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TITLE: Pharmacokinetic drug-drug interactions between vonoprazan and low-dose aspirin or nonsteroidal anti-inflammatory drugs: a phase 2, open-label, study in healthy Japanese men

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SUPPLEMENTARY TABLES

Supplementary Table 1. Pharmacokinetic Parameters of Vonoprazan and Its Metabolites when Administered in Combination with Aspirin (Cohort 1)

Vonoprazan-F Pharmacokinetic Parameters	Arithmetic Mean (SD)				Geometric Mean			
	n	Vonoprazan Alone	n	Vonoprazan + Aspirin	Vonoprazan Alone (R)	Vonoprazan + Aspirin (T)	Mean Ratio (T/R)	90% CI of Ratio
C_{max}, ng/mL	7	76.54 (23.853)	7	79.04 (16.713)	72.568	77.085	1.062	(0.897, 1.257)
$AUC_{0\text{-}inf}$, ng·hr/mL	7	544.5 (148.04)	7	543.1 (110.50)	525.743	532.951	1.014	(0.943, 1.090)
$AUC_{0\text{-}48}$, ng·hr/mL	7	534.8 (145.78)	7	534.3 (109.03)	516.240	524.177	1.015	(0.945, 1.091)
$T_{1/2}$, hr	7	8.871 (0.92064)	7	8.769 (0.86928)	–	–	–	–
T_{max}[a], hr	7	1.50 (1.0, 2.0)	7	1.50 (0.5, 2.0)	–	–	–	–
M-I Pharmacokinetic Parameters								
C_{max}, ng/mL	7	90.03 (21.931)	7	89.33 (23.824)	87.958	87.029	0.989	(0.857, 1.142)
$AUC_{0\text{-}inf}$, ng·hr/mL	7	836.3 (173.14)	7	926.2 (166.77)	820.416	914.473	1.115	(1.044, 1.190)
$AUC_{0\text{-}48}$, ng·hr/mL	7	803.0 (164.88)	7	887.8 (165.53)	788.066	875.966	1.112	(1.042, 1.186)
$T_{1/2}$, hr	7	10.61 (1.1208)	7	11.04 (1.1354)	–	–	–	–
T_{max}[a], hr	7	1.50 (1.0, 2.0)	7	1.50 (1.0, 2.0)	–	–	–	–
M-II Pharmacokinetic Parameters								
C_{max}, ng/mL	7	5.664 (2.3997)	7	7.001 (3.3960)	5.257	6.415	1.220	(1.048, 1.421)
$AUC_{0\text{-}inf}$, ng·hr/mL	7	147.4 (77.894)	7	162.5 (70.579)	132.443	149.958	1.132	(0.968, 1.324)
$AUC_{0\text{-}48}$, ng·hr/mL	7	118.2 (51.683)	7	143.6 (64.801)	108.834	132.325	1.216	(1.068, 1.384)
$T_{1/2}$, hr	7	15.78 (5.0904)	7	13.11 (4.4586)	–	–	–	–
T_{max}[a], hr	7	4.00 (4.0, 10.0)	7	6.00 (4.0, 10.0)	–	–	–	–
M-III Pharmacokinetic Parameters								
C_{max}, ng/mL	7	42.91 (3.8168)	7	45.27 (8.3835)	42.768	44.669	1.044	(0.957, 1.140)
$AUC_{0\text{-}inf}$, ng·hr/mL	7	364.2 (78.392)	7	375.8 (85.329)	356.375	366.976	1.030	(0.989, 1.072)

AUC_{0-48}, ng·hr/mL	7	360.8 (76.094)	7	374.3 (81.396)	353.374	366.369	1.037	(0.994, 1.081)
$T_{1/2}$, hr	7	7.743 (1.2302)	7	7.061 (1.1984)	–	–	–	–
T_{max}[a], hr	7	2.00 (1.0, 4.0)	7	2.00 (1.5, 3.0)	–	–	–	–
M-IV-Sul Pharmacokinetic Parameters								
C_{max}, ng/mL	7	80.24 (18.127)	7	76.11 (13.367)	78.613	75.190	0.956	(0.850, 1.077)
AUC_{0-inf}, ng·hr/mL	7	488.2 (136.85)	7	464.9 (97.993)	472.330	455.872	0.965	(0.899, 1.037)
AUC_{0-48}, ng·hr/mL	7	494.2 (138.02)	7	472.6 (98.070)	478.223	463.664	0.970	(0.898, 1.047)
$T_{1/2}$, hr	7	6.869 (0.70361)	7	6.309 (1.5329)	–	–	–	–
T_{max}[a], hr	7	2.00 (1.5, 3.0)	7	2.00 (1.5, 2.0)	–	–	–	–

