Supplementary Materials

Pharmacodynamic and Pharmacokinetic Drug Interactions Between Fexuprazan, a Novel Potassium-Competitive Inhibitor, and Aspirin, in Healthy Subjects

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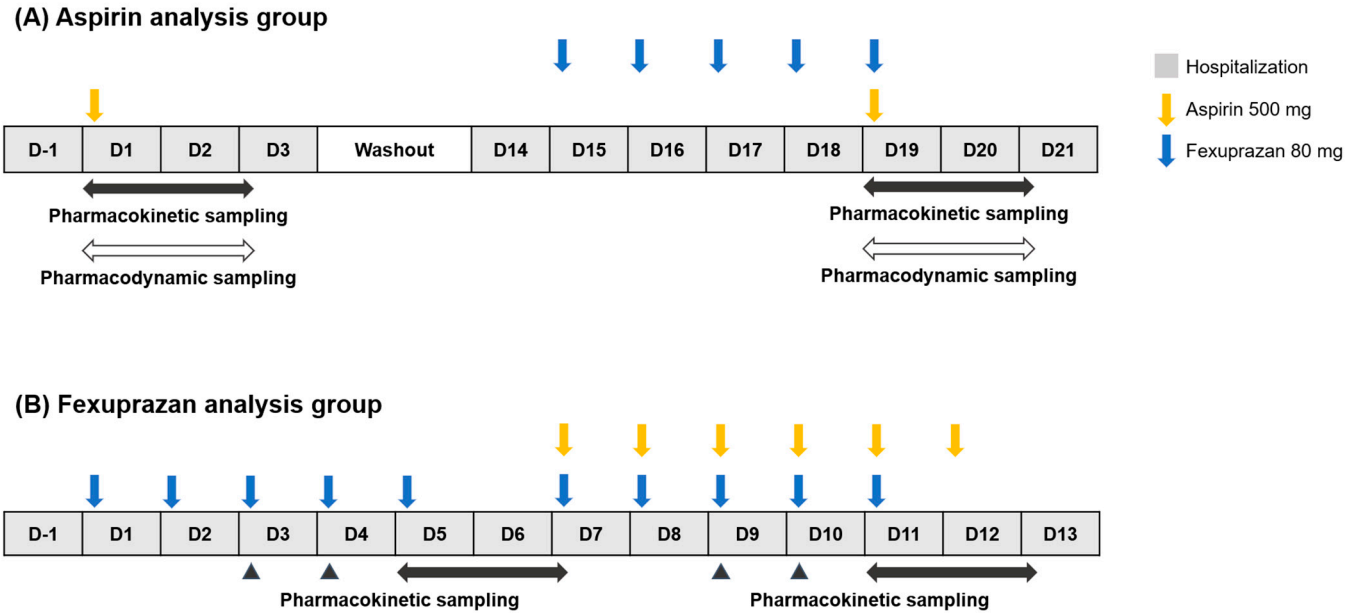

Supplementary Figure S1. Study design.

Supplementary Table S1. Analysis of variance (ANOVA) table for pharmacokinetic parameters of aspirin and fexuprazan.

Parameters	Source	df	SS	MS	F	p-value
Aspirin						
AUC_{last}	Treatment	1	0.0203	0.0203	3.38	0.1157
	Group	4	0.7364	0.1841	3.56	0.0812
	Treatment*Group	4	0.1667	0.0417	6.95	0.0194
	Subject	6	0.3107	0.0518	8.64	0.0095
	Error	6	0.0360	0.0060	.	.
AUC_{inf}	Treatment	1	0.0202	0.0202	3.28	0.1199
	Group	4	0.7358	0.1840	3.59	0.0799
	Treatment*Group	4	0.1645	0.0411	6.69	0.0212
	Subject	6	0.3078	0.0513	8.34	0.0104
	Error	6	0.0369	0.0062	.	.
C_{max}	Treatment	1	0.2974	0.2974	2.22	0.1668
	Group	4	1.9142	0.4786	2.15	0.1917
	Subject	6	1.3339	0.2223	1.66	0.2276
	Error	10	1.3372	0.1337	.	.
Fexuprazan						
$AUC_{\tau,ss}$	Treatment	1	0.2801	0.2801	44.31	<0.001
	Group	5	2.5811	0.5162	1.27	0.4012
	Subject	5	2.0394	0.4079	64.53	<0.001
	Error	10	0.0632	0.0063	.	.
$C_{max,ss}$	Treatment	1	0.0704	0.0704	5.09	0.0477
	Group	5	2.5896	0.5179	1.34	0.378
	Subject	5	1.9325	0.3865	27.96	<.0001
	Error	10	0.1382	0.0138	.	.

If the fixed effect of the interaction between treatment and group was not statistically significant, analysis of variance was performed excluding the corresponding effect.

Abbreviations: df, degree of freedom; SS, sum of squares; MS, mean square; F, F-test statstic.

Supplementary Table S2. Pharmacokinetic parameters of salicylic acid, an active metabolite of aspirin, determined after a single oral administration of aspirin 500 mg alone and coadministered with fexuprazan 80 mg.

Parameters	Aspirin 500 mg + Fexuprazan 80 mg (N=11)	Aspirin 500 mg only (N=11)
AUC_{last} (h·mg/L)	209.89 ± 121.86	207.98 ± 142.16
AUC_{inf} (h·mg/L)	214.58 ± 122.31	214.25 ± 142.05
C_{max} (mg/L)	29.79 ± 6.49	27.73 ± 6.23
Metabolic ratio[a]	40.93 ± 13.18	42.52 ± 16.61

All data are presented as mean ± standard deviation.

Abbreviations: AUC_{last}, area under the concentration-time curve (AUC) from time 0 to the time of the last quantifiable concentration; AUC_{inf}, AUC from 0 to infinity; C_{max}, maximum plasma concentration.

[a] Ratio of AUC_{inf} of salicylic acid to AUC_{inf} of aspirin

Supplementary Table S3. Pharmacokinetic parameters of M14, a metabolite of fexuprazan, determined after multiple oral administrations of fexuprazan 80 mg alone and coadministered with aspirin 500 mg.

Parameters	Fexuprazan 80 mg + Aspirin 500 mg (N=11)	Fexuprazan 80 mg only (N=11)
$AUC_{\tau,ss}$ (h·μg/L)	3095.05 ± 749.42	3089.57 ± 690.99
$C_{max,ss}$ (μg/L)	300.55 ± 107.88	282.00 ± 96.01
Metabolic ratio[a]	4.17 ± 2.68	3.16 ± 1.73

All data are presented as mean ± standard deviation.

Abbreviations: $AUC_{\tau,ss}$, area under the concentration-time curve for a dosing interval at steady state; $C_{max,ss}$, maximum plasma concentration at steady state.

[a] Ratio of AUC of M14 to $AUC_{\tau,ss}$ of fexuprazan