)	9 (69.2)
TIME TO AT LEAST 50% DECREASE ON COMPOSITE VAS FROM BASELINE (95 % CI) [3]		
25TH PERCENTILE	2.79 (0.34, 3.84)	1.27 (0.31, NE)
MEDIAN	4.55 (2.40, NE)	NE (0.77, NE)
75TH PERCENTILE	NE (4.55, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.4030	
HAZARD RATIO (95 % CI) [4]	1.67 (0.52, 5.38)	

2.8.5 Prophylaxe-Status (Variante 1)

- VAS=Visual Analogic Scale; CI=Confidence Interval; NE=Not Evaluable
- Composite VAS score is defined as the mean score across all 3 symptom scores.
- Time to at least 50% decrease (hours) = Date/time of first $\geq 50\%$ decrease in composite VAS score for 3 consecutive time points (with possible missing values in between) – Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for visit, treatment, subgroup, subgroup*treatment interaction, and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if a $\geq 50\%$ reduction in composite VAS score for 3 consecutive time points did not occur or received conventional attack treatment within considered time of IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 3 post-baseline assessments, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to at least 50% decrease on Composite VAS from baseline within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- [5] Stratified log-rank test controlling for the baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.0269†	
PROPHYLACTIC TREATMENT STATUS 1 = ON PROPHYLACTIC TREATMENT		
NUMBER OF IMP-TREATED HAE ATTACKS	19	18
EVENTS [1]	9 (47.4)	9 (50.0)
CENSORED [2]	10 (52.6)	9 (50.0)
TIME TO AT LEAST 50% DECREASE ON COMPOSITE VAS FROM BASELINE (95 % CI) [3]		
25TH PERCENTILE	2.83 (0.34, 7.52)	2.93 (0.77, 6.35)
MEDIAN	NE (2.83, NE)	NE (2.93, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.9133	
HAZARD RATIO (95 % CI) [4]	1.08 (0.37, 3.15)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 1 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	35 (51.5)	13 (19.7)
CENSORED [2]	33 (48.5)	53 (80.3)
TIME TO AT LEAST 50% DECREASE ON COMPOSITE VAS FROM BASELINE (95 % CI) [3]		
25TH PERCENTILE	2.34 (1.79, 3.37)	NE (3.03, NE)
MEDIAN	5.53 (3.77, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0002†	
HAZARD RATIO (95 % CI) [4]	3.68 (1.88, 7.19)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.0360†	
PROPHYLACTIC TREATMENT STATUS 1 = ON PROPHYLACTIC TREATMENT		
NUMBER OF IMP-TREATED HAE ATTACKS	19	18
EVENTS [1]	12 (63.2)	11 (61.1)
CENSORED [2]	7 (36.8)	7 (38.9)
TIME TO AT LEAST 50% DECREASE ON COMPOSITE VAS FROM BASELINE (95 % CI) [3]		
25TH PERCENTILE	2.83 (0.34, 7.52)	2.93 (0.77, 6.35)
MEDIAN	9.59 (2.83, NE)	7.18 (2.93, NE)
75TH PERCENTILE	NE (9.59, NE)	NE (7.80, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.7233	
HAZARD RATIO (95 % CI) [4]	1.27 (0.50, 3.24)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 1 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	39 (57.4)	18 (27.3)
CENSORED [2]	29 (42.6)	48 (72.7)
TIME TO AT LEAST 50% DECREASE ON COMPOSITE VAS FROM BASELINE (95 % CI) [3]		
25TH PERCENTILE	2.34 (1.79, 3.77)	11.53 (3.03, NE)
MEDIAN	5.73 (3.80, 19.10)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0004†	
HAZARD RATIO (95 % CI) [4]	3.32 (1.82, 6.05)	