Abbreviations: AUC, area under the plasma concentration-time curve; AUC_{0-48}, AUC from time 0 to 48 hour, calculated using the linear trapezoid rule; AUC_{0-inf}, AUC from time 0 to infinity; CI, Confidence interval; C_{max}, maximum observed plasma concentration; SD, standard deviation; $T_{1/2}$, terminal elimination half-life; T_{max}, time to reach C_{max}.

[a] Median (minimum, maximum) shown for T_{max}.

Supplementary Table 2. Pharmacokinetic Parameters of Vonoprazan and Its Metabolites when Administered in Combination with Loxoprofen Sodium (Cohort 2)

Vonoprazan-F Pharmacokinetic Parameters	Arithmetic Mean (SD)				Geometric Mean		Mean Ratio (T/R)	90% CI of Ratio
	n	Vonoprazan Alone	n	Vonoprazan + Loxoprofen sodium	Vonoprazan Alone (R)	Vonoprazan + Loxoprofen sodium (T)		
C_{max}, ng/mL	8	70.35 (13.184)	8	58.50 (9.8013)	69.194	57.768	0.835	(0.695, 1.002)
$AUC_{0\text{-}inf}$, ng·hr/mL	8	467.0 (129.50)	8	460.0 (135.93)	452.671	443.286	0.979	(0.894, 1.073)
$AUC_{0\text{-}48}$, ng·hr/mL	8	460.8 (124.83)	8	453.6 (131.34)	447.176	437.687	0.979	(0.894, 1.072)
$T_{1/2}$, hr	8	7.954 (0.81200)	8	7.991 (0.89185)	–	–	–	–
T_{max}[a], hr	8	1.25 (0.5, 3.0)	8	2.00 (1.0, 3.0)	–	–	–	–
M-I Pharmacokinetic Parameters								
C_{max}, ng/mL	8	96.46 (25.189)	8	85.66 (17.584)	93.575	84.209	0.900	(0.787, 1.029)
$AUC_{0\text{-}inf}$, ng·hr/mL	8	879.5 (67.887)	8	913.5 (128.78)	877.230	905.220	1.032	(0.957, 1.112)
$AUC_{0\text{-}48}$, ng·hr/mL	8	852.8 (64.555)	8	886.4 (112.65)	850.760	879.925	1.034	(0.961, 1.114)
$T_{1/2}$, hr	8	9.658 (1.5376)	8	9.803 (1.4405)	–	–	–	–
T_{max}[a], hr	8	1.25 (1.0, 3.0)	8	1.75 (1.0, 3.0)	–	–	–	–
M-II Pharmacokinetic Parameters								
C_{max}, ng/mL	8	6.648 (1.6141)	8	6.938 (1.6418)	6.488	6.782	1.045	(0.929, 1.177)
$AUC_{0\text{-}inf}$, ng·hr/mL	8	158.6 (37.918)	8	177.4 (37.461)	155.218	174.065	1.121	(1.000, 1.258)
$AUC_{0\text{-}48}$, ng·hr/mL	8	143.2 (38.438)	8	149.7 (32.192)	139.328	146.871	1.054	(0.941, 1.181)
$T_{1/2}$, hr	8	12.57 (4.0717)	8	14.54 (2.3656)	–	–	–	–
T_{max}[a], hr	8	9.00 (3.0, 10.0)	8	6.00 (4.0, 10.0)	–	–	–	–
M-III Pharmacokinetic Parameters								
C_{max}, ng/mL	8	44.68 (9.3384)	8	42.41 (7.3090)	43.793	41.869	0.956	(0.897, 1.019)
$AUC_{0\text{-}inf}$, ng·hr/mL	8	358.0 (100.98)	8	359.0 (113.28)	345.176	342.994	0.994	(0.960, 1.029)
$AUC_{0\text{-}48}$, ng·hr/mL	8	356.8 (98.015)	8	357.2 (110.97)	344.803	341.856	0.991	(0.957, 1.027)

