Table 8.3.5-2
Occurrence of Treatment-Related Adverse Events by Severity
Safety Set

Study	KLH2301											
Group	KLH-2109 200 mg						Leuprorelin					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
N	143	---	---	---	---	---	144	---	---	---	---	---
Any Treatment-Related AEs	116	81.1	3	2.1	1	0.7	120	83.3	11	7.6	0	0.0
感染症および寄生虫症	1	0.7	0	0.0	0	0.0	2	1.4	0	0.0	0	0.0
尿路感染	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
腟感染	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
外陰腟真菌感染	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
カンジダ感染	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
膿疱性ざ瘡	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
結膜炎	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胃腸炎	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
外陰部腟カンジダ症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
癜風	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
膀胱炎	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
細菌性外陰腟炎	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
毛包炎	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血管腫	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血液およびリンパ系障害	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
貧血	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
好中球減少症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血小板減少症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
代謝および栄養障害	5	3.5	0	0.0	0	0.0	2	1.4	0	0.0	0	0.0
脂質異常症	5	3.5	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0

A subject was counted only once based on the most severe event if a subject had multiple events of the same MedDRA term.
For KLH-2109 ALL group, the severity of "Headache" and "Pain in extremity" with Subject [redacted] in the 15-OBE2109-001 study was unknown.

Table 8.3.5-2
Occurrence of Treatment-Related Adverse Events by Severity
Safety Set

Study	KLH2301											
Group	KLH-2109 200 mg						Leuprorelin					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
食欲減退	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
過食	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
食欲亢進	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
２型糖尿病	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
高コレステロール血症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
高トリグリセリド血症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
精神障害	6	4.2	1	0.7	0	0.0	8	5.6	5	3.5	0	0.0
気分動揺	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
リビドー減退	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
不眠症	2	1.4	1	0.7	0	0.0	2	1.4	3	2.1	0	0.0
感情不安定	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
不安	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
易刺激性	1	0.7	0	0.0	0	0.0	2	1.4	0	0.0	0	0.0
うつ病	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0
中期不眠症	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
睡眠障害	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
気分変化	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
睡眠の質低下	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
錯乱状態	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
神経過敏	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
抑うつ気分	0	0.0	0	0.0	0	0.0	1	0.7	1	0.7	0	0.0
リビドー消失	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
注意欠如・多動性障害	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
抑うつ症状	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0

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Safety Set

Study	KLH2301											
Group	KLH-2109 200 mg						Leuprorelin					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
気分の落ち込み	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
神経系障害	15	10.5	1	0.7	1	0.7	14	9.7	4	2.8	0	0.0
頭痛	8	5.6	1	0.7	0	0.0	9	6.3	1	0.7	0	0.0
浮動性めまい	4	2.8	0	0.0	0	0.0	2	1.4	1	0.7	0	0.0
傾眠	3	2.1	0	0.0	0	0.0	2	1.4	0	0.0	0	0.0
片頭痛	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0
体位性めまい	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
くも膜下出血	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
認知障害	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
嗜眠	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
記憶障害	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
鎮静	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
振戦	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
感覚鈍麻	0	0.0	0	0.0	0	0.0	2	1.4	0	0.0	0	0.0
味覚不全	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
眼振	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
緊張性頭痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
手根管症候群	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0
頚腕症候群	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
神経痛	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0
起立不耐性	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
眼障害	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
眼部腫脹	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
霧視	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

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Safety Set

Study	KLH2301											
Group	KLH-2109 200 mg						Leuprorelin					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
緑内障	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
耳および迷路障害	2	1.4	0	0.0	0	0.0	2	1.4	0	0.0	0	0.0
回転性めまい	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
耳不快感	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
耳鳴	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
頭位性回転性めまい	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
心臓障害	7	4.9	0	0.0	0	0.0	3	2.1	0	0.0	0	0.0
動悸	7	4.9	0	0.0	0	0.0	2	1.4	0	0.0	0	0.0
頻脈	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
狭心症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
上室性期外収縮	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
心室性期外収縮	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
洞性徐脈	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
血管障害	76	53.1	1	0.7	0	0.0	74	51.4	3	2.1	0	0.0
ほてり	76	53.1	1	0.7	0	0.0	74	51.4	3	2.1	0	0.0
高血圧	1	0.7	0	0.0	0	0.0	2	1.4	0	0.0	0	0.0
潮紅	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
呼吸器、胸郭および縦隔障害	3	2.1	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
咽喉絞扼感	2	1.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
呼吸困難	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
アレルギー性咳嗽	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
喘息	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胃腸障害	6	4.2	0	0.0	0	0.0	4	2.8	0	0.0	0	0.0

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Safety Set

Study	KLH2301											
Group	KLH-2109 200 mg						Leuprorelin					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
悪心	2	1.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
上腹部痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
便秘	2	1.4	0	0.0	0	0.0	2	1.4	0	0.0	0	0.0
下痢	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
腹部不快感	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
腹痛	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
嘔吐	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
腹部膨満	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
鼓腸	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
消化不良	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
胃炎	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
下腹部痛	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
胃食道逆流性疾患	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胃酸過多	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
肛門周囲痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
肝胆道系障害	4	2.8	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
肝機能異常	4	2.8	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
脂肪肝	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
高トランスアミナーゼ血症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
皮膚および皮下組織障害	23	16.1	1	0.7	0	0.0	24	16.7	1	0.7	0	0.0
多汗症	18	12.6	1	0.7	0	0.0	17	11.8	0	0.0	0	0.0
脱毛症	4	2.8	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
ざ瘡	0	0.0	0	0.0	0	0.0	4	2.8	0	0.0	0	0.0
寝汗	0	0.0	0	0.0	0	0.0	2	1.4	0	0.0	0	0.0

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Safety Set

Study	KLH2301											
Group	KLH-2109 200 mg						Leuprorelin					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
蕁麻疹	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
アレルギー性皮膚炎	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
発疹	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0
冷汗	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
湿疹	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
そう痒症	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
皮膚炎	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
円形脱毛症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
男性型多毛症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
ばら色粃糠疹	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
脂漏性皮膚炎	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
乾皮症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
紅斑	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
丘疹性皮疹	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
皮膚局面	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
筋骨格系および結合組織障害	24	16.8	1	0.7	0	0.0	22	15.3	2	1.4	0	0.0
関節痛	12	8.4	1	0.7	0	0.0	13	9.0	0	0.0	0	0.0
筋骨格硬直	10	7.0	0	0.0	0	0.0	2	1.4	1	0.7	0	0.0
背部痛	2	1.4	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
骨吸収亢進	2	1.4	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
腱鞘炎	2	1.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
骨喪失	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
筋肉痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
筋痙縮	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0

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Group	KLH-2109 200 mg						Leuprorelin					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
四肢痛	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
骨痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
筋緊張	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
関節周囲炎	0	0.0	0	0.0	0	0.0	1	0.7	1	0.7	0	0.0
骨減少症	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
変形性関節症	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
弾発指	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
側腹部痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
関節腫脹	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
腎および尿路障害	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
頻尿	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
夜間頻尿	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
排尿困難	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
腎臓痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
生殖系および乳房障害	74	51.7	0	0.0	0	0.0	102	70.8	1	0.7	0	0.0
月経中間期出血	53	37.1	0	0.0	0	0.0	77	53.5	0	0.0	0	0.0
重度月経出血	6	4.2	0	0.0	0	0.0	4	2.8	0	0.0	0	0.0
閉経期症状	8	5.6	0	0.0	0	0.0	4	2.8	0	0.0	0	0.0
外陰腟乾燥	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
異常子宮出血	6	4.2	0	0.0	0	0.0	11	7.6	1	0.7	0	0.0
腟出血	1	0.7	0	0.0	0	0.0	2	1.4	0	0.0	0	0.0
子宮出血	6	4.2	0	0.0	0	0.0	6	4.2	0	0.0	0	0.0
無月経	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
骨盤痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

A subject was counted only once based on the most severe event if a subject had multiple events of the same MedDRA term.
For KLH-2109 ALL group, the severity of "Headache" and "Pain in extremity" with Subject [redacted] in the 15-OBE2109-001 study was unknown.

Table 8.3.5-2
Occurrence of Treatment-Related Adverse Events by Severity
Safety Set

Study	KLH2301											
Group	KLH-2109 200 mg						Leuprorelin					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
腟分泌物	1	0.7	0	0.0	0	0.0	2	1.4	0	0.0	0	0.0
不規則月経	3	2.1	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
乳房不快感	1	0.7	0	0.0	0	0.0	2	1.4	0	0.0	0	0.0
性器出血	1	0.7	0	0.0	0	0.0	2	1.4	0	0.0	0	0.0
外陰腟灼熱感	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
月経障害	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
月経困難症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
子宮内膜増殖症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
乳汁漏出症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
月経遅延	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
外陰腟不快感	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
卵巣嚢胞	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
外陰腟そう痒症	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
乳房圧痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
乳房痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
希発月経	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
月経前症候群	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
萎縮性外陰腟炎	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
乳房うっ滞	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
一般・全身障害および投与部位の状態	12	8.4	0	0.0	0	0.0	19	13.2	0	0.0	0	0.0
倦怠感	8	5.6	0	0.0	0	0.0	8	5.6	0	0.0	0	0.0
疲労	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
浮腫	3	2.1	0	0.0	0	0.0	3	2.1	0	0.0	0	0.0
異常感	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

A subject was counted only once based on the most severe event if a subject had multiple events of the same MedDRA term.
For KLH-2109 ALL group, the severity of "Headache" and "Pain in extremity" with Subject [redacted] in the 15-OBE2109-001 study was unknown.