2.8.6 Prophylaxe-Status (Variante 2)

- VAS=Visual Analogic Scale; CI=Confidence Interval; NE=Not Evaluable
- Composite VAS score is defined as the mean score across all 3 symptom scores.
- Time to at least 50% decrease (hours) = Date/time of first $\geq 50\%$ decrease in composite VAS score for 3 consecutive time points (with possible missing values in between) – Date/time of first IMP administration.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if a $\geq 50\%$ reduction in composite VAS score for 3 consecutive time points did not occur or received conventional attack treatment within considered time of IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 3 post-baseline assessments, attacks will be censored at time 0.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON KALLIKREIN		
NUMBER OF IMP-TREATED HAE ATTACKS	14	14
EVENTS [1]	8 (57.1)	9 (64.3)
CENSORED [2]	6 (42.9)	5 (35.7)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON OTHER		
NUMBER OF IMP-TREATED HAE ATTACKS	5	4
EVENTS [1]	1 (20.0)	0
CENSORED [2]	4 (80.0)	4 (100)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	35 (51.5)	13 (19.7)
CENSORED [2]	33 (48.5)	53 (80.3)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON KALLIKREIN		
NUMBER OF IMP-TREATED HAE ATTACKS	14	14
EVENTS [1]	9 (64.3)	10 (71.4)
CENSORED [2]	5 (35.7)	4 (28.6)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON OTHER		
NUMBER OF IMP-TREATED HAE ATTACKS	5	4
EVENTS [1]	3 (60.0)	1 (25.0)
CENSORED [2]	2 (40.0)	3 (75.0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	39 (57.4)	18 (27.3)
CENSORED [2]	29 (42.6)	48 (72.7)

2.8.7 Attacken-Schwere (PGIS) zu Baseline

- VAS=Visual Analogic Scale; CI=Confidence Interval; NE=Not Evaluable
- Composite VAS score is defined as the mean score across all 3 symptom scores.
- Time to at least 50% decrease (hours) = Date/time of first $\geq 50\%$ decrease in composite VAS score for 3 consecutive time points (with possible missing values in between) – Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for visit, treatment, subgroup, and subgroup*treatment interaction in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if a $\geq 50\%$ reduction in composite VAS score for 3 consecutive time points did not occur or received conventional attack treatment within considered time of IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 3 post-baseline assessments, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to at least 50% decrease on Composite VAS from baseline within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment in the model as a fixed effect and patient as a random effect.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.4336	
ATTACK SEVERITY AT BASELINE PGI-S = NONE OR MILD		
NUMBER OF IMP-TREATED HAE ATTACKS	36	38
EVENTS [1]	21 (58.3)	13 (34.2)
CENSORED [2]	15 (41.7)	25 (65.8)
TIME TO AT LEAST 50% DECREASE ON COMPOSITE VAS FROM BASELINE (95 % CI) [3]		
25TH PERCENTILE	2.40 (1.28, 3.80)	3.60 (0.79, NE)
MEDIAN	3.95 (2.79, NE)	NE (5.56, NE)
75TH PERCENTILE	NE (4.92, NE)	NE (NE, NE)
UNSTRATIFIED LOG-RANK P-VALUE	0.0655	
HAZARD RATIO (95 % CI) [4]	1.97 (0.96, 4.04)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = MODERATE		
NUMBER OF IMP-TREATED HAE ATTACKS	35	33
EVENTS [1]	14 (40.0)	7 (21.2)
CENSORED [2]	21 (60.0)	26 (78.8)
TIME TO AT LEAST 50% DECREASE ON COMPOSITE VAS FROM BASELINE (95 % CI) [3]		
25TH PERCENTILE	2.85 (1.33, 7.03)	NE (2.07, NE)
MEDIAN	NE (4.76, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
UNSTRATIFIED LOG-RANK P-VALUE	0.0833	
HAZARD RATIO (95 % CI) [4]	2.47 (0.93, 6.56)	

