

## **Pooled analysis of studies evaluating fosnetupitant and risk factors for cisplatin-induced nausea and vomiting during the extended overall phase**

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**Table S1 List of study sites in the phase II and phase III studies**

<Phase II study; jRCT20802233009>

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Sendai Kousei Hospital  
Hamamatsu University Hospital  
Hiroshima City Hiroshima Citizens Hospital  
Nagoya University Hospital  
Fukujuji Hospital  
Osaka International Cancer Institute  
Kitasato University Hospital, The Kitasato Institute  
Gunma Prefectural Cancer Center  
Nagaoka Chuo General Hospital  
Nagasaki University Hospital  
Aichi Cancer Center Hospital  
Yokohama Municipal Citizen's Hospital  
Osaka Medical College Hospital  
National Center for Global Health and Medicine Hospital  
Aichi Cancer Center Aichi Hospital  
Kyushu University Hospital  
Tottori University Hospital  
Teikyo University Hospital  
Kanagawa Cancer Center  
Niigata Cancer Center Hospital  
Kyorin University Hospital  
Tokyo Medical Center  
Nagaoka Red Cross Hospital  
Kameda General Hospital  
National Hospital Organization Tokyo National Hospital  
Ibaraki Prefectural Central Hospital  
Saitama Medical University International Medical Center  
Asahikawa Medical Center  
Osaka City University Hospital  
National Hospital Organization Kinki-Chuo Chest Medical Center  
Kanazawa University Hospital  
IUHW Mita Hospital  
National University Corporation Tohoku University  
Saitama Cardiovascular and Respiratory Center  
Funabashi Municipal Medical Center  
Kurume University Hospital  
Hokkaido University Hospital  
Fujita Health University Hospital  
Kobe City Medical Center General Hospital  
Yokosuka Kyosai Hospital

Hiroshima University Hospital  
St. Marianna University School of Medicine Hospital  
Niigata City General Hospital  
Fukushima Medical University Hospital  
Kumamoto University Hospital  
Tochigi Cancer Center  
Tokyo Metropolitan Tama Medical Center  
National Cancer Center Hospital  
National Hospital Organization Himeji Medical Center  
Toranomon Hospital  
Ishikawa Prefectural Central Hospital  
Shikoku Cancer Center  
National Hospital Organization Nagasaki Medical Center  
Okayama University Hospital  
Keio University Hospital  
Nara Medical University Hospital  
Tokai University Hospital  
St. Luke's International Hospital  
National Hospital Organization, Yamaguchi Ube Medical Center  
Tenri Hospital  
Tokyo Medical University Hospital  
Hyogo College Of Medicine College Hospital  
Osaka Habikino Medical Center  
National Hospital Organization Kyushu Medical Center  
Saitama Medical Center  
University of Tsukuba Hospital  
Chiba Cancer Center  
Hiratsuka Kyosai Hospital  
National Disaster Medical Center  
Jichi Medical University Hospital  
Chiba University Hospital  
University Hospital of Occupational and Environmental Health  
Institute of Biomedical Research and Innovation Hospital  
Iwate Prefectural Central Hospital

<Phase III study; jRCT2080224542>

Kobe Minimally Invasive Cancer Center  
Kyushu University Hospital  
Hamamatsu University Hospital  
Hiroshima University Hospital  
Nagoya University Hospital  
Osaka City General Hospital  
Kindai University Hospital

Saitama Cancer Center  
Sendai Kousei Hospital  
Hokkaido University Hospital  
Gunma Prefectural Cancer Center  
Osaka International Cancer Institute, Respiratory Internal Medicine  
Osaka City University Hospital  
Kitasato University Hospital  
Tohoku University Hospital  
Ureshino Medical Center  
Tottori University Hospital  
National Center for Global Health and Medicine  
Funabashi Municipal Medical Center  
Hiroshima City Hiroshima Citizens Hospital  
Yokohama Municipal Citizen's Hospital  
Shizuoka Cancer Center  
Yamaguchi Ube Medical Center  
Tokushima University Hospital  
Ishikawa Prefectural Central Hospital  
Kanazawa University Hospital  
Hokkaido Cancer Center  
Kanagawa Cancer Center  
National Hospital Organization Himeji Medical Center  
Tokyo Metropolitan Cancer and Infectious Diseases Center Komagome Hospital  
Kinki-chuo Chest Medical Center  
Hyogo Prefectural Amagasaki General Medical Center  
Nagasaki University Hospital  
The Cancer Institute Hospital of JFCR, Gastroenterological Chemotherapy  
Ibaraki Prefectural Central Hospital  
Nagaoka Red Cross Hospital  
Japan Anti-Tuberculosis Association Fukujuji Hospital  
Tochigi Cancer Center  
Niigata Cancer Center Hospital  
The Cancer Institute Hospital of JFCR, Thoracic Medical Oncology  
National Hospital Organization Kyushu Medical Center  
Saitama Medical University International Medical Center  
Hyogo College of Medicine College Hospital  
National Hospital Organization Tokyo National Hospital  
Nagaoka Chuo General Hospital  
Toho University Omori Medical Center  
International University of Health and Welfare Mita Hospital  
Osaka Medical College Hospital  
Kurume University Hospital  
Tokyo Medical University Hospital

Osaka International Cancer Institute, Head and Neck Surgery  
National Hospital Organization Nagasaki Medical Center  
Fujita Health University Hospital  
Toranomon Hospital  
Wakayama Medical University Hospital  
Kyorin University Hospital  
University Hospital, Kyoto Prefectural University of Medicine  
St. Marianna University School of Medicine Hospital  
Niigata University Medical & Dental Hospital  
Osaka Habikino Medical Center  
Yokosuka Kyosai Hospital  
Saitama Cardiovascular and Respiratory Center  
Nara Medical University Hospital  
Teikyo University Hospital  
Saitama Medical Center  
Asahikawa Medical Center  
St. Luke's International Hospital  
National Hospital Organization Tokyo Medical Center  
Okazaki City Hospital  
Tenri Hospital  
Kobe City Medical Center General Hospital  
National Cancer Center Hospital East  
Kumamoto University Hospital  
Tokyo Metropolitan Tama Medical Center  
Fukushima Medical University Hospital  
Kyoto University Hospital  
Okayama University Hospital  
Kameda General Hospital  
University of Tsukuba Hospital  
Shonan Kamakura General Hospital  
Niigata City General Hospital  
Tokai University Hospital  
Keiyukai Sapporo Hospital  
Keio University Hospital