Table 8.3.5-2
Occurrence of Treatment-Related Adverse Events by Severity
Safety Set

Study	KLH2301											
Group	KLH-2109 200 mg						Leuprorelin					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
無力症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
末梢性浮腫	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
疼痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
熱感	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
末梢腫脹	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
悪寒	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
口渇	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
注射部位硬結	0	0.0	0	0.0	0	0.0	3	2.1	0	0.0	0	0.0
投与部位硬結	0	0.0	0	0.0	0	0.0	2	1.4	0	0.0	0	0.0
胸部不快感	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
冷感	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
注射部位内出血	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
注射部位反応	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
投与部位疼痛	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
穿刺部位疼痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
顔面浮腫	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
空腹	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
発熱	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
臨床検査	35	24.5	0	0.0	0	0.0	30	20.8	0	0.0	0	0.0
アラニンアミノトランスフェラーゼ増加	7	4.9	0	0.0	0	0.0	2	1.4	0	0.0	0	0.0
アスパラギン酸アミノトランスフェラーゼ増加	4	2.8	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
γ－グルタミルトランスフェラーゼ増加	5	3.5	0	0.0	0	0.0	5	3.5	0	0.0	0	0.0
血中コレステロール増加	4	2.8	0	0.0	0	0.0	4	2.8	0	0.0	0	0.0
骨密度減少	8	5.6	0	0.0	0	0.0	4	2.8	0	0.0	0	0.0

A subject was counted only once based on the most severe event if a subject had multiple events of the same MedDRA term.
For KLH-2109 ALL group, the severity of "Headache" and "Pain in extremity" with Subject [redacted] in the 15-OBE2109-001 study was unknown.

Table 8.3.5-2
Occurrence of Treatment-Related Adverse Events by Severity
Safety Set

Study	KLH2301											
Group	KLH-2109 200 mg						Leuprorelin					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
低比重リポ蛋白増加	2	1.4	0	0.0	0	0.0	4	2.8	0	0.0	0	0.0
グアナーゼ増加	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
生化学的骨代謝マーカー上昇	10	7.0	0	0.0	0	0.0	6	4.2	0	0.0	0	0.0
血中トリグリセリド増加	3	2.1	0	0.0	0	0.0	5	3.5	0	0.0	0	0.0
酒石酸抵抗性酸ホスファターゼ増加	7	4.9	0	0.0	0	0.0	9	6.3	0	0.0	0	0.0
活性化部分トロンボプラスチン時間延長	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
体重増加	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
血中クレアチンホスホキナーゼ増加	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血中アルカリホスファターゼ増加	1	0.7	0	0.0	0	0.0	2	1.4	0	0.0	0	0.0
血圧上昇	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
高比重リポ蛋白増加	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血中ビリルビン増加	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
肝機能検査値上昇	2	1.4	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
肝酵素上昇	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
体重減少	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
遊離脂肪酸増加	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
心電図ＱＴ延長	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
プロトロンビン時間短縮	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Ｎ－テロペプチド	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血中乳酸脱水素酵素増加	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血小板数減少	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
尿中ブドウ糖陽性	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
トランスアミナーゼ上昇	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血中クレアチニン増加	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

A subject was counted only once based on the most severe event if a subject had multiple events of the same MedDRA term.
For KLH-2109 ALL group, the severity of "Headache" and "Pain in extremity" with Subject [redacted] in the 15-OBE2109-001 study was unknown.

Table 8.3.5-2
Occurrence of Treatment-Related Adverse Events by Severity
Safety Set

Study	KLH2301											
Group	KLH-2109 200 mg						Leuprorelin					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
血中尿素減少	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
体温低下	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
脂質増加	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
総蛋白増加	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
白血球数減少	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血小板数増加	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
尿中蛋白陽性	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
便潜血陽性	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
プロトロンビン時間延長	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
尿中ケトン体陽性	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

A subject was counted only once based on the most severe event if a subject had multiple events of the same MedDRA term.
For KLH-2109 ALL group, the severity of "Headache" and "Pain in extremity" with Subject [redacted] in the 15-OBE2109-001 study was unknown.

Table 8.3.5-2
Occurrence of Treatment-Related Adverse Events by Severity
Safety Set

Study	KLH2302											
Group	KLH-2109 200 mg						Placebo					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
N	48	---	---	---	---	---	41	---	---	---	---	---
Any Treatment-Related AEs	39	81.3	0	0.0	0	0.0	16	39.0	1	2.4	0	0.0
感染症および寄生虫症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
尿路感染	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
腟感染	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
外陰腟真菌感染	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
カンジダ感染	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
膿疱性ざ瘡	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
結膜炎	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胃腸炎	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
外陰部腟カンジダ症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
癜風	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
膀胱炎	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
細菌性外陰腟炎	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
毛包炎	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血管腫	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血液およびリンパ系障害	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
貧血	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
好中球減少症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血小板減少症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
代謝および栄養障害	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
脂質異常症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

A subject was counted only once based on the most severe event if a subject had multiple events of the same MedDRA term.
For KLH-2109 ALL group, the severity of "Headache" and "Pain in extremity" with Subject [redacted] in the 15-OBE2109-001 study was unknown.

Table 8.3.5-2
Occurrence of Treatment-Related Adverse Events by Severity
Safety Set

Study	KLH2302											
Group	KLH-2109 200 mg						Placebo					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
食欲減退	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
過食	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
食欲亢進	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
２型糖尿病	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
高コレステロール血症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
高トリグリセリド血症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
精神障害	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
気分動揺	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
リビドー減退	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
不眠症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
感情不安定	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
不安	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
易刺激性	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
うつ病	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
中期不眠症	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
睡眠障害	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
気分変化	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
睡眠の質低下	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
錯乱状態	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
神経過敏	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
抑うつ気分	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
リビドー消失	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
注意欠如・多動性障害	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
抑うつ症状	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

A subject was counted only once based on the most severe event if a subject had multiple events of the same MedDRA term.
For KLH-2109 ALL group, the severity of "Headache" and "Pain in extremity" with Subject [redacted] in the 15-OBE2109-001 study was unknown.

Table 8.3.5-2
Occurrence of Treatment-Related Adverse Events by Severity
Safety Set

Study	KLH2302											
Group	KLH-2109 200 mg						Placebo					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
気分の落ち込み	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
神経系障害	5	10.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
頭痛	3	6.3	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
浮動性めまい	2	4.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
傾眠	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
片頭痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
体位性めまい	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
くも膜下出血	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
認知障害	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
嗜眠	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
記憶障害	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
鎮静	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
振戦	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
感覚鈍麻	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
味覚不全	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
眼振	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
緊張性頭痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
手根管症候群	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
頚腕症候群	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
神経痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
起立不耐性	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
眼障害	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
眼部腫脹	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
霧視	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

A subject was counted only once based on the most severe event if a subject had multiple events of the same MedDRA term.
For KLH-2109 ALL group, the severity of "Headache" and "Pain in extremity" with Subject [redacted] in the 15-OBE2109-001 study was unknown.

Table 8.3.5-2
Occurrence of Treatment-Related Adverse Events by Severity
Safety Set

Study	KLH2302											
Group	KLH-2109 200 mg						Placebo					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
緑内障	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
耳および迷路障害	0	0.0	0	0.0	0	0.0	1	2.4	0	0.0	0	0.0
回転性めまい	0	0.0	0	0.0	0	0.0	1	2.4	0	0.0	0	0.0
耳不快感	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
耳鳴	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
頭位性回転性めまい	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
心臓障害	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
動悸	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
頻脈	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
狭心症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
上室性期外収縮	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
心室性期外収縮	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
洞性徐脈	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血管障害	23	47.9	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
ほてり	23	47.9	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
高血圧	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
潮紅	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
呼吸器、胸郭および縦隔障害	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
咽喉絞扼感	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
呼吸困難	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
アレルギー性咳嗽	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
喘息	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胃腸障害	3	6.3	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

A subject was counted only once based on the most severe event if a subject had multiple events of the same MedDRA term.
For KLH-2109 ALL group, the severity of "Headache" and "Pain in extremity" with Subject [redacted] in the 15-OBE2109-001 study was unknown.

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Safety Set

Study	KLH2302											
Group	KLH-2109 200 mg						Placebo					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
悪心	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
上腹部痛	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
便秘	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
下痢	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
腹部不快感	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
腹痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
嘔吐	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
腹部膨満	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
鼓腸	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
消化不良	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胃炎	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
下腹部痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胃食道逆流性疾患	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胃酸過多	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
肛門周囲痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
肝胆道系障害	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
肝機能異常	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
脂肪肝	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
高トランスアミナーゼ血症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
皮膚および皮下組織障害	6	12.5	0	0.0	0	0.0	1	2.4	0	0.0	0	0.0
多汗症	6	12.5	0	0.0	0	0.0	1	2.4	0	0.0	0	0.0
脱毛症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
ざ瘡	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
寝汗	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

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For KLH-2109 ALL group, the severity of "Headache" and "Pain in extremity" with Subject [redacted] in the 15-OBE2109-001 study was unknown.