$T_{1/2}$, hr	8	6.640 (1.0851)	8	6.762 (0.75364)	–	–	–	–
T_{max}[a], hr	8	1.75 (1.0, 4.0)	8	3.00 (1.0, 4.0)	–	–	–	–
M-IV-Sul Pharmacokinetic Parameters								
C_{max}, ng/mL	8	88.46 (30.110)	8	73.54 (18.774)	83.917	71.344	0.850	(0.772, 0.937)
$AUC_{0\text{-}inf}$, ng·hr/mL	8	524.3 (224.27)	8	481.4 (201.15)	481.166	443.241	0.921	(0.872, 0.973)
$AUC_{0\text{-}48}$, ng·hr/mL	8	534.0 (230.53)	8	491.6 (207.63)	489.364	451.815	0.923	(0.874, 0.976)
$T_{1/2}$, hr	8	6.108 (0.89092)	8	6.087 (0.72403)	–	–	–	–
T_{max}[a], hr	8	1.75 (1.0, 4.0)	8	2.50 (1.5, 4.0)	–	–	–	–

Abbreviations: AUC, area under the plasma concentration-time curve; $AUC_{0\text{-}48}$, AUC from time 0 to 48 hour, calculated using the linear trapezoid rule; $AUC_{0\text{-}inf}$, AUC from time 0 to infinity; CI, Confidence interval; C_{max}, maximum observed plasma concentration; SD, standard deviation; $T_{1/2}$, terminal elimination half-life; T_{max}, time to reach C_{max}..

[a] Median (minimum, maximum) shown for T_{max}.

Supplementary Table 3. Pharmacokinetic Parameters of Vonoprazan and Its Metabolites when Administered in Combination with Diclofenac Sodium (Cohort 3)

Vonoprazan-F Pharmacokinetic Parameters	Arithmetic Mean (SD)				Geometric Mean		Mean Ratio (T/R)	90% CI of Ratio
	n	Vonoprazan Alone	n	Vonoprazan + Diclofenac sodium	Vonoprazan Alone (R)	Vonoprazan + Diclofenac sodium (T)		
C_{max}, ng/mL	8	87.58 (21.272)	8	87.20 (17.723)	85.342	85.662	1.004	(0.945, 1.066)
$AUC_{0\text{-}inf}$, ng·hr/mL	8	568.2 (222.96)	8	558.0 (230.60)	536.179	522.870	0.975	(0.931, 1.022)
$AUC_{0\text{-}48}$, ng·hr/mL	8	558.2 (212.80)	8	549.2 (221.41)	528.474	516.272	0.977	(0.933, 1.023)
$T_{1/2}$, hr	8	8.346 (1.3819)	8	8.042 (1.2419)	–	–	–	–
T_{max}[a], hr	8	1.50 (0.5, 2.0)	8	1.25 (0.5, 2.0)	–	–	–	–
M-I Pharmacokinetic Parameters								
C_{max}, ng/mL	8	98.09 (25.361)	8	86.26 (27.257)	94.636	82.109	0.868	(0.759, 0.992)
$AUC_{0\text{-}inf}$, ng·hr/mL	8	851.8 (225.09)	8	756.4 (176.80)	824.897	739.168	0.896	(0.838, 0.958)
$AUC_{0\text{-}48}$, ng·hr/mL	8	826.2 (224.46)	8	733.4 (176.64)	798.257	715.560	0.896	(0.840, 0.956)
$T_{1/2}$, hr	8	9.910 (1.4406)	8	9.955 (1.6950)	–	–	–	–
T_{max}[a], hr	8	1.25 (1.0, 2.0)	8	1.25 (1.0, 2.0)	–	–	–	–
M-II Pharmacokinetic Parameters								
C_{max}, ng/mL	8	6.821 (2.3083)	8	6.161 (2.2411)	6.448	5.779	0.896	(0.801, 1.003)
$AUC_{0\text{-}inf}$, ng·hr/mL	8	192.1 (154.53)	8	148.4 (56.518)	158.159	139.465	0.882	(0.682, 1.139)
$AUC_{0\text{-}48}$, ng·hr/mL	8	132.5 (54.475)	8	121.9 (38.361)	124.639	116.907	0.938	(0.840, 1.047)
$T_{1/2}$, hr	8	21.83 (31.801)	8	14.68 (8.9495)	–	–	–	–
T_{max}[a], hr	8	4.00 (4.0, 10.0)	8	4.00 (4.0, 12.0)	–	–	–	–
M-III Pharmacokinetic Parameters								
C_{max}, ng/mL	8	50.89 (10.018)	8	46.48 (8.3983)	49.994	45.776	0.916	(0.876, 0.957)
$AUC_{0\text{-}inf}$, ng·hr/mL	8	411.6 (138.09)	8	392.9 (145.97)	391.604	368.891	0.942	(0.890, 0.997)
$AUC_{0\text{-}48}$, ng·hr/mL	8	406.7 (132.45)	8	388.8 (139.35)	388.149	366.791	0.945	(0.896, 0.997)