**Table S2** Summary of background factors

Factor	FosNTP 81 mg	FosNTP 235 mg	Placebo	FosAPR	Total
	( <i>N</i> = 195)	( <i>N</i> = 587)	( <i>N</i> = 193)	( <i>N</i> = 393)	( <i>N</i> = 1368)
	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)
<b>Age</b>					
≥55	170 (87.2)	515 (87.7)	169 (87.6)	343 (87.3)	1197 (87.5)
<55	25 (12.8)	72 (12.3)	24 (12.4)	50 (12.7)	171 (12.5)
<b>Sex</b>					
Male	146 (74.9)	449 (76.5)	147 (76.2)	302 (76.8)	1044 (76.3)
Female	49 (25.1)	138 (23.5)	46 (23.8)	91 (23.2)	324 (23.7)
<b>Performance status</b>					
0	125 (64.1)	368 (62.7)	123 (63.7)	260 (66.2)	876 (64.0)
1	70 (35.9)	219 (37.3)	70 (36.3)	133 (33.8)	492 (36.0)
<b>Drinking history</b>					
Yes	82 (42.1)	255 (43.4)	87 (45.1)	181 (46.1)	605 (44.2)
No or rarely	113 (57.9)	332 (56.6)	106 (54.9)	212 (53.9)	763 (55.8)
<b>Smoking history</b>					
Yes	162 (83.1)	485 (82.6)	153 (79.3)	321 (81.7)	1121 (81.9)

Factor	FosNTP 81 mg	FosNTP 235 mg	Placebo	FosAPR	Total
	(N = 195)	(N = 587)	(N = 193)	(N = 393)	(N = 1368)
	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)
No	33 (16.9)	102 (17.4)	40 (20.7)	72 (18.3)	247 (18.1)
Motion sickness					
No	176 (90.3)	524 (89.3)	166 (86.0)	360 (91.6)	1226 (89.6)
Yes	19 (9.7)	63 (10.7)	27 (14.0)	33 (8.4)	142 (10.4)
Pregnancy-related vomiting					
No	22 (44.9)	83 (60.1)	20 (43.5)	54 (59.3)	179 (55.2)
Yes	21 (42.9)	37 (26.8)	21 (45.7)	27 (29.7)	106 (32.7)
Not applicable	6 (12.2)	18 (13.0)	5 (10.9)	10 (11.0)	39 (12.0)
Cancer type					
Other	11 (5.6)	47 (8.0)	9 (4.7)	52 (13.2)	119 (8.7)
Lung	184 (94.4)	540 (92.0)	184 (95.3)	341 (86.8)	1249 (91.3)
CDDP dose					
<80 mg/m <sup>2</sup>	108 (55.4)	251 (42.8)	102 (52.8)	165 (42.0)	626 (45.8)
≥80 mg/m <sup>2</sup>	87 (44.6)	336 (57.2)	91 (47.2)	228 (58.0)	742 (54.2)

Factor	FosNTP 81 mg	FosNTP 235 mg	Placebo	FosAPR	Total
	(N = 195)	(N = 587)	(N = 193)	(N = 393)	(N = 1368)
	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)	<i>n</i> (%)
<b>NK-1RA</b>					
Placebo	0 (0.0)	0 (0.0)	193 (100.0)	0 (0.0)	193 (14.1)
FosAPR	0 (0.0)	0 (0.0)	0 (0.0)	393 (100.0)	393 (28.7)
FosNTP 81 mg	195 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	195 (14.3)
FosNTP 235 mg	0 (0.0)	587 (100.0)	0 (0.0)	0 (0.0)	587 (42.9)
<b>Treatment failure in 0–120 h</b>					
No	124 (63.6)	445 (75.8)	106 (54.9)	279 (71.0)	954 (69.7)
Yes	70 (35.9)	142 (24.2)	87 (45.1)	114 (29.0)	413 (30.2)

Data were obtained from the full analysis set

*FosNTP* fosnetupitant, *FosAPR* fosaprepitant, *CDDP* cisplatin, *NK-1RA* neurokinin 1 receptor antagonist





Factor	Overall (0–120 h)								Acute (0–24 h)				Delayed (24–120 h)						
	Univariate analysis		Multivariate analysis				Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis						
			Full model		Backward elimination				Full model		Backward elimination								
	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>					
No or rarely	763	2.000	<.001	1.686	<.001	1.663	<.001	2.199	<.001	1.708	.025	1.854	.008	2.118	<.001	1.764	<.001	1.746	<.001
		(1.570–2.546)		(1.298–2.189)		(1.283–2.155)		(1.433–3.376)		(1.071–2.726)		(1.176–2.923)		(1.653–2.713)		(1.350–2.305)		(1.339–2.278)	
Smoking history																			
Yes	1121	1		1		1		1		1		—		1		1		1	
No	247	2.258	<.001	1.454	.034	1.466	.030	2.816	<.001	1.601	.082	—		2.376	<.001	1.499	.023	1.514	.020
		(1.701–2.997)		(1.029–2.055)		(1.038–2.069)		(1.861–4.261)		(0.942–2.719)				(1.786–3.162)		(1.057–2.126)		(1.068–2.145)	
Motion sickness																			
No	1226	1		1		1		1		1		1		1		1		1	
Yes	142	1.930	<.001	1.491	.038	1.524	.028	2.470	<.001	1.676	.059	1.750	.039	2.118	<.001	1.632	.011	1.659	.009
		(1.355–2.750)		(1.022–2.175)		(1.047–2.219)		(1.504–4.055)		(0.980–2.866)		(1.028–2.978)		(1.485–3.020)		(1.117–2.384)		(1.138–2.420)	
Pregnancy-related vomiting																			
No	179	1		—		—		1		—		—		1		—		—	
Yes	106	3.393	<.001	—		—		1.790	.071	—		—		3.613	<.001	—		—	
		(2.054–5.603)						(0.952–3.364)						(2.179–5.989)					