Table 8.3.5-2
Occurrence of Treatment-Related Adverse Events by Severity
Safety Set

Study	KLH2302											
Group	KLH-2109 200 mg						Placebo					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
蕁麻疹	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
アレルギー性皮膚炎	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
発疹	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
冷汗	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
湿疹	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
そう痒症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
皮膚炎	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
円形脱毛症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
男性型多毛症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
ばら色粃糠疹	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
脂漏性皮膚炎	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
乾皮症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
紅斑	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
丘疹性皮疹	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
皮膚局面	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
筋骨格系および結合組織障害	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
関節痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
筋骨格硬直	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
背部痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
骨吸収亢進	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
腱鞘炎	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
骨喪失	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
筋肉痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
筋痙縮	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

A subject was counted only once based on the most severe event if a subject had multiple events of the same MedDRA term.
For KLH-2109 ALL group, the severity of "Headache" and "Pain in extremity" with Subject [redacted] in the 15-OBE2109-001 study was unknown.

Table 8.3.5-2
Occurrence of Treatment-Related Adverse Events by Severity
Safety Set

Study	KLH2302											
Group	KLH-2109 200 mg						Placebo					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
四肢痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
骨痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
筋緊張	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
関節周囲炎	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
骨減少症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
変形性関節症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
弾発指	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
側腹部痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
関節腫脹	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
腎および尿路障害	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
頻尿	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
夜間頻尿	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
排尿困難	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
腎臓痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
生殖系および乳房障害	25	52.1	0	0.0	0	0.0	14	34.1	1	2.4	0	0.0
月経中間期出血	20	41.7	0	0.0	0	0.0	12	29.3	1	2.4	0	0.0
重度月経出血	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
閉経期症状	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
外陰腟乾燥	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
異常子宮出血	4	8.3	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
腟出血	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
子宮出血	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
無月経	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
骨盤痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

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Table 8.3.5-2
Occurrence of Treatment-Related Adverse Events by Severity
Safety Set

Study	KLH2302											
Group	KLH-2109 200 mg						Placebo					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
腟分泌物	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
不規則月経	0	0.0	0	0.0	0	0.0	2	4.9	0	0.0	0	0.0
乳房不快感	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
性器出血	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
外陰腟灼熱感	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
月経障害	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
月経困難症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
子宮内膜増殖症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
乳汁漏出症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
月経遅延	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
外陰腟不快感	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
卵巣嚢胞	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
外陰腟そう痒症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
乳房圧痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
乳房痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
希発月経	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
月経前症候群	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
萎縮性外陰腟炎	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
乳房うっ滞	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
一般・全身障害および投与部位の状態	2	4.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
倦怠感	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
疲労	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
浮腫	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
異常感	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

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Safety Set

Study	KLH2302											
Group	KLH-2109 200 mg						Placebo					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
無力症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
末梢性浮腫	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
疼痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
熱感	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
末梢腫脹	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
悪寒	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
口渇	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
注射部位硬結	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
投与部位硬結	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胸部不快感	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
冷感	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
注射部位内出血	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
注射部位反応	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
投与部位疼痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
穿刺部位疼痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
顔面浮腫	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
空腹	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
発熱	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
臨床検査	3	6.3	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
アラニンアミノトランスフェラーゼ増加	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
アスパラギン酸アミノトランスフェラーゼ増加	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
γ－グルタミルトランスフェラーゼ増加	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血中コレステロール増加	2	4.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
骨密度減少	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

A subject was counted only once based on the most severe event if a subject had multiple events of the same MedDRA term.
For KLH-2109 ALL group, the severity of "Headache" and "Pain in extremity" with Subject [redacted] in the 15-OBE2109-001 study was unknown.

Table 8.3.5-2
Occurrence of Treatment-Related Adverse Events by Severity
Safety Set

Study	KLH2302											
Group	KLH-2109 200 mg						Placebo					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
低比重リポ蛋白増加	2	4.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
グアナーゼ増加	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
生化学的骨代謝マーカー上昇	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血中トリグリセリド増加	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
酒石酸抵抗性酸ホスファターゼ増加	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
活性化部分トロンボプラスチン時間延長	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
体重増加	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血中クレアチンホスホキナーゼ増加	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血中アルカリホスファターゼ増加	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血圧上昇	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
高比重リポ蛋白増加	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血中ビリルビン増加	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
肝機能検査値上昇	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
肝酵素上昇	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
体重減少	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
遊離脂肪酸増加	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
心電図ＱＴ延長	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
プロトロンビン時間短縮	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Ｎ－テロペプチド	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血中乳酸脱水素酵素増加	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血小板数減少	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
尿中ブドウ糖陽性	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
トランスアミナーゼ上昇	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血中クレアチニン増加	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

A subject was counted only once based on the most severe event if a subject had multiple events of the same MedDRA term.
For KLH-2109 ALL group, the severity of "Headache" and "Pain in extremity" with Subject [redacted] in the 15-OBE2109-001 study was unknown.

Table 8.3.5-2
Occurrence of Treatment-Related Adverse Events by Severity
Safety Set

Study	KLH2302											
Group	KLH-2109 200 mg						Placebo					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
血中尿素減少	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
体温低下	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
脂質増加	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
総蛋白増加	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
白血球数減少	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血小板数増加	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
尿中蛋白陽性	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
便潜血陽性	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
プロトロンビン時間延長	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
尿中ケトン体陽性	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

A subject was counted only once based on the most severe event if a subject had multiple events of the same MedDRA term.
For KLH-2109 ALL group, the severity of "Headache" and "Pain in extremity" with Subject [redacted] in the 15-OBE2109-001 study was unknown.

Table 8.3.5-2
Occurrence of Treatment-Related Adverse Events by Severity
Safety Set

Study	Overall Population											
Group	KLH-2109 200 mg						KLH-2109 ALL					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
N	498	---	---	---	---	---	1452	---	---	---	---	---
Any Treatment-Related AEs	253	50.8	47	9.4	15	3.0	583	40.2	114	7.9	31	2.1
感染症および寄生虫症	2	0.4	1	0.2	0	0.0	6	0.4	2	0.1	0	0.0
尿路感染	1	0.2	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
腟感染	1	0.2	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
外陰腟真菌感染	1	0.2	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
カンジダ感染	0	0.0	1	0.2	0	0.0	0	0.0	1	0.1	0	0.0
膿疱性ざ瘡	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
結膜炎	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
胃腸炎	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
外陰部腟カンジダ症	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
癜風	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
膀胱炎	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
細菌性外陰腟炎	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
毛包炎	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
血管腫	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
血液およびリンパ系障害	0	0.0	0	0.0	0	0.0	4	0.3	1	0.1	0	0.0
貧血	0	0.0	0	0.0	0	0.0	3	0.2	0	0.0	0	0.0
好中球減少症	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
血小板減少症	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
代謝および栄養障害	8	1.6	0	0.0	0	0.0	16	1.1	0	0.0	1	0.1
脂質異常症	5	1.0	0	0.0	0	0.0	10	0.7	0	0.0	0	0.0

A subject was counted only once based on the most severe event if a subject had multiple events of the same MedDRA term.
For KLH-2109 ALL group, the severity of "Headache" and "Pain in extremity" with Subject [redacted] in the 15-OBE2109-001 study was unknown.

Table 8.3.5-2
Occurrence of Treatment-Related Adverse Events by Severity
Safety Set

Study	Overall Population											
Group	KLH-2109 200 mg						KLH-2109 ALL					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
食欲減退	3	0.6	0	0.0	0	0.0	5	0.3	0	0.0	0	0.0
過食	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
食欲亢進	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1
２型糖尿病	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
高コレステロール血症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
高トリグリセリド血症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
精神障害	26	5.2	6	1.2	2	0.4	47	3.2	11	0.8	3	0.2
気分動揺	4	0.8	1	0.2	0	0.0	13	0.9	2	0.1	1	0.1
リビドー減退	5	1.0	2	0.4	0	0.0	8	0.6	2	0.1	0	0.0
不眠症	4	0.8	2	0.4	0	0.0	5	0.3	2	0.1	0	0.0
感情不安定	2	0.4	0	0.0	0	0.0	5	0.3	2	0.1	0	0.0
不安	3	0.6	0	0.0	2	0.4	3	0.2	1	0.1	2	0.1
易刺激性	1	0.2	1	0.2	0	0.0	4	0.3	1	0.1	0	0.0
うつ病	1	0.2	0	0.0	1	0.2	1	0.1	1	0.1	1	0.1
中期不眠症	2	0.4	0	0.0	0	0.0	2	0.1	0	0.0	0	0.0
睡眠障害	1	0.2	0	0.0	0	0.0	2	0.1	0	0.0	0	0.0
気分変化	0	0.0	0	0.0	0	0.0	2	0.1	0	0.0	0	0.0
睡眠の質低下	1	0.2	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
錯乱状態	1	0.2	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
神経過敏	1	0.2	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
抑うつ気分	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
リビドー消失	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
注意欠如・多動性障害	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
抑うつ症状	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

A subject was counted only once based on the most severe event if a subject had multiple events of the same MedDRA term.
For KLH-2109 ALL group, the severity of "Headache" and "Pain in extremity" with Subject [redacted] in the 15-OBE2109-001 study was unknown.