$T_{1/2}$, hr	8	7.548 (1.5410)	8	7.001 (1.8062)	–	–	–	–
T_{max}[a], hr	8	1.75 (1.0, 3.0)	8	2.00 (1.0, 3.0)	–	–	–	–
M-IV-Sul Pharmacokinetic Parameters								
C_{max}, ng/mL	8	99.50 (18.157)	8	86.30 (18.916)	98.099	84.421	0.861	(0.805, 0.920)
AUC_{0-inf}, ng·hr/mL	8	585.5 (207.34)	8	534.8 (194.40)	552.357	504.797	0.914	(0.853, 0.979)
AUC_{0-48}, ng·hr/mL	8	591.8 (208.23)	8	537.8 (187.18)	558.781	509.725	0.912	(0.852, 0.976)
$T_{1/2}$, hr	8	6.412 (1.9972)	8	6.415 (1.9314)	–	–	–	–
T_{max}[a], hr	8	2.00 (1.5, 3.0)	8	2.00 (1.5, 2.0)	–	–	–	–

Abbreviations: AUC, area under the plasma concentration-time curve; AUC_{0-48}, AUC from time 0 to 48 hour, calculated using the linear trapezoid rule; AUC_{0-inf}, AUC from time 0 to infinity; CI, Confidence interval; C_{max}, maximum observed plasma concentration; SD, standard deviation; $T_{1/2}$, terminal elimination half-life; T_{max}, time to reach C_{max}.

[a] Median (minimum, maximum) shown for T_{max}.

Supplementary Table 4. Pharmacokinetic Parameters of Vonoprazan and Its Metabolites when Administered in Combination with Meloxicam (Cohort 4)