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = SEVERE OR VERY SEVERE		
NUMBER OF IMP-TREATED HAE ATTACKS	14	13
EVENTS [1]	9 (64.3)	2 (15.4)
CENSORED [2]	5 (35.7)	11 (84.6)
TIME TO AT LEAST 50% DECREASE ON COMPOSITE VAS FROM BASELINE (95 % CI) [3]		
25TH PERCENTILE	2.28 (0.77, 5.73)	NE (1.27, NE)
MEDIAN	6.16 (1.79, NE)	NE (3.77, NE)
75TH PERCENTILE	NE (5.73, NE)	NE (NE, NE)
UNSTRATIFIED LOG-RANK P-VALUE	0.0197†	
HAZARD RATIO (95 % CI) [4]	5.79 (1.00, 33.52)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.7990	
ATTACK SEVERITY AT BASELINE PGI-S = NONE OR MILD		
NUMBER OF IMP-TREATED HAE ATTACKS	36	38
EVENTS [1]	23 (63.9)	14 (36.8)
CENSORED [2]	13 (36.1)	24 (63.2)
TIME TO AT LEAST 50% DECREASE ON COMPOSITE VAS FROM BASELINE (95 % CI) [3]		
25TH PERCENTILE	2.40 (1.28, 3.80)	3.60 (0.79, 7.80)
MEDIAN	3.96 (2.83, 17.24)	NE (5.56, NE)
75TH PERCENTILE	NE (7.52, NE)	NE (NE, NE)
UNSTRATIFIED LOG-RANK P-VALUE	0.0568	
HAZARD RATIO (95 % CI) [4]	1.93 (0.98, 3.79)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = MODERATE		
NUMBER OF IMP-TREATED HAE ATTACKS	35	33
EVENTS [1]	19 (54.3)	10 (30.3)
CENSORED [2]	16 (45.7)	23 (69.7)
TIME TO AT LEAST 50% DECREASE ON COMPOSITE VAS FROM BASELINE (95 % CI) [3]		
25TH PERCENTILE	3.31 (1.33, 7.03)	10.69 (2.07, NE)
MEDIAN	10.83 (4.76, NE)	NE (13.12, NE)
75TH PERCENTILE	NE (19.10, NE)	NE (NE, NE)
UNSTRATIFIED LOG-RANK P-VALUE	0.0372†	
HAZARD RATIO (95 % CI) [4]	2.48 (1.07, 5.73)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = SEVERE OR VERY SEVERE		
NUMBER OF IMP-TREATED HAE ATTACKS	14	13
EVENTS [1]	9 (64.3)	5 (38.5)
CENSORED [2]	5 (35.7)	8 (61.5)
TIME TO AT LEAST 50% DECREASE ON COMPOSITE VAS FROM BASELINE (95 % CI) [3]		
25TH PERCENTILE	2.28 (0.77, 5.73)	14.38 (1.27, NE)
MEDIAN	6.16 (1.79, NE)	NE (13.02, NE)
75TH PERCENTILE	NE (5.73, NE)	NE (NE, NE)
UNSTRATIFIED LOG-RANK P-VALUE	0.0934	
HAZARD RATIO (95 % CI) [4]	3.75 (0.83, 16.98)	

2.9 Zeit bis zu einer Verringerung des VAS von mindestens 15 % der Gesamtskala

2.9.1 Geschlecht

- VAS=Visual Analogic Scale; CI=Confidence Interval; NE=Not Evaluable
- Composite VAS score is defined as the mean score across all 3 symptom scores.
- Time to at least 15 points decrease (hours) = Date/time of first ≥ 15 points decrease in composite VAS score for 3 consecutive time points (with possible missing values in between) – Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for visit, treatment, subgroup, subgroup*treatment interaction, and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if a ≥ 15 points reduction in composite VAS score for 3 consecutive time points did not occur or received conventional attack treatment within considered time of IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 3 post-baseline assessments, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to at least 15 points decrease on Composite VAS from baseline within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- [5] Stratified log-rank test controlling for the baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.4905	
SEX = MALE		
NUMBER OF IMP-TREATED HAE ATTACKS	33	29
EVENTS [1]	10 (30.3)	3 (10.3)
CENSORED [2]	23 (69.7)	26 (89.7)
TIME TO FIRST INCIDENCE OF AT LEAST 15 POINTS DECREASE ON COMPOSITE VAS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	7.03 (1.28, NE)	NE (0.77, NE)
MEDIAN	NE (8.52, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.1112	
HAZARD RATIO (95 % CI) [4]	2.97 (0.74, 11.90)	

 Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
SEX = FEMALE		
NUMBER OF IMP-TREATED HAE ATTACKS	54	55
EVENTS [1]	15 (27.8)	12 (21.8)
CENSORED [2]	39 (72.2)	43 (78.2)
TIME TO FIRST INCIDENCE OF AT LEAST 15 POINTS DECREASE ON COMPOSITE VAS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	5.51 (1.79, NE)	NE (2.77, NE)
MEDIAN	NE (NE, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.3936	
HAZARD RATIO (95 % CI) [4]	1.58 (0.72, 3.45)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.5125	
SEX = MALE		
NUMBER OF IMP-TREATED HAE ATTACKS	33	29
EVENTS [1]	13 (39.4)	6 (20.7)
CENSORED [2]	20 (60.6)	23 (79.3)
TIME TO FIRST INCIDENCE OF AT LEAST 15 POINTS DECREASE ON COMPOSITE VAS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	7.03 (1.28, 17.03)	NE (0.78, NE)
MEDIAN	NE (8.52, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.1481	
HAZARD RATIO (95 % CI) [4]	2.75 (0.92, 8.27)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
SEX = FEMALE		
NUMBER OF IMP-TREATED HAE ATTACKS	54	55
EVENTS [1]	20 (37.0)	17 (30.9)
CENSORED [2]	34 (63.0)	38 (69.1)
TIME TO FIRST INCIDENCE OF AT LEAST 15 POINTS DECREASE ON COMPOSITE VAS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	5.51 (1.79, 11.73)	6.55 (2.77, NE)
MEDIAN	NE (11.20, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.4161	
HAZARD RATIO (95 % CI) [4]	1.51 (0.77, 2.98)	

2.9.2 Alter

- VAS=Visual Analogic Scale; CI=Confidence Interval; NE=Not Evaluable
- Composite VAS score is defined as the mean score across all 3 symptom scores.
- Time to at least 15 points decrease (hours) = Date/time of first ≥ 15 points decrease in composite VAS score for 3 consecutive time points (with possible missing values in between) – Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for visit, treatment, subgroup, subgroup*treatment interaction, and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if a ≥ 15 points reduction in composite VAS score for 3 consecutive time points did not occur or received conventional attack treatment within considered time of IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 3 post-baseline assessments, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to at least 15 points decrease on Composite VAS from baseline within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- [5] Stratified log-rank test controlling for the baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.7081	
AGE GROUP = <18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	10	9
EVENTS [1]	1 (10.0)	1 (11.1)
CENSORED [2]	9 (90.0)	8 (88.9)
TIME TO FIRST INCIDENCE OF AT LEAST 15 POINTS DECREASE ON COMPOSITE VAS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	NE (1.28, NE)	NE (2.83, NE)
MEDIAN	NE (1.28, NE)	NE (2.83, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.8638	
HAZARD RATIO (95 % CI) [4]	1.29 (0.06, 26.00)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
AGE GROUP = >=18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	77	75
EVENTS [1]	24 (31.2)	14 (18.7)
CENSORED [2]	53 (68.8)	61 (81.3)
TIME TO FIRST INCIDENCE OF AT LEAST 15 POINTS DECREASE ON COMPOSITE VAS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	5.21 (1.89, NE)	NE (2.77, NE)
MEDIAN	NE (NE, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.1069	
HAZARD RATIO (95 % CI) [4]	1.87 (0.94, 3.73)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.9320	
AGE GROUP = <18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	10	9
EVENTS [1]	2 (20.0)	1 (11.1)
CENSORED [2]	8 (80.0)	8 (88.9)
TIME TO FIRST INCIDENCE OF AT LEAST 15 POINTS DECREASE ON COMPOSITE VAS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	NE (1.28, NE)	NE (2.83, NE)
MEDIAN	NE (1.28, NE)	NE (2.83, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.9710	
HAZARD RATIO (95 % CI) [4]	0.81 (0.04, 15.99)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
AGE GROUP = >=18 YEARS		
NUMBER OF IMP-TREATED HAE ATTACKS	77	75
EVENTS [1]	31 (40.3)	22 (29.3)
CENSORED [2]	46 (59.7)	53 (70.7)
TIME TO FIRST INCIDENCE OF AT LEAST 15 POINTS DECREASE ON COMPOSITE VAS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	5.36 (1.89, 10.97)	11.12 (2.59, NE)
MEDIAN	NE (11.53, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.1360	
HAZARD RATIO (95 % CI) [4]	1.80 (1.00, 3.23)	