Factor	N	Overall (0–120 h)						Acute (0–24 h)						Delayed (24–120 h)					
		Univariate analysis		Multivariate analysis				Univariate analysis		Multivariate analysis				Univariate analysis		Multivariate analysis			
				Full model		Backward elimination				Full model		Backward elimination				Full model		Backward elimination	
		OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>
Not applicable	39	1.834	.091	—	—	—	—	0.538	.333	—	—	—	—	1.788	.108	—	—	—	
		(0.908–3.708)						(0.154–1.886)						(0.880–3.633)					
Cancer type																			
Other	119	1		1	—	—	—	1		1	—	—	1		1	—	—	—	
Lung	1249	1.090	.683	0.822	.392	—	—	2.136	.105	1.197	.714	—	—	1.095	.675	0.833	.434	—	
		(0.720–1.652)		(0.526–1.287)				(0.854–5.345)		(0.457–3.138)				(0.717–1.672)		(0.527–1.316)			
CDDP dose																			
<80 mg/m <sup>2</sup>	626	1		1	—	—	—	1		1		1		1		1		—	
≥80 mg/m <sup>2</sup>	742	0.957	.707	1.128	.343	—	—	1.790	.005	2.176	<.001	2.175	<.001	0.910	.430	1.073	.584	—	
		(0.759–1.206)		(0.880–1.445)				(1.189–2.695)		(1.407–3.366)		(1.417–3.338)		(0.719–1.151)		(0.833–1.382)			
NK-1RA																			
Placebo	193	1		1	1	1	1	1		1		1		1		1		1	
FosAPR	393	0.498	<.001	0.486	<.001	0.503	<.001	0.416	.001	0.393	.001	0.383	<.001	0.481	<.001	0.471	<.001	0.483	<.001
		(0.348–0.712)		(0.335–0.706)		(0.347–0.727)		(0.243–0.714)		(0.223–0.692)		(0.218–0.671)		(0.335–0.690)		(0.322–0.688)		(0.332–0.703)	



Factor	Extended overall (0–168 h)		Extended delayed (24–168 h)						Beyond delayed (120–168 h)									
			Multivariate analysis			Univariate analysis			Multivariate analysis			Univariate analysis			Multivariate analysis			
	Univariate analysis		Full model		Backward elimination		Univariate analysis		Full model		Backward elimination		Univariate analysis		Full model		Backward elimination	
	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>
Age																		
≥55	1197	1	1	—	—	—	1	1	—	—	—	1	1	—	—	—	—	—
<55	171	1.355	.071	1.280	.159	—	1.267	.167	1.183	.346	—	1.086	.697	0.811	.400	—	—	—
	(0.974–1.886)		(0.908–1.806)				(0.906–1.771)		(0.834–1.678)				(0.716–1.649)		(0.498–1.321)			
Sex																		
Male	1044	1	1	—	—	—	1	1	—	—	—	1	1	—	—	—	—	—
Female	324	2.042	<.001	1.486	.013	1.512	.009	2.070	<.001	1.465	.018	1.455	.019	1.690	<.001	0.917	.700	—
	(1.580–2.638)		(1.087–2.031)		(1.111–2.059)		(1.599–2.680)		(1.069–2.008)		(1.063–1.991)		(1.241–2.302)		(0.590–1.425)			
Performance status																		
0	876	1	1	—	—	—	1	1	—	—	—	1	1	—	—	—	—	—
1	492	1.326	.017	1.344	.017	1.336	.019	1.336	.016	1.340	.020	1.329	.023	1.434	.014	1.251	.202	—
	(1.051–1.674)		(1.053–1.714)		(1.049–1.701)		(1.056–1.690)		(1.048–1.714)		(1.040–1.697)		(1.076–1.911)		(0.887–1.762)			
Drinking history																		
Yes	605	1	1	—	—	—	1	1	—	—	—	1	1	—	—	—	—	—

Factor	Extended overall (0–168 h)		Extended												Beyond delayed (120–168 h)			
			delayed (24–168 h)															
			Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis					
			Full model		Backward elimination		Full model		Backward elimination		Full model		Backward elimination					
			OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>			OR (95% CI)	<i>p</i>
No or rarely	763	2.015	<.001	1.746	<.001	1.733	<.001	2.094	<.001	1.796	<.001	1.780	<.001	1.809	<.001	1.257	.228	—
		(1.593–2.549)		(1.355–2.250)		(1.348–2.227)		(1.649–2.660)		(1.388–2.324)		(1.378–2.298)		(1.343–2.436)		(0.866–1.825)		
Smoking history																		
Yes	1121	1		1		1		1		1		1		1		1		—
No	247	2.150	<.001	1.415	.046	1.443	.034	2.221	<.001	1.451	.034	1.454	.032	1.975	<.001	1.269	.320	—
		(1.624–2.846)		(1.006–1.992)		(1.028–2.025)		(1.675–2.945)		(1.029–2.047)		(1.032–2.047)		(1.422–2.743)		(0.793–2.029)		
Motion sickness																		
No	1226	1		1		—		1		1		1		1		1		—
Yes	142	1.768	.001	1.388	.086	—		1.907	<.001	1.501	.034	1.521	.028	1.547	.041	0.984	.951	—
		(1.244–2.513)		(0.955–2.018)				(1.340–2.712)		(1.032–2.184)		(1.047–2.210)		(1.019–2.350)		(0.595–1.630)		
Pregnancy-related vomiting																		
No	179	1		—		—		1		—		—		1		—		—

Factor	N	Extended														
		Extended overall (0–168 h)				Extended delayed (24–168 h)				Beyond delayed (120–168 h)						
		Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis				
		Full model		Backward elimination		Full model		Backward elimination		Full model		Backward elimination				
		OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>			
Yes	106	3.242 (1.965–5.348)	<.001	—	—	3.442 (2.080–5.696)	<.001	—	—	2.297 (1.315–4.011)	.003	—	—			
Not applicable	39	1.793 (0.891–3.608)	.102	—	—	1.743 (0.864–3.519)	.121	—	—	1.185 (0.499–2.819)	.700	—	—			
Cancer type																
Other	119	1	1	—	—	1	1	—	—	1	1	—	—			
Lung	1249	1.154 (0.767–1.736)	.491	0.885 (0.571–1.371)	.583	—	1.173 (0.775–1.777)	.450	0.918 (0.587–1.433)	.706	—	0.957 (0.584–1.569)	.862	0.882 (0.478–1.628)	.688	—
CDDP dose																
<80 mg/m <sup>2</sup>	626	1	1	—	—	1	1	—	—	1	1	—	—			
≥80 mg/m <sup>2</sup>	742	1.011 (0.806–1.267)	.926	1.185 (0.930–1.509)	.170	—	0.957 (0.762–1.203)	.709	1.117 (0.875–1.427)	.374	—	1.016 (0.766–1.349)	.912	1.123 (0.797–1.584)	.507	—