Vonoprazan-F Pharmacokinetic Parameters	Arithmetic Mean (SD)				Geometric Mean		Mean Ratio (T/R)	90% CI of Ratio
	n	Vonoprazan Alone	n	Vonoprazan + Meloxicam	Vonoprazan Alone (R)	Vonoprazan + Meloxicam (T)		
C_{max}, ng/mL	7	77.21 (25.670)	7	75.37 (24.059)	73.974	72.024	0.974	(0.816, 1.162)
$AUC_{0\text{-}inf}$, ng·hr/mL	7	475.8 (122.55)	7	471.4 (128.50)	464.304	459.112	0.989	(0.947, 1.032)
$AUC_{0\text{-}48}$, ng·hr/mL	7	470.5 (119.85)	7	466.4 (125.76)	459.299	454.369	0.989	(0.948, 1.033)
$T_{1/2}$, hr	7	7.978 (0.50383)	7	7.808 (0.79508)	–	–	–	–
T_{max}[a], hr	7	1.50 (1.5, 2.0)	7	1.50 (1.0, 2.0)	–	–	–	–
M-I Pharmacokinetic Parameters								
C_{max}, ng/mL	7	94.59 (15.985)	7	95.29 (21.530)	93.389	93.204	0.998	(0.858, 1.162)
$AUC_{0\text{-}inf}$, ng·hr/mL	7	815.6 (152.47)	7	964.0 (229.08)	803.277	941.069	1.172	(1.112, 1.234)
$AUC_{0\text{-}48}$, ng·hr/mL	7	790.9 (143.94)	7	928.5 (208.89)	779.565	908.303	1.165	(1.108, 1.225)
$T_{1/2}$, hr	7	10.05 (0.49815)	7	10.13 (1.4436)	–	–	–	–
T_{max}[a], hr	7	1.50 (1.0, 2.0)	7	1.50 (1.0, 1.5)	–	–	–	–
M-II Pharmacokinetic Parameters								
C_{max}, ng/mL	7	5.697 (1.3809)	7	6.143 (1.2208)	5.559	6.041	1.087	(0.998, 1.183)
$AUC_{0\text{-}inf}$, ng·hr/mL	7	130.3 (44.899)	7	147.5 (53.625)	125.263	139.955	1.117	(0.995, 1.255)
$AUC_{0\text{-}48}$, ng·hr/mL	7	111.0 (33.911)	7	130.1 (47.314)	107.252	123.788	1.154	(1.086, 1.226)
$T_{1/2}$, hr	7	14.22 (3.1973)	7	13.34 (2.6069)	–	–	–	–
T_{max}[a], hr	7	4.00 (4.0, 10.0)	7	4.00 (4.0, 10.0)	–	–	–	–
M-III Pharmacokinetic Parameters								
C_{max}, ng/mL	7	42.49 (10.915)	7	40.13 (8.2158)	41.367	39.429	0.953	(0.872, 1.041)
$AUC_{0\text{-}inf}$, ng·hr/mL	7	320.5 (125.28)	7	314.6 (130.08)	303.148	296.456	0.978	(0.947, 1.010)
$AUC_{0\text{-}48}$, ng·hr/mL	7	320.4 (123.08)	7	314.9 (126.46)	303.543	297.614	0.980	(0.952, 1.010)

$T_{1/2}$, hr	7	6.512 (1.0307)	7	6.759 (1.3653)	–	–	–	–
T_{max}[a], hr	7	1.50 (1.5,2.0)	7	2.00 (1.5, 3.0)	–	–	–	–
M-IV-Sul Pharmacokinetic Parameters								
C_{max}, ng/mL	7	92.83 (30.442)	7	84.20 (22.002)	88.743	81.566	0.919	(0.829, 1.019)
AUC_{0-inf}, ng·hr/mL	7	516.7 (161.51)	7	517.8 (172.99)	494.688	493.702	0.998	(0.953, 1.045)
AUC_{0-48}, ng·hr/mL	7	526.1 (164.73)	7	526.3 (175.28)	503.534	501.786	0.997	(0.952, 1.043)
$T_{1/2}$, hr	7	5.916 (0.60512)	7	6.253 (0.75441)	–	–	–	–
T_{max}[a], hr	7	2.00 (2.0, 2.0)	7	2.00 (2.0, 3.0)	–	–	–	–

Abbreviations: AUC, area under the plasma concentration-time curve; AUC_{0-48}, AUC from time 0 to 48 hour, calculated using the linear trapezoid rule; AUC_{0-inf}, AUC from time 0 to infinity; CI, Confidence interval; C_{max}, maximum observed plasma concentration; SD, standard deviation; $T_{1/2}$, terminal elimination half-life; T_{max}, time to reach C_{max}.

[a] Median (minimum, maximum) shown for T_{max}.

Supplementary Table 5. Pharmacokinetic Parameters of Aspirin and Its Metabolites when Administered in Combination with Vonoprazan (Cohort 5)