2.9.3 Region (Variante 1)

- VAS=Visual Analogic Scale; CI=Confidence Interval; NE=Not Evaluable
- Composite VAS score is defined as the mean score across all 3 symptom scores.
- Time to at least 15 points decrease (hours) = Date/time of first ≥ 15 points decrease in composite VAS score for 3 consecutive time points (with possible missing values in between) – Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for visit, treatment, subgroup, subgroup*treatment interaction, and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if a ≥ 15 points reduction in composite VAS score for 3 consecutive time points did not occur or received conventional attack treatment within considered time of IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 3 post-baseline assessments, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to at least 15 points decrease on Composite VAS from baseline within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- [5] Stratified log-rank test controlling for the baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.3845	
REGION 1 = US		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	6 (22.2)	5 (21.7)
CENSORED [2]	21 (77.8)	18 (78.3)
TIME TO FIRST INCIDENCE OF AT LEAST 15 POINTS DECREASE ON COMPOSITE VAS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	8.52 (0.77, NE)	NE (1.27, NE)
MEDIAN	NE (NE, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.9091	
HAZARD RATIO (95 % CI) [4]	1.02 (0.30, 3.44)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 1 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	60	61
EVENTS [1]	19 (31.7)	10 (16.4)
CENSORED [2]	41 (68.3)	51 (83.6)
TIME TO FIRST INCIDENCE OF AT LEAST 15 POINTS DECREASE ON COMPOSITE VAS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	5.51 (1.89, NE)	NE (2.32, NE)
MEDIAN	NE (NE, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0561	
HAZARD RATIO (95 % CI) [4]	2.17 (0.96, 4.90)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.2367	
REGION 1 = US		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	8 (29.6)	8 (34.8)
CENSORED [2]	19 (70.4)	15 (65.2)
TIME TO FIRST INCIDENCE OF AT LEAST 15 POINTS DECREASE ON COMPOSITE VAS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	8.52 (0.77, NE)	6.55 (1.27, NE)
MEDIAN	NE (10.55, NE)	NE (6.55, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.7303	
HAZARD RATIO (95 % CI) [4]	0.91 (0.32, 2.59)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 1 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	60	61
EVENTS [1]	25 (41.7)	15 (24.6)
CENSORED [2]	35 (58.3)	46 (75.4)
TIME TO FIRST INCIDENCE OF AT LEAST 15 POINTS DECREASE ON COMPOSITE VAS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	5.51 (1.89, 11.73)	17.87 (2.32, NE)
MEDIAN	NE (11.73, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0439†	
HAZARD RATIO (95 % CI) [4]	2.21 (1.11, 4.43)	

2.9.4 Region (Variante 2)

- VAS=Visual Analogic Scale; CI=Confidence Interval; NE=Not Evaluable
- Composite VAS score is defined as the mean score across all 3 symptom scores.
- Time to at least 15 points decrease (hours) = Date/time of first ≥ 15 points decrease in composite VAS score for 3 consecutive time points (with possible missing values in between) – Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for visit, treatment, subgroup, subgroup*treatment interaction, and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if a ≥ 15 points reduction in composite VAS score for 3 consecutive time points did not occur or received conventional attack treatment within considered time of IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 3 post-baseline assessments, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to at least 15 points decrease on Composite VAS from baseline within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- [5] Stratified log-rank test controlling for the baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.6164	
REGION 2 = NORTH AMERICA		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	6 (22.2)	5 (21.7)
CENSORED [2]	21 (77.8)	18 (78.3)
TIME TO FIRST INCIDENCE OF AT LEAST 15 POINTS DECREASE ON COMPOSITE VAS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	8.52 (0.77, NE)	NE (1.27, NE)
MEDIAN	NE (NE, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.9091	
HAZARD RATIO (95 % CI) [4]	1.02 (0.30, 3.44)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = EUROPE		
NUMBER OF IMP-TREATED HAE ATTACKS	44	48
EVENTS [1]	16 (36.4)	8 (16.7)
CENSORED [2]	28 (63.6)	40 (83.3)
TIME TO FIRST INCIDENCE OF AT LEAST 15 POINTS DECREASE ON COMPOSITE VAS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	3.78 (1.28, 9.27)	NE (2.29, NE)
MEDIAN	NE (7.55, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0531	
HAZARD RATIO (95 % CI) [4]	2.56 (1.00, 6.56)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	16	13
EVENTS [1]	3 (18.8)	2 (15.4)
CENSORED [2]	13 (81.3)	11 (84.6)
TIME TO FIRST INCIDENCE OF AT LEAST 15 POINTS DECREASE ON COMPOSITE VAS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	NE (2.79, NE)	NE (0.77, NE)
MEDIAN	NE (5.51, NE)	NE (2.83, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.9633	
HAZARD RATIO (95 % CI) [4]	0.95 (0.16, 5.78)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.4980	
REGION 2 = NORTH AMERICA		
NUMBER OF IMP-TREATED HAE ATTACKS	27	23
EVENTS [1]	8 (29.6)	8 (34.8)
CENSORED [2]	19 (70.4)	15 (65.2)
TIME TO FIRST INCIDENCE OF AT LEAST 15 POINTS DECREASE ON COMPOSITE VAS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	8.52 (0.77, NE)	6.55 (1.27, NE)
MEDIAN	NE (10.55, NE)	NE (6.55, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.7303	
HAZARD RATIO (95 % CI) [4]	0.91 (0.32, 2.59)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = EUROPE		
NUMBER OF IMP-TREATED HAE ATTACKS	44	48
EVENTS [1]	21 (47.7)	13 (27.1)
CENSORED [2]	23 (52.3)	35 (72.9)
TIME TO FIRST INCIDENCE OF AT LEAST 15 POINTS DECREASE ON COMPOSITE VAS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	3.79 (1.28, 11.20)	14.90 (2.07, NE)
MEDIAN	NE (7.55, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0664	
HAZARD RATIO (95 % CI) [4]	2.59 (1.19, 5.66)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
REGION 2 = REST OF THE WORLD		
NUMBER OF IMP-TREATED HAE ATTACKS	16	13
EVENTS [1]	4 (25.0)	2 (15.4)
CENSORED [2]	12 (75.0)	11 (84.6)
TIME TO FIRST INCIDENCE OF AT LEAST 15 POINTS DECREASE ON COMPOSITE VAS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	15.13 (2.79, NE)	NE (0.77, NE)
MEDIAN	NE (5.51, NE)	NE (2.83, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.6613	
HAZARD RATIO (95 % CI) [4]	1.42 (0.25, 7.91)	