Factor	Extended overall (0–168 h)		Extended															
			delayed (24–168 h)						Beyond delayed (120–168 h)									
			Univariate analysis			Multivariate analysis			Univariate analysis			Multivariate analysis						
			Full model		Backward elimination		Full model		Backward elimination		Full model		Backward elimination					
			OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>				
NK-IRA																		
Placebo	193	1	1	1	1	1	1	1	1	1	1	1	1	1	1	—		
FosAPR	393	0.543 (0.382–0.772)	<.001	0.531 (0.368–0.766)	<.001	0.539 (0.375–0.774)	<.001	0.533 (0.374–0.760)	<.001	0.526 (0.364–0.762)	<.001	0.538 (0.373–0.775)	<.001	0.719 (0.473–1.092)	.122	1.120 (0.677–1.855)	.659	—
FosNTP 81 mg	195	0.722 (0.483–1.081)	.114	0.716 (0.472–1.085)	.116	0.707 (0.468–1.070)	.101	0.683 (0.455–1.026)	.066	0.674 (0.443–1.026)	.066	0.675 (0.444–1.027)	.066	0.743 (0.456–1.210)	.233	0.916 (0.516–1.625)	.763	—
FosNTP 235 mg	587	0.388 (0.277–0.544)	<.001	0.363 (0.256–0.516)	<.001	0.370 (0.261–0.523)	<.001	0.388 (0.276–0.544)	<.001	0.364 (0.255–0.518)	<.001	0.370 (0.260–0.526)	<.001	0.477 (0.317–0.718)	<.001	0.779 (0.480–1.263)	.311	—
Treatment failure in 0–120 h																		
No	954	—	—	—	—	—	—	—	—	—	—	—	1	1	1	1	1	
Yes	413	—	—	—	—	—	—	—	—	—	—	—	20.951 (14.407–30.466)	<.001	19.766 (13.453–29.043)	<.001	20.951 (14.407–30.466)	<.001

Data were obtained from the full analysis set.

*h* hours, *OR* odds ratio, *CI* confidence interval, *CDDP* cisplatin, *NK-IRA* neurokinin 1 receptor antagonist, *FosAPR* fosaprepitant, *FosNTP* fosnetupitant



**Table S4** Multivariate logistic analysis of the association of treatment failure with clinical variables in each phase in the neurokinin 1 receptor antagonist evaluable population

Treatment		Overall (0–120 h)						Acute (0–24 h)						Delayed (24–120 h)									
Group	Factor	Univariate analysis		Multivariate analysis				Univariate analysis		Multivariate analysis				Univariate analysis		Multivariate analysis							
				Full model		Backward elimination				Full model		Backward elimination				Full model		Backward elimination					
		OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>				
FosNTP																							
Age																							
235 mg	≥55	515	1	1	—	—	—	1	1	1	—	—	—	1	1	—	—	—					
	<55	72	1.449	.180	1.263	.418	—	2.674	.023	2.615	.031	2.641	.026	1.338	.305	1.127	.687	—					
		(0.843–2.489)		(0.718–2.224)				(1.148–6.229)		(1.090–6.272)				(1.126–6.191)		(0.767–2.332)				(0.629–2.021)			
Sex																							
	Male	449	1	1	—	—	—	1	1	—	—	—	1	1	—	—	—						
	Female	138	2.108	<.001	1.357	.233	—	1.592	.242	1.085	.861	—	2.119	<.001	1.286	.336	—						
		(1.389–3.197)		(0.821–2.241)				(0.731–3.468)		(0.437–2.690)				(1.389–3.232)		(0.770–2.147)							
Performance status																							
	0	368	1	1	—	—	—	1	1	—	—	—	1	1	—	—							
	1	219	1.368	.111	1.275	.233	—	1.065	.868	1.131	.752	—	1.417	.081	1.311	.192	—						
		(0.931–2.010)		(0.855–1.903)				(0.507–2.238)		(0.526–2.434)				(0.958–2.095)		(0.872–1.971)							
Drinking history 1																							
	Yes	255	1	1	1	—	—	1	1	—	—	—	1	1	—	—	1						
	No or rarely	332	2.384	<.001	1.906	.004	2.017	.001	1.940	.102	1.855	.157	—	2.585	<.001	2.045	.002	2.172	<.001				
		(1.582–3.593)		(1.231–2.952)				(1.317–3.089)		(0.877–4.289)				(0.788–4.370)		(1.692–3.949)				(1.303–3.211)		(1.399–3.374)	
Drinking history 2																							



Treatment		Overall (0–120 h)						Acute (0–24 h)				Delayed (24–120 h)							
Group	Factor	Univariate analysis		Multivariate analysis				Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis					
				Full model		Backward elimination				Full model		Backward elimination							
		OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>				
	Stop smoking prior to 180 days before registration	—	—	—	—	—	—	—	—	—	—	—	—	—	—				
	Non-smoker	—	—	—	—	—	—	—	—	—	—	—	—	—	—				
	Motion sickness																		
	No	524	1	1	1	1	1	1	1	—	—	1	1	1	1				
	Yes	63	2.289	.003	1.797	.045	1.901	.026	1.651	.323	1.245	.680	—	2.476	.001	1.964	.021	2.045	.013
			(1.327–3.947)		(1.014–3.183)		(1.082–3.342)		(0.611–4.466)		(0.439–3.532)			(1.433–4.278)		(1.106–3.490)		(1.160–3.606)	
	Pregnancy-related vomiting																		
	No	83	1	—	—	—	—	1	—	—	—	—	—	1	—	—	—	—	—
	Yes	37	2.595	.020	—	—	—	1.132	.866	—	—	—	—	2.926	.009	—	—	—	—
			(1.165–5.777)					(0.267–4.796)						(1.304–6.566)					
	Not applicable	18	1.229	.710	—	—	—	0.755	.801	—	—	—	—	1.386	.559	—	—	—	—
			(0.414–3.651)					(0.085–6.687)						(0.464–4.142)					
	Cancer type																		
	Other	47	1	1	—	—	—	1	1	1	—	—	—	1	1	—	—	—	—