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Table 8.3.5-2
Occurrence of Treatment-Related Adverse Events by Severity
Safety Set

Study	Overall Population											
Group	KLH-2109 200 mg						KLH-2109 ALL					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
気分の落ち込み	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
神経系障害	45	9.0	15	3.0	4	0.8	99	6.8	42	2.9	10	0.7
頭痛	26	5.2	11	2.2	3	0.6	65	4.5	32	2.2	6	0.4
浮動性めまい	14	2.8	0	0.0	0	0.0	26	1.8	4	0.3	1	0.1
傾眠	7	1.4	0	0.0	0	0.0	12	0.8	1	0.1	0	0.0
片頭痛	0	0.0	3	0.6	0	0.0	2	0.1	5	0.3	1	0.1
体位性めまい	0	0.0	0	0.0	0	0.0	3	0.2	0	0.0	0	0.0
くも膜下出血	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	2	0.1
認知障害	1	0.2	0	0.0	0	0.0	2	0.1	0	0.0	0	0.0
嗜眠	0	0.0	1	0.2	0	0.0	0	0.0	1	0.1	0	0.0
記憶障害	1	0.2	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
鎮静	0	0.0	1	0.2	0	0.0	0	0.0	1	0.1	0	0.0
振戦	0	0.0	1	0.2	0	0.0	0	0.0	1	0.1	0	0.0
感覚鈍麻	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
味覚不全	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
眼振	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
緊張性頭痛	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
手根管症候群	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
頚腕症候群	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
神経痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
起立不耐性	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
眼障害	2	0.4	0	0.0	0	0.0	2	0.1	0	0.0	0	0.0
眼部腫脹	1	0.2	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
霧視	1	0.2	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0

A subject was counted only once based on the most severe event if a subject had multiple events of the same MedDRA term.
For KLH-2109 ALL group, the severity of "Headache" and "Pain in extremity" with Subject [redacted] in the 15-OBE2109-001 study was unknown.

Table 8.3.5-2
Occurrence of Treatment-Related Adverse Events by Severity
Safety Set

Study Group	Overall Population											
	KLH-2109 200 mg						KLH-2109 ALL					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
緑内障	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
耳および迷路障害	2	0.4	0	0.0	0	0.0	5	0.3	1	0.1	0	0.0
回転性めまい	1	0.2	0	0.0	0	0.0	4	0.3	1	0.1	0	0.0
耳不快感	1	0.2	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
耳鳴	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
頭位性回転性めまい	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
心臓障害	8	1.6	0	0.0	0	0.0	13	0.9	3	0.2	0	0.0
動悸	7	1.4	0	0.0	0	0.0	9	0.6	1	0.1	0	0.0
頻脈	1	0.2	0	0.0	0	0.0	1	0.1	1	0.1	0	0.0
狭心症	0	0.0	0	0.0	0	0.0	1	0.1	1	0.1	0	0.0
上室性期外収縮	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
心室性期外収縮	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
洞性徐脈	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血管障害	174	34.9	30	6.0	11	2.2	292	20.1	52	3.6	15	1.0
ほてり	173	34.7	30	6.0	11	2.2	290	20.0	51	3.5	15	1.0
高血圧	1	0.2	0	0.0	0	0.0	2	0.1	1	0.1	0	0.0
潮紅	1	0.2	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
呼吸器、胸郭および縦隔障害	4	0.8	0	0.0	0	0.0	5	0.3	1	0.1	0	0.0
咽喉絞扼感	2	0.4	0	0.0	0	0.0	3	0.2	0	0.0	0	0.0
呼吸困難	1	0.2	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
アレルギー性咳嗽	1	0.2	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
喘息	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
胃腸障害	27	5.4	8	1.6	1	0.2	62	4.3	27	1.9	3	0.2

A subject was counted only once based on the most severe event if a subject had multiple events of the same MedDRA term.
For KLH-2109 ALL group, the severity of "Headache" and "Pain in extremity" with Subject [redacted] in the 15-OBE2109-001 study was unknown.

Table 8.3.5-2
Occurrence of Treatment-Related Adverse Events by Severity
Safety Set

Study Group	Overall Population											
	KLH-2109 200 mg						KLH-2109 ALL					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
悪心	16	3.2	3	0.6	1	0.2	29	2.0	10	0.7	1	0.1
上腹部痛	1	0.2	2	0.4	0	0.0	6	0.4	5	0.3	0	0.0
便秘	4	0.8	1	0.2	0	0.0	8	0.6	2	0.1	0	0.0
下痢	2	0.4	1	0.2	0	0.0	6	0.4	3	0.2	0	0.0
腹部不快感	2	0.4	0	0.0	0	0.0	7	0.5	0	0.0	0	0.0
腹痛	2	0.4	0	0.0	0	0.0	3	0.2	3	0.2	1	0.1
嘔吐	1	0.2	1	0.2	0	0.0	2	0.1	3	0.2	1	0.1
腹部膨満	1	0.2	0	0.0	0	0.0	3	0.2	2	0.1	0	0.0
鼓腸	0	0.0	0	0.0	0	0.0	1	0.1	1	0.1	0	0.0
消化不良	0	0.0	1	0.2	0	0.0	0	0.0	1	0.1	0	0.0
胃炎	1	0.2	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
下腹部痛	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
胃食道逆流性疾患	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
胃酸過多	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
肛門周囲痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
肝胆道系障害	6	1.2	0	0.0	0	0.0	7	0.5	0	0.0	0	0.0
肝機能異常	5	1.0	0	0.0	0	0.0	5	0.3	0	0.0	0	0.0
脂肪肝	1	0.2	0	0.0	0	0.0	2	0.1	0	0.0	0	0.0
高トランスアミナーゼ血症	1	0.2	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
皮膚および皮下組織障害	45	9.0	3	0.6	1	0.2	79	5.4	7	0.5	1	0.1
多汗症	35	7.0	1	0.2	0	0.0	47	3.2	1	0.1	0	0.0
脱毛症	5	1.0	1	0.2	0	0.0	10	0.7	2	0.1	0	0.0
ざ瘡	2	0.4	0	0.0	0	0.0	10	0.7	1	0.1	0	0.0
寝汗	2	0.4	1	0.2	1	0.2	6	0.4	1	0.1	1	0.1

A subject was counted only once based on the most severe event if a subject had multiple events of the same MedDRA term.
For KLH-2109 ALL group, the severity of "Headache" and "Pain in extremity" with Subject [redacted] in the 15-OBE2109-001 study was unknown.

Table 8.3.5-2
Occurrence of Treatment-Related Adverse Events by Severity
Safety Set

Study	Overall Population											
Group	KLH-2109 200 mg						KLH-2109 ALL					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
蕁麻疹	1	0.2	0	0.0	0	0.0	2	0.1	2	0.1	0	0.0
アレルギー性皮膚炎	0	0.0	1	0.2	0	0.0	1	0.1	1	0.1	0	0.0
発疹	0	0.0	0	0.0	0	0.0	2	0.1	0	0.0	0	0.0
冷汗	1	0.2	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
湿疹	1	0.2	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
そう痒症	1	0.2	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
皮膚炎	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
円形脱毛症	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
男性型多毛症	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
ばら色粃糠疹	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
脂漏性皮膚炎	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
乾皮症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
紅斑	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
丘疹性皮疹	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
皮膚局面	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
筋骨格系および結合組織障害	30	6.0	3	0.6	0	0.0	47	3.2	6	0.4	0	0.0
関節痛	16	3.2	3	0.6	0	0.0	23	1.6	4	0.3	0	0.0
筋骨格硬直	11	2.2	0	0.0	0	0.0	18	1.2	0	0.0	0	0.0
背部痛	2	0.4	0	0.0	0	0.0	3	0.2	0	0.0	0	0.0
骨吸収亢進	2	0.4	0	0.0	0	0.0	2	0.1	0	0.0	0	0.0
腱鞘炎	2	0.4	0	0.0	0	0.0	2	0.1	0	0.0	0	0.0
骨喪失	1	0.2	0	0.0	0	0.0	2	0.1	0	0.0	0	0.0
筋肉痛	0	0.0	0	0.0	0	0.0	0	0.0	2	0.1	0	0.0
筋痙縮	1	0.2	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0

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Table 8.3.5-2
Occurrence of Treatment-Related Adverse Events by Severity
Safety Set

Study	Overall Population											
Group	KLH-2109 200 mg						KLH-2109 ALL					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
四肢痛	1	0.2	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
骨痛	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
筋緊張	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
関節周囲炎	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
骨減少症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
変形性関節症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
弾発指	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
側腹部痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
関節腫脹	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
腎および尿路障害	3	0.6	0	0.0	0	0.0	5	0.3	0	0.0	1	0.1
頻尿	2	0.4	0	0.0	0	0.0	4	0.3	0	0.0	0	0.0
夜間頻尿	1	0.2	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
排尿困難	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1
腎臓痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
生殖系および乳房障害	134	26.9	5	1.0	2	0.4	317	21.8	13	0.9	6	0.4
月経中間期出血	95	19.1	0	0.0	0	0.0	237	16.3	1	0.1	2	0.1
重度月経出血	11	2.2	0	0.0	1	0.2	53	3.7	3	0.2	2	0.1
閉経期症状	8	1.6	0	0.0	0	0.0	12	0.8	0	0.0	0	0.0
外陰腟乾燥	4	0.8	1	0.2	1	0.2	8	0.6	2	0.1	1	0.1
異常子宮出血	10	2.0	0	0.0	0	0.0	10	0.7	0	0.0	0	0.0
腟出血	3	0.6	2	0.4	0	0.0	3	0.2	5	0.3	0	0.0
子宮出血	6	1.2	0	0.0	0	0.0	6	0.4	1	0.1	0	0.0
無月経	1	0.2	0	0.0	0	0.0	7	0.5	0	0.0	0	0.0
骨盤痛	2	0.4	1	0.2	0	0.0	4	0.3	2	0.1	0	0.0

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For KLH-2109 ALL group, the severity of "Headache" and "Pain in extremity" with Subject [redacted] in the 15-OBE2109-001 study was unknown.