2.9.5 Prophylaxe-Status (Variante 1)

- VAS=Visual Analogic Scale; CI=Confidence Interval; NE=Not Evaluable
- Composite VAS score is defined as the mean score across all 3 symptom scores.
- Time to at least 15 points decrease (hours) = Date/time of first ≥ 15 points decrease in composite VAS score for 3 consecutive time points (with possible missing values in between) – Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for visit, treatment, subgroup, subgroup*treatment interaction, and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- †: p-value < 0.05.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if a ≥ 15 points reduction in composite VAS score for 3 consecutive time points did not occur or received conventional attack treatment within considered time of IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 3 post-baseline assessments, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to at least 15 points decrease on Composite VAS from baseline within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment and baseline PGI-S category (none or mild, moderate, and severe or very severe) in the model as fixed effects and patient as a random effect.
- [5] Stratified log-rank test controlling for the baseline PGI-S category (none or mild, moderate, and severe or very severe).

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.1657	
PROPHYLACTIC TREATMENT STATUS 1 = ON PROPHYLACTIC TREATMENT		
NUMBER OF IMP-TREATED HAE ATTACKS	19	18
EVENTS [1]	7 (36.8)	7 (38.9)
CENSORED [2]	12 (63.2)	11 (61.1)
TIME TO FIRST INCIDENCE OF AT LEAST 15 POINTS DECREASE ON COMPOSITE VAS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	3.29 (0.77, NE)	3.77 (0.77, NE)
MEDIAN	NE (3.29, NE)	NE (3.77, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.9292	
HAZARD RATIO (95 % CI) [4]	1.01 (0.35, 2.87)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 1 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	18 (26.5)	8 (12.1)
CENSORED [2]	50 (73.5)	58 (87.9)
TIME TO FIRST INCIDENCE OF AT LEAST 15 POINTS DECREASE ON COMPOSITE VAS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	7.03 (1.89, NE)	NE (2.95, NE)
MEDIAN	NE (NE, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0345†	
HAZARD RATIO (95 % CI) [4]	2.68 (1.09, 6.60)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.2316	
PROPHYLACTIC TREATMENT STATUS 1 = ON PROPHYLACTIC TREATMENT		
NUMBER OF IMP-TREATED HAE ATTACKS	19	18
EVENTS [1]	9 (47.4)	9 (50.0)
CENSORED [2]	10 (52.6)	9 (50.0)
TIME TO FIRST INCIDENCE OF AT LEAST 15 POINTS DECREASE ON COMPOSITE VAS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	3.29 (0.77, 10.97)	3.77 (0.77, 6.55)
MEDIAN	NE (3.29, NE)	NE (3.77, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.9833	
HAZARD RATIO (95 % CI) [4]	1.00 (0.40, 2.53)	