Treatment Group	Extended						Extended						Beyond					
Factor	overall (0–168 h)						delayed (24–168 h)						delayed (120–168 h)					
	Univariate analysis		Multivariate analysis				Univariate analysis		Multivariate analysis				Univariate analysis		Multivariate analysis			
			Full model		Backward elimination				Full model		Backward elimination				Full model		Backward elimination	
	OR		OR		OR		OR		OR		OR		OR		OR		OR	
	(95% CI)	<i>p</i>	(95% CI)	<i>p</i>	(95% CI)	<i>p</i>	(95% CI)	<i>p</i>	(95% CI)	<i>p</i>	(95% CI)	<i>p</i>	(95% CI)	<i>p</i>	(95% CI)	<i>p</i>	(95% CI)	<i>p</i>
Age																		
≥55	515	1	1	—	—	—	1	1	1	—	—	—	1	1	—	—	—	—
<55	72	1.387	.230	1.218	.487	—	1.268	.394	1.078	.797	—	1.549	.190	1.122	.788	—	—	—
	(0.813–2.365)		(0.699–2.122)				(0.734–2.190)		(0.609–1.909)				(0.805–2.983)		(0.487–2.585)			
Sex																		
Male	449	1	1	—	—	—	1	1	1	—	—	1	1	—	—	—	—	—
Female	138	1.904	.002	1.184	.503	—	1.880	.003	1.103	.703	—	1.807	.025	0.797	.548	—	—	—
	(1.262–2.871)		(0.721–1.944)				(1.241–2.848)		(0.666–1.828)				(1.078–3.030)		(0.381–1.669)			
Performance status																		
0	368	1	1	—	—	—	1	1	1	—	—	1	1	—	—	—	—	—
1	219	1.255	.237	1.174	.422	—	1.323	.150	1.232	.302	—	1.397	.177	1.158	.637	—	—	—
	(0.861–1.831)		(0.794–1.736)				(0.904–1.937)		(0.829–1.832)				(0.860–2.268)		(0.629–2.130)			





Treatment Group	Extended overall (0–168 h)						Extended delayed (24–168 h)						Beyond delayed (120–168 h)					
Factor	Univariate analysis			Multivariate analysis			Univariate analysis			Multivariate analysis			Univariate analysis			Multivariate analysis		
	Full model		Backward elimination		Full model		Backward elimination		Full model		Backward elimination		Full model		Backward elimination			
	OR		OR		OR		OR		OR		OR		OR		OR			
	(95% CI)	<i>p</i>	(95% CI)	<i>p</i>	(95% CI)	<i>p</i>	(95% CI)	<i>p</i>	(95% CI)	<i>p</i>	(95% CI)	<i>p</i>	(95% CI)	<i>p</i>	(95% CI)	<i>p</i>		
Stop smoking prior to 180 days before registration	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—		
Non-smoker	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—		
Motion sickness																		
No	524	1	1	—	1	—	1	—	1	—	1	—	1	—	1	—		
Yes	63	2.030	.011	1.618	.097	—	2.162	.005	1.743	.056	1.785	.044	2.086	.027	1.106	.811		
	(1.180–3.493)		(0.917–2.853)			(1.255–3.725)		(0.986–3.083)		(1.016–3.138)		(1.089–3.995)		(0.485–2.521)				
Pregnancy-related vomiting																		
No	83	1	—	—	1	—	—	—	—	—	1	—	—	—	—	—		
Yes	37	2.449	.028	—	—	—	2.753	.014	—	—	2.769	.035	—	—	—	—		
	(1.103–5.434)					(1.232–6.153)					(1.073–7.149)							



Treatment Group	Extended overall (0–168 h)						Extended delayed (24–168 h)						Beyond delayed (120–168 h)					
Factor	Univariate analysis			Multivariate analysis			Univariate analysis			Multivariate analysis			Univariate analysis			Multivariate analysis		
	Full model		Backward elimination		Full model		Backward elimination		Full model		Backward elimination		Full model		Backward elimination			
	OR	(95% CI)	<i>p</i>	OR	(95% CI)	<i>p</i>	OR	(95% CI)	<i>p</i>	OR	(95% CI)	<i>p</i>	OR	(95% CI)	<i>p</i>	OR	(95% CI)	<i>p</i>
Not applicable	18	1.160	.789	—	—	—	1.304	.633	—	—	—	—	1.870	.338	—	—	—	—
		(0.391–3.438)						(0.438–3.885)						(0.520–6.723)				
Cancer type																		
Other	47	1		1		—	1		1		—		1		1		—	
Lung	540	1.171	.660	0.970	.937	—	1.453	.330	1.235	.603	—		1.684	.332	1.476	.542	—	
		(0.580–2.362)		(0.463–2.036)				(0.685–3.081)		(0.557–2.737)				(0.587–4.831)		(0.422–5.156)		
CDDP dose																		
<80 mg/m <sup>2</sup>	251	1		1		—	1		1		—		1		1		—	
≥80 mg/m <sup>2</sup>	336	1.057	.771	1.165	.446	—	1.076	.705	1.183	.411	—		1.280	.326	1.617	.135	—	
		(0.728–1.535)		(0.787–1.726)				(0.737–1.571)		(0.793–1.763)				(0.782–2.096)		(0.861–3.037)		
Treatment failure in 0–120 h																		
No	445	—		—		—	—		—		—		1		1		1	

Treatment Group	Extended overall (0–168 h)				Extended delayed (24–168 h)				Beyond delayed (120–168 h)					
Factor	Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis			
	Full model		Backward elimination		Full model		Backward elimination		Full model		Backward elimination			
	OR	<i>p</i>	OR	<i>p</i>	OR	<i>p</i>	OR	<i>p</i>	OR	<i>p</i>	OR	<i>p</i>		
	(95% CI)		(95% CI)		(95% CI)		(95% CI)		(95% CI)		(95% CI)			
Yes	142	—	—	—	—	—	—	—	34.184	<.001	31.191	<.001	34.184	<.001
									(17.262–67.696)		(15.534–62.628)		(17.262–67.696)	