Aspirin Pharmacokinetic Parameters	Arithmetic Mean (SD)				Geometric Mean		Mean Ratio (T/R)	90% CI of Ratio
	n	Aspirin Alone	n	Aspirin + Vonoprazan	Aspirin Alone (R)	Aspirin + Vonoprazan (T)		
C_{max}, ng/mL	8	402.8 (338.27)	8	509.4 (270.58)	227.931	418.125	1.834	(0.798, 4.215)
$AUC_{0\text{-}inf}$, ng·hr/mL	3	1265 (127.19)	5	1049 (232.73)	–	–	–	–
$AUC_{0\text{-}48}$, ng·hr/mL	8	839.2 (570.17)	8	869.1 (372.05)	649.089	766.847	1.181	(0.670, 2.083)
$T_{1/2}$, hr	3	0.5585 (0.087943)	5	0.4866 (0.073375)	–	–	–	–
T_{max}[a], hr	8	6.00 (4.0, 24.0)	8	3.50 (3.0, 6.0)	–	–	–	–
Salicylic acid Pharmacokinetic Parameters								
C_{max}, ng/mL	8	5289 (1492.8)	8	5479 (802.54)	5068.022	5427.404	1.071	(0.804, 1.427)
$AUC_{0\text{-}inf}$, ng·hr/mL	7	28640 (4623.9)	8	25010 (4032.4)	28334.760	24093.339	0.850	(0.783, 0.923)
$AUC_{0\text{-}48}$, ng·hr/mL	8	30460 (6205.3)	8	25120 (4107.1)	29932.672	24820.145	0.829	(0.765, 0.899)
$T_{1/2}$, hr	7	1.968 (0.31985)	8	2.068 (0.36624)	–	–	–	–
T_{max}[a], hr	8	6.00 (6.0, 24.0)	8	5.00 (3.0, 8.0)	–	–	–	–
					Results excluding 1 subject [b]			
Aspirin Pharmacokinetic Parameters								
C_{max}, ng/mL	7	–		–	336.217	525.074	1.562	(0.624, 3.905)
$AUC_{0\text{-}48}$, ng·hr/mL	7	–		–	748.225	923.180	1.234	(0.635, 2.398)
Salicylic acid Pharmacokinetic Parameters								
C_{max}, ng/mL	7	–		–	5581.191	5256.484	0.942	(0.787, 1.127)
$AUC_{0\text{-}48}$, ng·hr/mL	7	–		–	28589.296	24169.084	0.845	(0.776, 0.921)

Abbreviations: AUC, area under the plasma concentration-time curve; $AUC_{0\text{-}48}$, AUC from time 0 to 48 hour, calculated using the linear trapezoid rule; $AUC_{0\text{-}inf}$, AUC from time 0 to infinity; CI, Confidence interval; C_{max}, maximum observed plasma concentration; SD, standard deviation; $T_{1/2}$, terminal elimination half-life; T_{max}, time to reach C_{max}.

[a] Median (minimum, maximum) shown for T_{max}.

[b] 1 subject presented a slow absorption of aspirin (T_{max} = 24 hours) and was excluded from the analysis

Supplementary Table 6. Pharmacokinetic Parameters of Loxoprofen Sodium and Its Metabolites when Administered in Combination with Vonoprazan (Cohort 6)

Loxoprofen Pharmacokinetic Parameters	Arithmetic Mean (SD)				Geometric Mean		Mean Ratio (T/R)	90% CI of Ratio
	n	Loxoprofen sodium Alone	n	Loxoprofen sodium + Vonoprazan	Loxoprofen sodium Alone (R)	Loxoprofen sodium + Vonoprazan (T)		
C_{max}, ng/mL	8	3181 (557.56)	8	3106 (620.99)	3133.552	3056.677	0.975	(0.895, 1.064)
$AUC_{0\text{-}inf}$, ng·hr/mL	8	7808 (1188.8)	8	8266 (503.30)	7734.164	8252.867	1.067	(0.993, 1.146)
$AUC_{0\text{-}48}$, ng·hr/mL	8	7800 (1188.1)	8	8255 (508.47)	7725.589	8241.412	1.067	(0.993, 1.146)
$T_{1/2}$, hr	8	1.671 (0.23560)	8	1.856 (0.21860)	–	–	–	–
T_{max}[a], hr	8	1.00 (0.5, 1.5)	8	1.00 (1.0, 2.0)	–	–	–	–
Trans-OH Pharmacokinetic Parameters								
C_{max}, ng/mL	8	577.1 (32.721)	8	580.3 (39.561)	576.287	579.050	1.005	(0.979, 1.031)
$AUC_{0\text{-}inf}$, ng·hr/mL	8	2124 (206.19)	8	2279 (212.40)	2115.592	2270.793	1.073	(0.992, 1.162)
$AUC_{0\text{-}48}$, ng·hr/mL	8	2128 (210.28)	8	2284 (216.43)	2118.649	2275.114	1.074	(0.992, 1.163)
$T_{1/2}$, hr	8	2.070 (0.32918)	8	2.507 (0.73226)	–	–	–	–
T_{max}[a], hr	8	1.50 (1.0, 2.0)	8	1.75 (1.5, 2.0)	–	–	–	–