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 1 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	24 (35.3)	14 (21.2)
CENSORED [2]	44 (64.7)	52 (78.8)
TIME TO FIRST INCIDENCE OF AT LEAST 15 POINTS DECREASE ON COMPOSITE VAS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	7.03 (1.89, 15.13)	NE (2.83, NE)
MEDIAN	NE (17.03, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
STRATIFIED LOG-RANK P-VALUE [5]	0.0488†	
HAZARD RATIO (95 % CI) [4]	2.48 (1.19, 5.16)	

2.9.6 Prophylaxe-Status (Variante 2)

- VAS=Visual Analogic Scale; CI=Confidence Interval; NE=Not Evaluable
- Composite VAS score is defined as the mean score across all 3 symptom scores.
- Time to at least 15 points decrease (hours) = Date/time of first ≥ 15 points decrease in composite VAS score for 3 consecutive time points (with possible missing values in between) – Date/time of first IMP administration.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if a ≥ 15 points reduction in composite VAS score for 3 consecutive time points did not occur or received conventional attack treatment within considered time of IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 3 post-baseline assessments, attacks will be censored at time 0.

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON KALLIKREIN		
NUMBER OF IMP-TREATED HAE ATTACKS	14	14
EVENTS [1]	4 (28.6)	7 (50.0)
CENSORED [2]	10 (71.4)	7 (50.0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON OTHER		
NUMBER OF IMP-TREATED HAE ATTACKS	5	4
EVENTS [1]	3 (60.0)	0
CENSORED [2]	2 (40.0)	4 (100)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	18 (26.5)	8 (12.1)
CENSORED [2]	50 (73.5)	58 (87.9)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON KALLIKREIN		
NUMBER OF IMP-TREATED HAE ATTACKS	14	14
EVENTS [1]	6 (42.9)	8 (57.1)
CENSORED [2]	8 (57.1)	6 (42.9)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON OTHER		
NUMBER OF IMP-TREATED HAE ATTACKS	5	4
EVENTS [1]	3 (60.0)	1 (25.0)
CENSORED [2]	2 (40.0)	3 (75.0)

Medizinischer Nutzen, medizinischer Zusatznutzen, Patientengruppen mit therap. bedeutsamem Zusatznutzen

WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
PROPHYLACTIC TREATMENT STATUS 2 = ON DEMAND		
NUMBER OF IMP-TREATED HAE ATTACKS	68	66
EVENTS [1]	24 (35.3)	14 (21.2)
CENSORED [2]	44 (64.7)	52 (78.8)

2.9.7 Attacken-Schwere (PGIS) zu Baseline

- VAS=Visual Analogic Scale; CI=Confidence Interval; NE=Not Evaluable
- Composite VAS score is defined as the mean score across all 3 symptom scores.
- Time to at least 15 points decrease (hours) = Date/time of first ≥ 15 points decrease in composite VAS score for 3 consecutive time points (with possible missing values in between) – Date/time of first IMP administration.
- ** Interaction p-values were calculated using a Cox proportional hazards model including terms for visit, treatment, subgroup, and subgroup*treatment interaction in the model as fixed effects and patient as a random effect.
- [1] Attacks that achieved the described event within considered time.
- [2] Attacks are treated as right-censored at considered time if a ≥ 15 points reduction in composite VAS score for 3 consecutive time points did not occur or received conventional attack treatment within considered time of IMP administration. In the case of discontinuation that prevented the event, attack is censored at the time of discontinuation. In the case of underivable time-to-event results due to lack of at least 3 post-baseline assessments, attacks will be censored at time 0.
- [3] Kaplan-Meier estimates for time to at least 15 points decrease on Composite VAS from baseline within considered time.
- [4] Hazard ratio and associated 95% CI were calculated using a Cox proportional hazards model including terms for treatment in the model as a fixed effect and patient as a random effect.