Treatment		Overall (0–120 h)								Acute (0–24 h)								Delayed (24–120 h)							
Group	Factor	Univariate analysis		Multivariate analysis				Univariate analysis		Multivariate analysis				Univariate analysis		Multivariate analysis									
				Backward elimination						Backward elimination						Backward elimination									
		OR		OR		OR		OR		OR		OR		OR		OR		OR							
		(95% CI)		(95% CI)		(95% CI)		OR (95% CI)		(95% CI)		(95% CI)		OR (95% CI)		(95% CI)		OR (95% CI)							
		<i>p</i>		<i>p</i>		<i>p</i>		<i>p</i>		<i>p</i>		<i>p</i>		<i>p</i>		<i>p</i>		<i>p</i>							
FosAPR	Age																								
	≥55	343	1	1	—	—	—	1	1	—	—	—	—	1	1	—	—	—	—						
	<55	50	0.842	.616	0.780	.485	—	1.477	.451	1.266	.660	—	0.824	.584	0.752	.437	—	—	—						
			(0.429–1.650)		(0.388–1.566)			(0.536–4.066)		(0.443–3.620)			(0.413–1.645)		(0.366–1.543)										
	Sex																								
	Male	302	1	1	—	—	—	1	1	—	—	—	1	1	—	—	—	—	—						
	Female	91	2.133	.003	1.685	.080	—	3.479	.002	2.684	.036	—	3.479	.002	2.421	<.001	1.875	.037	—						
			(1.305–3.485)		(0.940–3.020)			(1.610–7.518)		(1.066–6.757)			(1.610–7.518)		(1.475–3.975)		(1.039–3.385)								
	Performance status																								
	0	260	1	1	—	—	—	1	1	—	—	—	1	1	—	—	—	—	—						
	1	133	1.493	.082	1.549	.066	—	1.418	.374	1.533	.297	—	1.385	.166	1.433	.142	—	—	—						
			(0.950–2.346)		(0.971–2.469)			(0.656–3.064)		(0.687–3.424)			(0.873–2.195)		(0.886–2.316)										
	Drinking history																								
	1																								
	Yes	181	1	1	—	—	—	1	1	—	—	—	1	1	—	—	—	—	—						

Treatment	Overall (0–120 h)										Delayed (24–120 h)											
Group	Factor	N	Univariate analysis				Multivariate analysis				Acute (0–24 h)		Univariate analysis		Multivariate analysis		Delayed (24–120 h)		Univariate analysis		Multivariate analysis	
			Backward elimination		Backward elimination		Backward elimination		Backward elimination		Backward elimination		Backward elimination		Backward elimination		Backward elimination		Backward elimination		Backward elimination	
			OR	OR	OR	OR	OR	OR	OR	OR	OR	OR	OR	OR	OR	OR	OR	OR	OR	OR	OR	OR
			(95% CI)	<i>p</i>	(95% CI)	<i>p</i>	(95% CI)	<i>p</i>	OR (95% CI)	<i>p</i>	(95% CI)	<i>p</i>	(95% CI)	<i>p</i>	(95% CI)	<i>p</i>	(95% CI)	<i>p</i>	(95% CI)	<i>p</i>	(95% CI)	<i>p</i>
	No or rarely	212	1.458	.095	1.205	.461	—	—	1.683	.198	1.126	.795	—	—	1.544	.061	1.245	.400	—	—	—	—
			(0.936–2.271)		(0.734–1.976)				(0.762–3.720)		(0.459–2.761)				(0.981–2.429)		(0.747–2.075)					
Drinking history																						
2																						
	Regularly (once per day)	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
	Occasionally (once per week)	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
	Rarely (once per month)	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
	No	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Smoking history																						
1																						
	Yes	321	1	—	1	—	—	—	1	—	1	—	—	—	1	—	1	—	—	—	1	—



Treatment Group	Factor	N	Overall (0–120 h)						Acute (0–24 h)						Delayed (24–120 h)					
			Univariate analysis		Multivariate analysis				Univariate analysis		Multivariate analysis				Univariate analysis		Multivariate analysis			
				Backward Full model		Backward elimination				Backward Full model		Backward elimination				Backward Full model		Backward elimination		
		OR (95% CI)		OR (95% CI)		OR (95% CI)		OR (95% CI)		OR (95% CI)		OR (95% CI)		OR (95% CI)		OR (95% CI)		OR (95% CI)		
		<i>p</i>		<i>p</i>		<i>p</i>		<i>p</i>		<i>p</i>		<i>p</i>		<i>p</i>		<i>p</i>		<i>p</i>		
Motion sickness																				
	No	360	1	1	1	1	1	1	—	—	—	—	1	1	1	1	1	1	1	
	Yes	33	2.197 (1.066–4.529)	.033	2.052 (0.958–4.394)	.064	2.181 (1.049–4.534)	.037	3.256 (1.222–8.678)	.018	2.227 (0.781–6.350)	.134	—	2.428 (1.176–5.014)	.016	2.274 (1.055–4.898)	.036	2.422 (1.159–5.061)	.019	
Pregnancy-related vomiting																				
	No	54	1	—	—	—	1	—	—	—	—	—	1	—	—	—	—	—	—	
	Yes	27	3.700 (1.403–9.754)	.008	—	—	1.136 (0.340–3.797)	.835	—	—	—	—	3.700 (1.403–9.754)	.008	—	—	—	—	—	
	Not applicable	10	1.451 (0.362–5.821)	.600	—	—	<0.001 (<0.001–>999.999)	.971	—	—	—	—	1.451 (0.362–5.821)	.600	—	—	—	—	—	
Cancer type																				
	Other	52	1	1	—	—	1	1	—	—	—	—	1	1	—	—	—	—	—	
	Lung	341	0.818 (0.438–1.530)	.530	0.658 (0.334–1.294)	.225	—	4.562 (0.607–34.269)	.140	3.128 (0.396–24.716)	.280	—	0.738 (0.394–1.383)	.343	0.574 (0.289–1.137)	.111	—	—	—	



Treatment Group	Extended				Extended				Beyond									
Factor	overall (0–168 h)				delayed (24–168 h)				delayed (120–168 h)									
	Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis							
			Full model		Backward elimination		Full model		Backward elimination		Full model		Backward elimination					
	OR	p	OR	p	OR	p	OR	p	OR	p	OR	p	OR	p				
	(95% CI)		(95% CI)		(95% CI)		(95% CI)		(95% CI)		(95% CI)		(95% CI)					
<b>Age</b>																		
≥55	343	1	1	—	1	1	1	—	1	1	1	—	1	—				
<55	50	0.761	.415	0.683	.274	—	0.734	.367	0.649	.227	—	0.562	.206	0.571	.283	—		
		(0.395–1.467)		(0.344–1.353)			(0.375–1.437)		(0.322–1.309)			(0.230–1.373)		(0.205–1.588)				
<b>Sex</b>																		
Male	302	1	1	1	1	1	1	1	1	1	1	1	1	—				
Female	91	2.351	<.001	1.959	.021	2.351	<.001	2.598	<.001	2.130	.010	2.446	<.001	2.170	.006	1.540	.283	—
		(1.453–3.804)		(1.108–3.465)		(1.453–3.804)		(1.601–4.216)		(1.201–3.780)		(1.498–3.994)		(1.251–3.765)		(0.700–3.388)		
<b>Performance status</b>																		
0	260	1	1	—	1	1	1	—	1	1	1	—	1	—				
1	133	1.425	.113	1.484	.089	—	1.299	.249	1.343	.214	—	1.692	.047	1.484	.216	—		
		(0.919–2.209)		(0.941–2.340)			(0.833–2.025)		(0.844–2.136)			(1.007–2.844)		(0.795–2.771)				
<b>Drinking history 1</b>																		
Yes	181	1	1	—	1	1	1	—	1	1	1	—	1	—				