Table 8.3.5-2
Occurrence of Treatment-Related Adverse Events by Severity
Safety Set

Study	Overall Population											
Group	KLH-2109 200 mg						KLH-2109 ALL					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
腟分泌物	2	0.4	0	0.0	0	0.0	4	0.3	0	0.0	1	0.1
不規則月経	3	0.6	0	0.0	0	0.0	3	0.2	0	0.0	0	0.0
乳房不快感	2	0.4	0	0.0	0	0.0	3	0.2	0	0.0	0	0.0
性器出血	2	0.4	0	0.0	0	0.0	2	0.1	0	0.0	0	0.0
外陰腟灼熱感	1	0.2	0	0.0	0	0.0	2	0.1	0	0.0	0	0.0
月経障害	0	0.0	0	0.0	0	0.0	0	0.0	2	0.1	0	0.0
月経困難症	0	0.0	1	0.2	0	0.0	0	0.0	1	0.1	0	0.0
子宮内膜増殖症	0	0.0	1	0.2	0	0.0	0	0.0	1	0.1	0	0.0
乳汁漏出症	1	0.2	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
月経遅延	1	0.2	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
外陰腟不快感	1	0.2	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
卵巣嚢胞	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
外陰腟そう痒症	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
乳房圧痛	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
乳房痛	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
希発月経	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
月経前症候群	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
萎縮性外陰腟炎	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
乳房うっ滞	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
一般・全身障害および投与部位の状態	23	4.6	2	0.4	0	0.0	48	3.3	4	0.3	0	0.0
倦怠感	12	2.4	0	0.0	0	0.0	19	1.3	0	0.0	0	0.0
疲労	5	1.0	0	0.0	0	0.0	8	0.6	0	0.0	0	0.0
浮腫	4	0.8	0	0.0	0	0.0	7	0.5	0	0.0	0	0.0
異常感	1	0.2	0	0.0	0	0.0	5	0.3	0	0.0	0	0.0

A subject was counted only once based on the most severe event if a subject had multiple events of the same MedDRA term.
For KLH-2109 ALL group, the severity of "Headache" and "Pain in extremity" with Subject [redacted] in the 15-OBE2109-001 study was unknown.

Table 8.3.5-2
Occurrence of Treatment-Related Adverse Events by Severity
Safety Set

Study Group	Overall Population											
	KLH-2109 200 mg						KLH-2109 ALL					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
無力症	0	0.0	1	0.2	0	0.0	2	0.1	2	0.1	0	0.0
末梢性浮腫	0	0.0	0	0.0	0	0.0	3	0.2	0	0.0	0	0.0
疼痛	1	0.2	1	0.2	0	0.0	1	0.1	1	0.1	0	0.0
熱感	1	0.2	0	0.0	0	0.0	2	0.1	0	0.0	0	0.0
末梢腫脹	1	0.2	0	0.0	0	0.0	2	0.1	0	0.0	0	0.0
悪寒	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
口渇	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
注射部位硬結	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
投与部位硬結	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胸部不快感	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
冷感	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
注射部位内出血	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
注射部位反応	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
投与部位疼痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
穿刺部位疼痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
顔面浮腫	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
空腹	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
発熱	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
臨床検査	64	12.9	5	1.0	0	0.0	129	8.9	16	1.1	0	0.0
アラニンアミノトランスフェラーゼ増加	17	3.4	1	0.2	0	0.0	43	3.0	3	0.2	0	0.0
アスパラギン酸アミノトランスフェラーゼ増加	10	2.0	1	0.2	0	0.0	32	2.2	3	0.2	0	0.0
γ－グルタミルトランスフェラーゼ増加	10	2.0	2	0.4	0	0.0	19	1.3	3	0.2	0	0.0
血中コレステロール増加	11	2.2	0	0.0	0	0.0	18	1.2	3	0.2	0	0.0
骨密度減少	10	2.0	2	0.4	0	0.0	16	1.1	3	0.2	0	0.0

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Occurrence of Treatment-Related Adverse Events by Severity
Safety Set

Study	Overall Population											
Group	KLH-2109 200 mg						KLH-2109 ALL					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
低比重リポ蛋白増加	9	1.8	0	0.0	0	0.0	13	0.9	1	0.1	0	0.0
グアナーゼ増加	6	1.2	0	0.0	0	0.0	14	1.0	0	0.0	0	0.0
生化学的骨代謝マーカー上昇	10	2.0	0	0.0	0	0.0	10	0.7	0	0.0	0	0.0
血中トリグリセリド増加	4	0.8	0	0.0	0	0.0	7	0.5	1	0.1	0	0.0
酒石酸抵抗性酸ホスファターゼ増加	7	1.4	0	0.0	0	0.0	7	0.5	0	0.0	0	0.0
活性化部分トロンボプラスチン時間延長	3	0.6	0	0.0	0	0.0	7	0.5	0	0.0	0	0.0
体重増加	1	0.2	0	0.0	0	0.0	6	0.4	0	0.0	0	0.0
血中クレアチンホスホキナーゼ増加	0	0.0	0	0.0	0	0.0	3	0.2	2	0.1	0	0.0
血中アルカリホスファターゼ増加	2	0.4	0	0.0	0	0.0	4	0.3	0	0.0	0	0.0
血圧上昇	1	0.2	0	0.0	0	0.0	2	0.1	2	0.1	0	0.0
高比重リポ蛋白増加	1	0.2	0	0.0	0	0.0	4	0.3	0	0.0	0	0.0
血中ビリルビン増加	0	0.0	0	0.0	0	0.0	2	0.1	2	0.1	0	0.0
肝機能検査値上昇	3	0.6	0	0.0	0	0.0	3	0.2	0	0.0	0	0.0
肝酵素上昇	2	0.4	0	0.0	0	0.0	3	0.2	0	0.0	0	0.0
体重減少	1	0.2	0	0.0	0	0.0	3	0.2	0	0.0	0	0.0
遊離脂肪酸増加	2	0.4	0	0.0	0	0.0	2	0.1	0	0.0	0	0.0
心電図ＱＴ延長	1	0.2	0	0.0	0	0.0	2	0.1	0	0.0	0	0.0
プロトロンビン時間短縮	1	0.2	0	0.0	0	0.0	2	0.1	0	0.0	0	0.0
Ｎ－テロペプチド	0	0.0	0	0.0	0	0.0	2	0.1	0	0.0	0	0.0
血中乳酸脱水素酵素増加	0	0.0	0	0.0	0	0.0	2	0.1	0	0.0	0	0.0
血小板数減少	0	0.0	0	0.0	0	0.0	2	0.1	0	0.0	0	0.0
尿中ブドウ糖陽性	1	0.2	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
トランスアミナーゼ上昇	0	0.0	1	0.2	0	0.0	0	0.0	1	0.1	0	0.0
血中クレアチニン増加	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0

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Safety Set

Study	Overall Population											
Group	KLH-2109 200 mg						KLH-2109 ALL					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
血中尿素減少	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
体温低下	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
脂質増加	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
総蛋白増加	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
白血球数減少	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
血小板数増加	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
尿中蛋白陽性	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
便潜血陽性	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
プロトロンビン時間延長	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
尿中ケトン体陽性	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

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For KLH-2109 ALL group, the severity of "Headache" and "Pain in extremity" with Subject [redacted] in the 15-OBE2109-001 study was unknown.