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WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.0625	
ATTACK SEVERITY AT BASELINE PGI-S = NONE OR MILD		
NUMBER OF IMP-TREATED HAE ATTACKS	36	38
EVENTS [1]	3 (8.3)	6 (15.8)
CENSORED [2]	33 (91.7)	32 (84.2)
TIME TO FIRST INCIDENCE OF AT LEAST 15 POINTS DECREASE ON COMPOSITE VAS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	NE (NE, NE)	NE (2.83, NE)
MEDIAN	NE (NE, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
UNSTRATIFIED LOG-RANK P-VALUE	0.2685	
HAZARD RATIO (95 % CI) [4]	0.47 (0.12, 1.86)	

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WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = MODERATE		
NUMBER OF IMP-TREATED HAE ATTACKS	35	33
EVENTS [1]	13 (37.1)	6 (18.2)
CENSORED [2]	22 (62.9)	27 (81.8)
TIME TO FIRST INCIDENCE OF AT LEAST 15 POINTS DECREASE ON COMPOSITE VAS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	3.78 (0.98, 9.27)	NE (2.32, NE)
MEDIAN	NE (5.53, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
UNSTRATIFIED LOG-RANK P-VALUE	0.0821	
HAZARD RATIO (95 % CI) [4]	2.56 (0.88, 7.44)	

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WITHIN 12 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = SEVERE OR VERY SEVERE		
NUMBER OF IMP-TREATED HAE ATTACKS	14	13
EVENTS [1]	9 (64.3)	3 (23.1)
CENSORED [2]	5 (35.7)	10 (76.9)
TIME TO FIRST INCIDENCE OF AT LEAST 15 POINTS DECREASE ON COMPOSITE VAS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	1.79 (0.28, 2.34)	NE (0.29, NE)
MEDIAN	2.81 (1.77, NE)	NE (0.78, NE)
75TH PERCENTILE	NE (2.34, NE)	NE (NE, NE)
UNSTRATIFIED LOG-RANK P-VALUE	0.0739	
HAZARD RATIO (95 % CI) [4]	2.97 (0.67, 13.11)	

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WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
P-VALUE** FOR SUBGROUP BY TREATMENT INTERACTION	0.3592	
ATTACK SEVERITY AT BASELINE PGI-S = NONE OR MILD		
NUMBER OF IMP-TREATED HAE ATTACKS	36	38
EVENTS [1]	7 (19.4)	7 (18.4)
CENSORED [2]	29 (80.6)	31 (81.6)
TIME TO FIRST INCIDENCE OF AT LEAST 15 POINTS DECREASE ON COMPOSITE VAS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	NE (10.55, NE)	NE (2.83, NE)
MEDIAN	NE (NE, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
UNSTRATIFIED LOG-RANK P-VALUE	0.8681	
HAZARD RATIO (95 % CI) [4]	0.92 (0.32, 2.61)	

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WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = MODERATE		
NUMBER OF IMP-TREATED HAE ATTACKS	35	33
EVENTS [1]	16 (45.7)	9 (27.3)
CENSORED [2]	19 (54.3)	24 (72.7)
TIME TO FIRST INCIDENCE OF AT LEAST 15 POINTS DECREASE ON COMPOSITE VAS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	4.49 (0.98, 9.27)	13.10 (2.32, NE)
MEDIAN	NE (5.53, NE)	NE (NE, NE)
75TH PERCENTILE	NE (NE, NE)	NE (NE, NE)
UNSTRATIFIED LOG-RANK P-VALUE	0.0914	
HAZARD RATIO (95 % CI) [4]	2.41 (0.95, 6.13)	

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WITHIN 24 HOURS	300 mg KVD900 (ATTACK=87)	Placebo (ATTACK=84)
ATTACK SEVERITY AT BASELINE PGI-S = SEVERE OR VERY SEVERE		
NUMBER OF IMP-TREATED HAE ATTACKS	14	13
EVENTS [1]	10 (71.4)	7 (53.8)
CENSORED [2]	4 (28.6)	6 (46.2)
TIME TO FIRST INCIDENCE OF AT LEAST 15 POINTS DECREASE ON COMPOSITE VAS FROM BASELINE (95% CI) [3]		
25TH PERCENTILE	1.79 (0.28, 2.34)	2.29 (0.29, 16.71)
MEDIAN	2.81 (1.77, NE)	16.71 (1.50, NE)
75TH PERCENTILE	NE (2.34, NE)	NE (10.70, NE)
UNSTRATIFIED LOG-RANK P-VALUE	0.3389	
HAZARD RATIO (95 % CI) [4]	1.68 (0.44, 6.41)	