Treatment Group	Extended						Extended						Beyond					
Factor	overall (0–168 h)						delayed (24–168 h)						delayed (120–168 h)					
	Univariate analysis			Multivariate analysis			Univariate analysis			Multivariate analysis			Univariate analysis			Multivariate analysis		
	Full model		Backward elimination	Full model		Backward elimination	Full model		Backward elimination	Full model		Backward elimination	Full model		Backward elimination	Full model		Backward elimination
	OR	(95% CI)	<i>p</i>	OR	(95% CI)	<i>p</i>	OR	(95% CI)	<i>p</i>	OR	(95% CI)	<i>p</i>	OR	(95% CI)	<i>p</i>	OR	(95% CI)	<i>p</i>
No or rarely	212	1.588	.034	1.359	.209	—	1.626	.028	1.358	.219	—	1.373	.230	1.060	.864	—		
		(1.035–2.436)		(0.843–2.190)			(1.053–2.511)		(0.834–2.209)			(0.818–2.303)		(0.543–2.072)				
Drinking history 2																		
Regularly (once per day)	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Occasionally (once per week)	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Rarely (once per month)	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
No	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—	—
Smoking history 1																		
Yes	321	1	—	1	—	—	1	1	—	1	—	1	1	—	—	—	—	—
No	72	2.097	.005	1.408	.290	—	2.297	.002	1.466	.239	—	1.945	.028	1.069	.879	—		
		(1.246–3.530)		(0.748–2.652)			(1.361–3.874)		(0.776–2.771)			(1.074–3.522)		(0.453–2.522)				

Treatment Group	Extended				Extended				Beyond								
Factor	overall (0–168 h)				delayed (24–168 h)				delayed (120–168 h)								
	Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis		Univariate analysis		Multivariate analysis						
			Full model		Backward elimination		Full model		Backward elimination		Full model		Backward elimination				
	OR		OR		OR		OR		OR		OR		OR				
	(95% CI)	<i>p</i>	(95% CI)	<i>p</i>	(95% CI)	<i>p</i>	(95% CI)	<i>p</i>	(95% CI)	<i>p</i>	(95% CI)	<i>p</i>	(95% CI)	<i>p</i>			
Smoking history 2																	
Smoker	—	—	—	—	—	—	—	—	—	—	—	—	—	—			
Stop smoking within 180 days before registration	—	—	—	—	—	—	—	—	—	—	—	—	—	—			
Stop smoking prior to 180 days before registration	—	—	—	—	—	—	—	—	—	—	—	—	—	—			
Non-smoker	—	—	—	—	—	—	—	—	—	—	—	—	—	—			
Motion sickness																	
No	360	1	1	—	1	1	1	1	1	1	1	1	1	—			
Yes	33	2.322	.021	2.076	.060	—	2.512	.012	2.256	.036	2.143	.043	2.801	.008	2.240	.102	—
		(1.133–4.761)		(0.971–4.438)			(1.224–5.156)		(1.053–4.834)		(1.023–4.489)		(1.309–5.994)		(0.851–5.895)		

Treatment	Extended						Extended						Beyond					
Group	overall (0–						delayed (24–						delayed (120–					
Factor	N 168 h)						168 h)						168 h)					
	Univariate analysis			Multivariate analysis			Univariate analysis			Multivariate analysis			Univariate analysis			Multivariate analysis		
	Full model		Backward elimination		Full model		Backward elimination		Full model		Backward elimination		Full model		Backward elimination			
	OR		OR		OR		OR		OR		OR		OR		OR			
	(95% CI)	<i>p</i>	(95% CI)	<i>p</i>	(95% CI)	<i>p</i>	(95% CI)	<i>p</i>	(95% CI)	<i>p</i>	(95% CI)	<i>p</i>	(95% CI)	<i>p</i>	(95% CI)	<i>p</i>		
Pregnancy-related																		
vomiting																		
No	54	1	—	—	1	—	—	—	1	—	—	—	1	—	—	—		
Yes	27	4.037	.006	—	—	—	4.037	.006	—	—	—	—	1.855	.226	—	—		
		(1.495–					(1.495–						(0.683–5.042)					
		10.906)					10.906)											
Not applicable	10	1.700	.443	—	—	—	1.700	.443	—	—	—	—	1.352	.692	—	—		
		(0.438–6.604)					(0.438–6.604)						(0.305–5.994)					
Cancer type																		
Other	52	1	1	—	1	—	1	—	1	—	—	—	1	1	—	—		
Lung	341	0.924	.800	0.692	.278	—	0.852	.610	0.632	.180	—	—	0.641	.204	0.540	.166		
		(0.500–1.708)		(0.355–1.347)			(0.460–1.577)		(0.324–1.236)				(0.322–1.273)		(0.226–1.292)			
CDDP dose																		
<80 mg/m <sup>2</sup>	165	1	1	—	1	—	1	—	1	—	—	—	1	1	—	—		
≥80 mg/m <sup>2</sup>	228	1.243	.320	1.452	.109	—	1.160	.501	1.360	.192	—	—	1.046	.865	1.013	.969		
		(0.809–1.910)		(0.920–2.291)			(0.752–1.790)		(0.857–2.160)				(0.624–1.753)		(0.544–1.886)			