Table 8.3.5-2
Occurrence of Treatment-Related Adverse Events by Severity
Safety Set

Study	Overall Population											
Group	Placebo						Leuprorelin					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
N	415	---	---	---	---	---	187	---	---	---	---	---
Any Treatment-Related AEs	64	15.4	19	4.6	7	1.7	155	82.9	17	9.1	0	0.0
感染症および寄生虫症	1	0.2	0	0.0	0	0.0	2	1.1	0	0.0	0	0.0
尿路感染	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
腟感染	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
外陰腟真菌感染	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
カンジダ感染	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
膿疱性ざ瘡	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
結膜炎	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胃腸炎	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
外陰部腟カンジダ症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
癜風	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
膀胱炎	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
細菌性外陰腟炎	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
毛包炎	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血管腫	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血液およびリンパ系障害	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
貧血	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
好中球減少症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血小板減少症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
代謝および栄養障害	1	0.2	1	0.2	0	0.0	4	2.1	0	0.0	0	0.0
脂質異常症	0	0.0	0	0.0	0	0.0	3	1.6	0	0.0	0	0.0

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Group	Placebo						Leuprorelin					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
食欲減退	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
過食	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
食欲亢進	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
２型糖尿病	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
高コレステロール血症	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
高トリグリセリド血症	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
精神障害	6	1.4	2	0.5	1	0.2	10	5.3	6	3.2	0	0.0
気分動揺	4	1.0	2	0.5	0	0.0	0	0.0	0	0.0	0	0.0
リビドー減退	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
不眠症	1	0.2	1	0.2	0	0.0	2	1.1	4	2.1	0	0.0
感情不安定	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
不安	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
易刺激性	2	0.5	0	0.0	0	0.0	2	1.1	0	0.0	0	0.0
うつ病	0	0.0	1	0.2	0	0.0	0	0.0	1	0.5	0	0.0
中期不眠症	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
睡眠障害	1	0.2	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
気分変化	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
睡眠の質低下	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
錯乱状態	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
神経過敏	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
抑うつ気分	0	0.0	0	0.0	0	0.0	1	0.5	1	0.5	0	0.0
リビドー消失	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
注意欠如・多動性障害	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
抑うつ症状	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0

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Group	Placebo						Leuprorelin					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
気分の落ち込み	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
神経系障害	11	2.7	7	1.7	2	0.5	18	9.6	7	3.7	0	0.0
頭痛	6	1.4	5	1.2	1	0.2	12	6.4	3	1.6	0	0.0
浮動性めまい	1	0.2	0	0.0	0	0.0	3	1.6	1	0.5	0	0.0
傾眠	3	0.7	0	0.0	0	0.0	3	1.6	0	0.0	0	0.0
片頭痛	0	0.0	2	0.5	1	0.2	0	0.0	1	0.5	0	0.0
体位性めまい	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
くも膜下出血	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
認知障害	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
嗜眠	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
記憶障害	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
鎮静	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
振戦	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
感覚鈍麻	0	0.0	0	0.0	0	0.0	2	1.1	0	0.0	0	0.0
味覚不全	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
眼振	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
緊張性頭痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
手根管症候群	0	0.0	0	0.0	0	0.0	0	0.0	2	1.1	0	0.0
頚腕症候群	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
神経痛	0	0.0	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0
起立不耐性	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
眼障害	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
眼部腫脹	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
霧視	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

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Safety Set

Study	Overall Population											
Group	Placebo						Leuprorelin					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
緑内障	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
耳および迷路障害	1	0.2	1	0.2	0	0.0	3	1.6	0	0.0	0	0.0
回転性めまい	1	0.2	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
耳不快感	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
耳鳴	0	0.0	0	0.0	0	0.0	2	1.1	0	0.0	0	0.0
頭位性回転性めまい	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
心臓障害	0	0.0	1	0.2	0	0.0	6	3.2	0	0.0	0	0.0
動悸	0	0.0	1	0.2	0	0.0	5	2.7	0	0.0	0	0.0
頻脈	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
狭心症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
上室性期外収縮	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
心室性期外収縮	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
洞性徐脈	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
血管障害	14	3.4	2	0.5	1	0.2	96	51.3	6	3.2	0	0.0
ほてり	14	3.4	2	0.5	1	0.2	96	51.3	6	3.2	0	0.0
高血圧	0	0.0	0	0.0	0	0.0	2	1.1	0	0.0	0	0.0
潮紅	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
呼吸器、胸郭および縦隔障害	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
咽喉絞扼感	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
呼吸困難	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
アレルギー性咳嗽	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
喘息	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胃腸障害	7	1.7	2	0.5	0	0.0	6	3.2	0	0.0	0	0.0

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Safety Set

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Group	Placebo						Leuprorelin					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
悪心	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
上腹部痛	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
便秘	0	0.0	0	0.0	0	0.0	4	2.1	0	0.0	0	0.0
下痢	2	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
腹部不快感	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
腹痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
嘔吐	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
腹部膨満	2	0.5	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
鼓腸	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
消化不良	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
胃炎	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
下腹部痛	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
胃食道逆流性疾患	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胃酸過多	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
肛門周囲痛	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
肝胆道系障害	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
肝機能異常	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
脂肪肝	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
高トランスアミナーゼ血症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
皮膚および皮下組織障害	6	1.4	1	0.2	0	0.0	30	16.0	1	0.5	0	0.0
多汗症	1	0.2	0	0.0	0	0.0	22	11.8	0	0.0	0	0.0
脱毛症	1	0.2	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
ざ瘡	2	0.5	0	0.0	0	0.0	4	2.1	0	0.0	0	0.0
寝汗	1	0.2	0	0.0	0	0.0	2	1.1	0	0.0	0	0.0

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Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
蕁麻疹	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
アレルギー性皮膚炎	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
発疹	0	0.0	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0
冷汗	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
湿疹	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
そう痒症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
皮膚炎	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
円形脱毛症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
男性型多毛症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
ばら色粃糠疹	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
脂漏性皮膚炎	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
乾皮症	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
紅斑	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
丘疹性皮疹	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
皮膚局面	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
筋骨格系および結合組織障害	3	0.7	1	0.2	0	0.0	26	13.9	4	2.1	0	0.0
関節痛	0	0.0	0	0.0	0	0.0	15	8.0	0	0.0	0	0.0
筋骨格硬直	0	0.0	0	0.0	0	0.0	3	1.6	3	1.6	0	0.0
背部痛	0	0.0	1	0.2	0	0.0	1	0.5	0	0.0	0	0.0
骨吸収亢進	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
腱鞘炎	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
骨喪失	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
筋肉痛	0	0.0	0	0.0	0	0.0	2	1.1	0	0.0	0	0.0
筋痙縮	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0

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Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
四肢痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
骨痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
筋緊張	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
関節周囲炎	0	0.0	0	0.0	0	0.0	1	0.5	1	0.5	0	0.0
骨減少症	1	0.2	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
変形性関節症	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
弾発指	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
側腹部痛	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
関節腫脹	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
腎および尿路障害	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
頻尿	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
夜間頻尿	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
排尿困難	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
腎臓痛	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
生殖系および乳房障害	34	8.2	2	0.5	1	0.2	135	72.2	1	0.5	0	0.0
月経中間期出血	24	5.8	1	0.2	0	0.0	103	55.1	0	0.0	0	0.0
重度月経出血	4	1.0	1	0.2	0	0.0	9	4.8	0	0.0	0	0.0
閉経期症状	0	0.0	0	0.0	0	0.0	5	2.7	0	0.0	0	0.0
外陰腟乾燥	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
異常子宮出血	0	0.0	0	0.0	0	0.0	11	5.9	1	0.5	0	0.0
腟出血	1	0.2	0	0.0	1	0.2	2	1.1	0	0.0	0	0.0
子宮出血	0	0.0	0	0.0	0	0.0	6	3.2	0	0.0	0	0.0
無月経	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
骨盤痛	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

A subject was counted only once based on the most severe event if a subject had multiple events of the same MedDRA term.
For KLH-2109 ALL group, the severity of "Headache" and "Pain in extremity" with Subject [redacted] in the 15-OBE2109-001 study was unknown.

Table 8.3.5-2
Occurrence of Treatment-Related Adverse Events by Severity
Safety Set

Study	Overall Population											
Group	Placebo						Leuprorelin					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
腟分泌物	0	0.0	0	0.0	0	0.0	2	1.1	0	0.0	0	0.0
不規則月経	2	0.5	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
乳房不快感	0	0.0	0	0.0	0	0.0	2	1.1	0	0.0	0	0.0
性器出血	0	0.0	0	0.0	0	0.0	2	1.1	0	0.0	0	0.0
外陰腟灼熱感	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
月経障害	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
月経困難症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
子宮内膜増殖症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
乳汁漏出症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
月経遅延	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
外陰腟不快感	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
卵巣嚢胞	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
外陰腟そう痒症	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
乳房圧痛	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
乳房痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
希発月経	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
月経前症候群	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
萎縮性外陰腟炎	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
乳房うっ滞	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
一般・全身障害および投与部位の状態	4	1.0	4	1.0	0	0.0	23	12.3	0	0.0	0	0.0
倦怠感	1	0.2	0	0.0	0	0.0	9	4.8	0	0.0	0	0.0
疲労	0	0.0	2	0.5	0	0.0	1	0.5	0	0.0	0	0.0
浮腫	0	0.0	0	0.0	0	0.0	4	2.1	0	0.0	0	0.0
異常感	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

A subject was counted only once based on the most severe event if a subject had multiple events of the same MedDRA term.
For KLH-2109 ALL group, the severity of "Headache" and "Pain in extremity" with Subject [redacted] in the 15-OBE2109-001 study was unknown.