Abbreviations: AUC, area under the plasma concentration-time curve; $AUC_{0\text{-}48}$, AUC from time 0 to 48 hour, calculated using the linear trapezoid rule; $AUC_{0\text{-}inf}$, AUC from time 0 to infinity; CI, Confidence interval; C_{max}, maximum observed plasma concentration; SD, standard deviation; $T_{1/2}$, terminal elimination half-life; T_{max}, time to reach $C_{max.}$

[a] Median (minimum, maximum) shown for T_{max}.

Supplementary Table 7. Pharmacokinetic Parameters of Diclofenac Sodium when Administered in Combination with Vonoprazan (Cohort 7)

Diclofenac Pharmacokinetic Parameters	Arithmetic Mean (SD)				Geometric Mean		Mean Ratio (T/R)	90% CI of Ratio
	n	Diclofenac sodium Alone	n	Diclofenac sodium + Vonoprazan	Diclofenac sodium Alone (R)	Diclofenac sodium + Vonoprazan (T)		
C_{max}, ng/mL	7	371.0 (101.45)	7	477.4 (150.83)	359.931	458.400	1.274	(0.920, 1.764)
$AUC_{0\text{-}inf}$, ng·hr/mL	7	616.0 (76.668)	7	643.9 (107.72)	611.741	636.315	1.040	(0.922, 1.174)
$AUC_{0\text{-}48}$, ng·hr/mL	7	613.7 (77.451)	7	641.2 (106.62)	609.281	633.778	1.040	(0.923, 1.172)
$T_{1/2}$, hr	7	2.849 (0.58700)	7	2.658 (0.90342)	–	–	–	–
T_{max} [a], hr	7	1.00 (1.0, 3.0)	7	1.00 (0.5, 1.5)	–	–	–	–

Abbreviations: AUC, area under the plasma concentration-time curve; $AUC_{0\text{-}48}$, AUC from time 0 to 48 hour, calculated using the linear trapezoid rule; $AUC_{0\text{-}inf}$, AUC from time 0 to infinity; CI, Confidence interval; C_{max}, maximum observed plasma concentration; SD, standard deviation; $T_{1/2}$, terminal elimination half-life; T_{max}, time to reach C_{max}.

[a] Median (minimum, maximum) shown for T_{max}.

Supplementary Table 8. Pharmacokinetic Parameters of Meloxicam when Administered in Combination with Vonoprazan (Cohort 8)

Meloxicam Pharmacokinetic Parameters	Arithmetic Mean (SD)				Geometric Mean			
	n	Meloxicam Alone	n	Meloxicam + Vonoprazan	Meloxicam Alone (R)	Meloxicam + Vonoprazan (T)	Mean Ratio (T/R)	90% CI of Ratio
C_{max}, ng/mL	8	1047 (175.79)	8	1088 (132.68)	1033.917	1080.803	1.045	(0.972, 1.124)
$AUC_{0\text{-}inf}$, ng·hr/mL	8	28820 (9466.7)	8	34290 (11562)	27593.436	32687.603	1.185	(1.111, 1.263)
$AUC_{0\text{-}48}$, ng·hr/mL	8	22220 (4078.4)	8	25360 (4794.5)	21900.568	24948.672	1.139	(1.075, 1.207)
$T_{1/2}$, hr	8	21.64 (8.3564)	8	23.43 (7.9625)	–	–	–	–
T_{max}[a], hr	8	4.00 (3.0, 4.0)	8	4.00 (1.0, 4.0)	–	–	–	–

Abbreviations: AUC, area under the plasma concentration-time curve; $AUC_{0\text{-}48}$, AUC from time 0 to 48 hour, calculated using the linear trapezoid rule; $AUC_{0\text{-}inf}$, AUC from time 0 to infinity; CI, Confidence interval; C_{max}, maximum observed plasma concentration; SD, standard deviation; $T_{1/2}$, terminal elimination half-life; T_{max}, time to reach C_{max}.

[a] Median (minimum, maximum) shown for T_{max}.