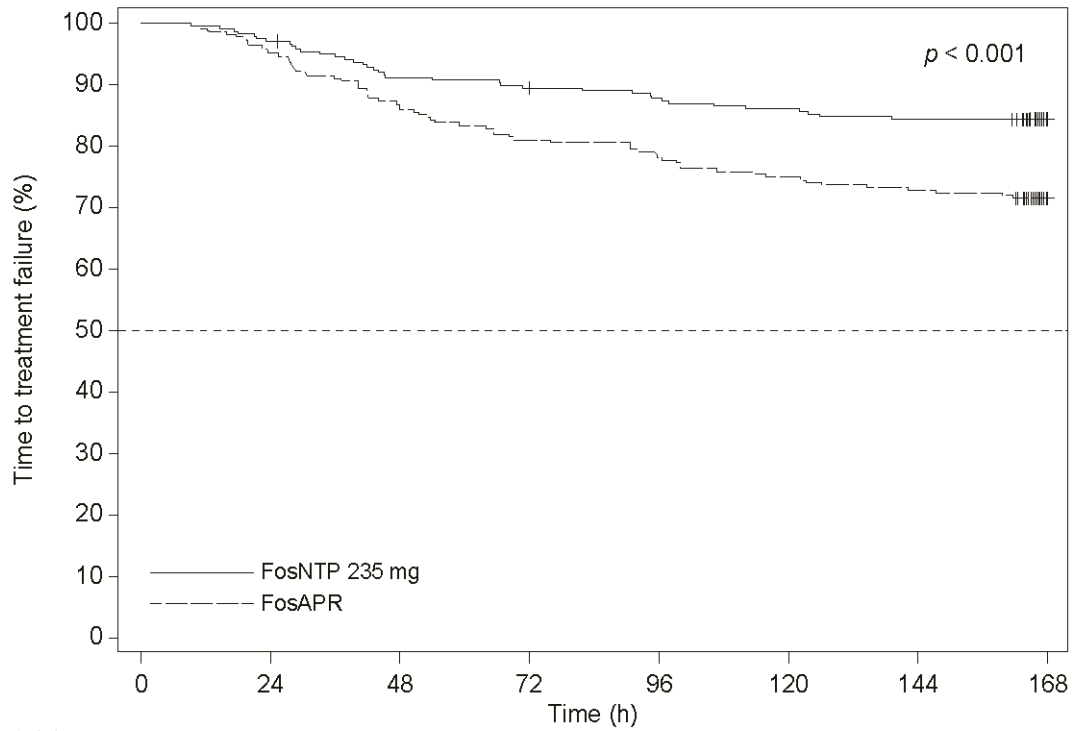
Treatment	Extended						Extended						Beyond								
Group	overall (0–						delayed (24–						delayed (120–								
Factor	N 168 h)						168 h)						168 h)								
	Univariate analysis			Multivariate analysis			Univariate analysis			Multivariate analysis			Univariate analysis			Multivariate analysis					
	Full model		Backward elimination	Full model		Backward elimination	Full model		Backward elimination	Full model		Backward elimination	Full model		Backward elimination	Full model		Backward elimination			
	OR	(95% CI)	<i>p</i>	OR	(95% CI)	<i>p</i>	OR	(95% CI)	<i>p</i>	OR	(95% CI)	<i>p</i>	OR	(95% CI)	<i>p</i>	OR	(95% CI)	<i>p</i>			
Treatment failure																					
in 0–120 h																					
No	279	—	—	—	—	—	—	—	—	—	—	—	1	—	—	1	—	—	1		
Yes	114	—	—	—	—	—	—	—	—	—	—	—	16.437	(8.806–30.681)	<.001	14.673	(7.755–27.762)	<.001	16.437	(8.806–30.681)	<.001

Data were obtained from the full analysis set.

*h* hours, *OR* odds ratio, *CI* confidence interval, *CDDP* cisplatin, *FosAPR* fosaprepitant, *FosNTP* fosnetupitant

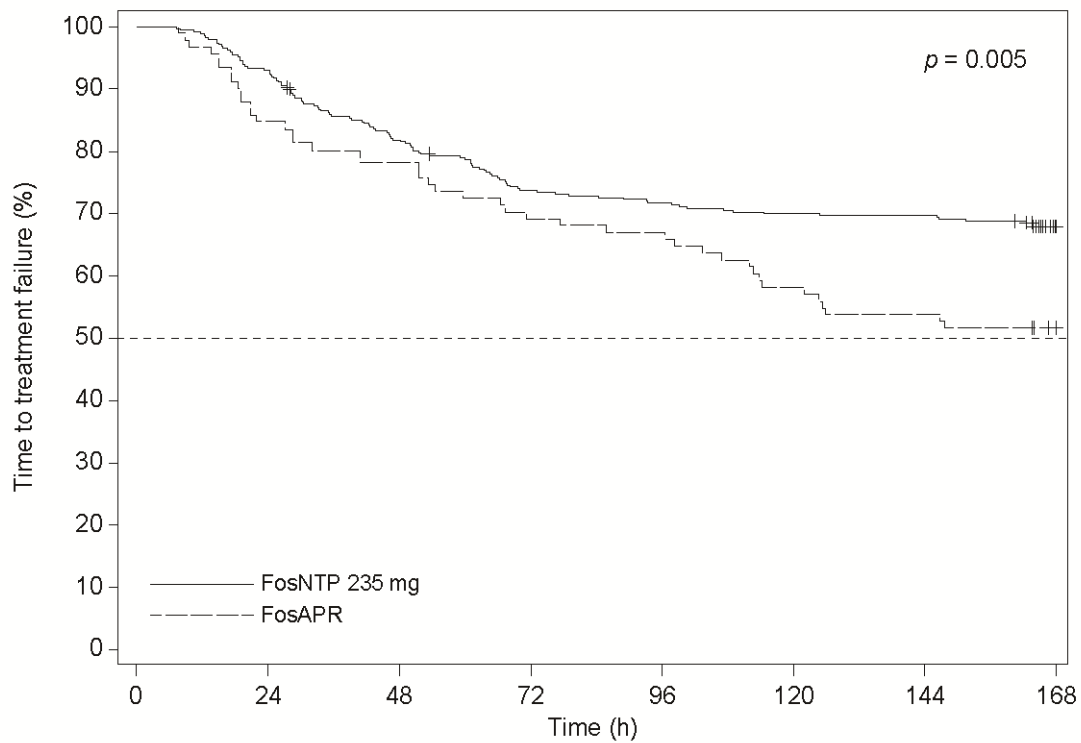
Figure S1 Comparison of the time to treatment failure curve classified by the number of risk factors at 0–168 hours in the neurokinin 1 receptor antagonist-evaluable population. **a** No risk factors; **b** One or more risk factors

a. No risk factors.



Number at risk		0	24	48	72	96	120	144	168
FosNTP 235 mg		238	231	216	212	207	203	199	167
FosAPR		302	287	262	245	235	226	219	183

b. One or more risk factors.



Number at risk		0	24	48	72	96	120	144	168
FosNTP 235 mg		348	324	283	254	247	241	240	212
FosAPR		91	77	71	63	61	53	49	43