Table 8.3.5-2
Occurrence of Treatment-Related Adverse Events by Severity
Safety Set

Study	Overall Population											
Group	Placebo						Leuprorelin					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
無力症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
末梢性浮腫	0	0.0	0	0.0	0	0.0	2	1.1	0	0.0	0	0.0
疼痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
熱感	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
末梢腫脹	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
悪寒	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
口渇	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
注射部位硬結	0	0.0	0	0.0	0	0.0	3	1.6	0	0.0	0	0.0
投与部位硬結	0	0.0	0	0.0	0	0.0	2	1.1	0	0.0	0	0.0
胸部不快感	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
冷感	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
注射部位内出血	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
注射部位反応	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
投与部位疼痛	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
穿刺部位疼痛	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
顔面浮腫	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
空腹	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
発熱	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
臨床検査	6	1.4	1	0.2	2	0.5	33	17.6	0	0.0	0	0.0
アラニンアミノトランスフェラーゼ増加	1	0.2	1	0.2	0	0.0	2	1.1	0	0.0	0	0.0
アスパラギン酸アミノトランスフェラーゼ増加	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
γ－グルタミルトランスフェラーゼ増加	0	0.0	1	0.2	0	0.0	5	2.7	0	0.0	0	0.0
血中コレステロール増加	1	0.2	0	0.0	0	0.0	4	2.1	0	0.0	0	0.0
骨密度減少	0	0.0	0	0.0	1	0.2	4	2.1	0	0.0	0	0.0

A subject was counted only once based on the most severe event if a subject had multiple events of the same MedDRA term.
For KLH-2109 ALL group, the severity of "Headache" and "Pain in extremity" with Subject [redacted] in the 15-OBE2109-001 study was unknown.

Table 8.3.5-2
Occurrence of Treatment-Related Adverse Events by Severity
Safety Set

Study	Overall Population											
Group	Placebo						Leuprorelin					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
低比重リポ蛋白増加	1	0.2	0	0.0	0	0.0	4	2.1	0	0.0	0	0.0
グアナーゼ増加	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
生化学的骨代謝マーカー上昇	0	0.0	0	0.0	0	0.0	6	3.2	0	0.0	0	0.0
血中トリグリセリド増加	0	0.0	0	0.0	0	0.0	5	2.7	0	0.0	0	0.0
酒石酸抵抗性酸ホスファターゼ増加	0	0.0	0	0.0	0	0.0	9	4.8	0	0.0	0	0.0
活性化部分トロンボプラスチン時間延長	1	0.2	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
体重増加	1	0.2	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
血中クレアチンホスホキナーゼ増加	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血中アルカリホスファターゼ増加	0	0.0	0	0.0	0	0.0	3	1.6	0	0.0	0	0.0
血圧上昇	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
高比重リポ蛋白増加	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血中ビリルビン増加	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
肝機能検査値上昇	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
肝酵素上昇	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
体重減少	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
遊離脂肪酸増加	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
心電図ＱＴ延長	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
プロトロンビン時間短縮	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Ｎ－テロペプチド	0	0.0	0	0.0	0	0.0	3	1.6	0	0.0	0	0.0
血中乳酸脱水素酵素増加	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血小板数減少	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
尿中ブドウ糖陽性	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
トランスアミナーゼ上昇	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血中クレアチニン増加	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

A subject was counted only once based on the most severe event if a subject had multiple events of the same MedDRA term.
For KLH-2109 ALL group, the severity of "Headache" and "Pain in extremity" with Subject [redacted] in the 15-OBE2109-001 study was unknown.

Table 8.3.5-2
Occurrence of Treatment-Related Adverse Events by Severity
Safety Set

Study	Overall Population											
Group	Placebo						Leuprorelin					
Severity	Mild		Moderate		Severe		Mild		Moderate		Severe	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%
血中尿素減少	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
体温低下	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
脂質増加	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
総蛋白増加	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
白血球数減少	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血小板数増加	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
尿中蛋白陽性	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
便潜血陽性	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
プロトロンビン時間延長	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
尿中ケトン体陽性	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

A subject was counted only once based on the most severe event if a subject had multiple events of the same MedDRA term.
For KLH-2109 ALL group, the severity of "Headache" and "Pain in extremity" with Subject [redacted] in the 15-OBE2109-001 study was unknown.

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: KLH2301
Group: KLH-2109 200 mg

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
N	143	---	143	---	143	---	139	---	139	---	136	---	136	---	132	---
Any AEs	139	97.2	101	70.6	70	49.0	61	43.9	47	33.8	45	33.1	37	27.2	32	24.2
Leading to Death	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Other Serious Events	2	1.4	0	0.0	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
Leading to Discontinuation	8	5.6	4	2.8	3	2.1	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
Leading to Interruption	3	2.1	2	1.4	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
感染症および寄生虫症	63	44.1	16	11.2	10	7.0	9	6.5	13	9.4	14	10.3	12	8.8	12	9.1
上咽頭炎	33	23.1	8	5.6	6	4.2	6	4.3	6	4.3	7	5.1	4	2.9	5	3.8
インフルエンザ	7	4.9	0	0.0	0	0.0	0	0.0	1	0.7	1	0.7	3	2.2	3	2.3
ＣＯＶＩＤ－１９	7	4.9	1	0.7	0	0.0	1	0.7	1	0.7	2	1.5	2	1.5	0	0.0
膀胱炎	5	3.5	1	0.7	0	0.0	1	0.7	2	1.4	1	0.7	1	0.7	0	0.0
外陰部腟カンジダ症	4	2.8	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	1	0.7	1	0.8
気管支炎	2	1.4	0	0.0	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
胃腸炎	2	1.4	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	1	0.8
歯周炎	2	1.4	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
コロナウイルス感染	2	1.4	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	1	0.8
急性副鼻腔炎	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
爪の皮膚糸状菌症	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
帯状疱疹	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
麦粒腫	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
中耳炎	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
爪囲炎	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
咽頭炎	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
鼻炎	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
皮膚感染	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.8
扁桃炎	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0
腟感染	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: KLH2301
Group: KLH-2109 200 mg

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
細菌性膀胱炎	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
細菌性外陰膣炎	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
免疫系障害	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
季節性アレルギー	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
代謝および栄養障害	6	4.2	0	0.0	4	2.8	2	1.4	0	0.0	0	0.0	0	0.0	0	0.0
脂質異常症	5	3.5	0	0.0	3	2.1	2	1.4	0	0.0	0	0.0	0	0.0	0	0.0
食欲減退	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
精神障害	10	7.0	2	1.4	3	2.1	2	1.4	2	1.4	1	0.7	0	0.0	0	0.0
不眠症	5	3.5	0	0.0	2	1.4	1	0.7	1	0.7	1	0.7	0	0.0	0	0.0
睡眠障害	2	1.4	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
うつ病	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
易刺激性	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
中期不眠症	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
神経系障害	23	16.1	9	6.3	10	7.0	1	0.7	2	1.4	3	2.2	3	2.2	1	0.8
頭痛	15	10.5	6	4.2	5	3.5	1	0.7	0	0.0	3	2.2	2	1.5	1	0.8
浮動性めまい	4	2.8	2	1.4	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0
傾眠	3	2.1	1	0.7	2	1.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
記憶障害	2	1.4	0	0.0	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
くも膜下出血	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
緊張性頭痛	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
眼障害	5	3.5	0	0.0	3	2.1	0	0.0	1	0.7	0	0.0	0	0.0	1	0.8
ドライアイ	2	1.4	0	0.0	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
眼瞼炎	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.8
眼そう痒症	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
マイボーム腺機能不全	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
耳および迷路障害	5	3.5	2	1.4	1	0.7	0	0.0	2	1.4	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: KLH2301
Group: KLH-2109 200 mg

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
耳痛	2	1.4	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
回転性めまい	2	1.4	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
耳不快感	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
心臓障害	8	5.6	4	2.8	2	1.4	1	0.7	1	0.7	0	0.0	0	0.0	1	0.8
動悸	7	4.9	4	2.8	2	1.4	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0
洞性不整脈	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.8
血管障害	78	54.5	31	21.7	26	18.2	14	10.1	5	3.6	4	2.9	0	0.0	0	0.0
ほてり	77	53.8	31	21.7	26	18.2	14	10.1	4	2.9	3	2.2	0	0.0	0	0.0
高血圧	3	2.1	0	0.0	1	0.7	0	0.0	1	0.7	1	0.7	0	0.0	0	0.0
呼吸器、胸郭および縦隔障害	15	10.5	2	1.4	4	2.8	2	1.4	1	0.7	4	2.9	2	1.5	2	1.5
咳嗽	5	3.5	1	0.7	1	0.7	1	0.7	1	0.7	1	0.7	1	0.7	0	0.0
口腔咽頭痛	4	2.8	0	0.0	0	0.0	0	0.0	0	0.0	2	1.5	1	0.7	2	1.5
咽喉絞扼感	2	1.4	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
喘息	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
呼吸困難	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
鼻閉	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
アレルギー性鼻炎	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胃腸障害	23	16.1	6	4.2	4	2.8	3	2.2	2	1.4	5	3.7	2	1.5	4	3.0
上腹部痛	4	2.8	0	0.0	0	0.0	0	0.0	1	0.7	1	0.7	1	0.7	1	0.8
下痢	4	2.8	1	0.7	1	0.7	1	0.7	0	0.0	1	0.7	0	0.0	1	0.8
悪心	4	2.8	3	2.1	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
歯痛	3	2.1	1	0.7	0	0.0	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0
腹痛	2	1.4	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	1	0.8
便秘	2	1.4	0	0.0	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
齲歯	2	1.4	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0
腹部不快感	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: KLH2301
Group: KLH-2109 200 mg

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
腹部膨満	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.8
胃炎	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
痔核	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
肝胆道系障害	5	3.5	0	0.0	0	0.0	1	0.7	2	1.4	1	0.7	0	0.0	1	0.8
肝機能異常	5	3.5	0	0.0	0	0.0	1	0.7	2	1.4	1	0.7	0	0.0	1	0.8
脂肪肝	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
皮膚および皮下組織障害	39	27.3	15	10.5	10	7.0	5	3.6	5	3.6	3	2.2	2	1.5	2	1.5
多汗症	19	13.3	8	5.6	7	4.9	2	1.4	1	0.7	1	0.7	0	0.0	0	0.0
湿疹	5	3.5	1	0.7	1	0.7	3	2.2	0	0.0	0	0.0	0	0.0	0	0.0
脱毛症	4	2.8	2	1.4	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
接触皮膚炎	3	2.1	2	1.4	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0
発疹	3	2.1	2	1.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.8
皮膚嚢腫	2	1.4	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	1	0.8
そう痒症	2	1.4	2	1.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
蕁麻疹	2	1.4	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
円形脱毛症	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
冷汗	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
皮膚炎	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0
貨幣状湿疹	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
汗疹	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
皮膚硬結	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
手皮膚炎	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
筋骨格系および結合組織障害	43	30.1	9	6.3	8	5.6	10	7.2	9	6.5	4	2.9	8	5.9	2	1.5
関節痛	18	12.6	4	2.8	2	1.4	4	2.9	3	2.2	3	2.2	1	0.7	1	0.8
背部痛	13	9.1	3	2.1	2	1.4	3	2.2	2	1.4	0	0.0	4	2.9	0	0.0
筋骨格硬直	11	7.7	3	2.1	2	1.4	1	0.7	3	2.2	1	0.7	1	0.7	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: KLH2301
Group: KLH-2109 200 mg

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
四肢痛	3	2.1	1	0.7	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
骨吸収亢進	2	1.4	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	1	0.8
腱鞘炎	2	1.4	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0
筋痙縮	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
変形性脊椎症	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
椎間板突出	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0
腎および尿路障害	4	2.8	0	0.0	0	0.0	2	1.4	2	1.4	0	0.0	0	0.0	0	0.0
頻尿	2	1.4	0	0.0	0	0.0	2	1.4	0	0.0	0	0.0	0	0.0	0	0.0
緊張性膀胱	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
夜間頻尿	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
生殖系および乳房障害	78	54.5	68	47.6	15	10.5	9	6.5	5	3.6	8	5.9	7	5.1	5	3.8
月経中間期出血	57	39.9	47	32.9	11	7.7	5	3.6	3	2.2	6	4.4	4	2.9	4	3.0
閉経期症状	8	5.6	4	2.8	2	1.4	2	1.4	0	0.0	0	0.0	0	0.0	0	0.0
重度月経出血	7	4.9	7	4.9	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
子宮出血	6	4.2	6	4.2	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
異常子宮出血	6	4.2	4	2.8	3	2.1	1	0.7	1	0.7	1	0.7	2	1.5	1	0.8
不規則月経	3	2.1	2	1.4	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
腟分泌物	2	1.4	2	1.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
腟出血	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	1	0.7	0	0.0
乳房不快感	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
性器出血	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
一般・全身障害および投与部位の状態	19	13.3	7	4.9	6	4.2	3	2.2	4	2.9	1	0.7	1	0.7	0	0.0
倦怠感	11	7.7	4	2.8	4	2.8	2	1.4	2	1.4	1	0.7	0	0.0	0	0.0
浮腫	3	2.1	0	0.0	1	0.7	0	0.0	2	1.4	0	0.0	1	0.7	0	0.0
発熱	2	1.4	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
胸痛	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: KLH2301
Group: KLH-2109 200 mg

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
疲労	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
異常感	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
注射部位疼痛	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
臨床検査	40	28.0	4	2.8	9	6.3	14	10.1	9	6.5	3	2.2	5	3.7	5	3.8
生化学的骨代謝マーカー上昇	10	7.0	0	0.0	0	0.0	8	5.8	1	0.7	1	0.7	0	0.0	0	0.0
アラニンアミノトランスフェラーゼ増加	9	6.3	1	0.7	3	2.1	1	0.7	2	1.4	1	0.7	1	0.7	0	0.0
骨密度減少	9	6.3	0	0.0	0	0.0	0	0.0	3	2.2	0	0.0	3	2.2	3	2.3
酒石酸抵抗性酸ホスファターゼ増加	7	4.9	0	0.0	0	0.0	2	1.4	2	1.4	0	0.0	2	1.5	1	0.8
アスパラギン酸アミノトランスフェラーゼ増加	6	4.2	1	0.7	2	1.4	1	0.7	1	0.7	1	0.7	0	0.0	0	0.0
γ－グルタミルトランスフェラーゼ増加	6	4.2	1	0.7	1	0.7	2	1.4	1	0.7	0	0.0	0	0.0	1	0.8
血中コレステロール増加	4	2.8	0	0.0	2	1.4	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0
血中トリグリセリド増加	4	2.8	0	0.0	2	1.4	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0
低比重リポ蛋白増加	2	1.4	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
肝機能検査値上昇	2	1.4	0	0.0	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
活性化部分トロンボプラスチン時間延長	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
血中乳酸脱水素酵素増加	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
心電図ＱＴ延長	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
心電図Ｔ波逆転	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血中アルカリホスファターゼ増加	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.8
肝酵素上昇	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
ＳＡＲＳ－ＣｏＶ－２検査陽性	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
傷害、中毒および処置合併症	7	4.9	1	0.7	1	0.7	2	1.4	0	0.0	1	0.7	1	0.7	1	0.8
靱帯捻挫	2	1.4	0	0.0	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
足関節部骨折	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
節足動物刺傷	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: KLH2301
Group: KLH-2109 200 mg

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
肋骨骨折	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.8
ワクチン接種合併症	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
挫傷	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0
外科および内科処置	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
大腸ポリープ切除	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: KLH2301
Group: Leuprorelin

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
N	144	---	144	---	144	---	142	---	140	---	137	---	135	---	133	---
Any AEs	139	96.5	117	81.3	78	54.2	71	50.0	59	42.1	46	33.6	35	25.9	35	26.3
Leading to Death	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Other Serious Events	2	1.4	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0
Leading to Discontinuation	7	4.9	3	2.1	1	0.7	2	1.4	0	0.0	1	0.7	0	0.0	0	0.0
Leading to Interruption	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
感染症および寄生虫症	71	49.3	14	9.7	4	2.8	16	11.3	12	8.6	18	13.1	16	11.9	12	9.0
上咽頭炎	29	20.1	6	4.2	2	1.4	5	3.5	6	4.3	5	3.6	5	3.7	6	4.5
ＣＯＶＩＤ－１９	11	7.6	3	2.1	0	0.0	2	1.4	3	2.1	2	1.5	1	0.7	0	0.0
コロナウイルス感染	8	5.6	1	0.7	1	0.7	1	0.7	2	1.4	0	0.0	1	0.7	2	1.5
胃腸炎	4	2.8	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	2	1.5	0	0.0
副鼻腔炎	4	2.8	2	1.4	0	0.0	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0
細菌性外陰腟炎	4	2.8	0	0.0	1	0.7	2	1.4	0	0.0	0	0.0	1	0.7	0	0.0
インフルエンザ	3	2.1	0	0.0	0	0.0	0	0.0	0	0.0	2	1.5	0	0.0	1	0.8
咽頭炎	3	2.1	0	0.0	0	0.0	0	0.0	0	0.0	2	1.5	1	0.7	0	0.0
扁桃炎	3	2.1	0	0.0	0	0.0	0	0.0	1	0.7	2	1.5	0	0.0	0	0.0
細菌性腟症	2	1.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	1	0.8
陰部ヘルペス	2	1.4	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0
外陰部腟カンジダ症	2	1.4	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	1	0.7	0	0.0
口腔ヘルペス	2	1.4	0	0.0	0	0.0	2	1.4	0	0.0	0	0.0	0	0.0	0	0.0
結膜炎	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
膀胱炎	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
喉頭蓋炎	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
毛包炎	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
歯肉炎	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
膿痂疹	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
爪囲炎	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.8

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: KLH2301
Group: Leuprorelin

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
歯冠周囲炎	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
歯髄炎	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
腎盂腎炎	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.8
鼻炎	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
前庭神経炎	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0
外陰部炎	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
咽喉頭炎	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1	0.7	0	0.0	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
メラノサイト性母斑	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
皮膚乳頭腫	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
免疫系障害	7	4.9	2	1.4	0	0.0	2	1.4	0	0.0	2	1.5	0	0.0	1	0.8
免疫反応	4	2.8	2	1.4	0	0.0	0	0.0	0	0.0	2	1.5	0	0.0	0	0.0
季節性アレルギー	3	2.1	0	0.0	0	0.0	2	1.4	0	0.0	0	0.0	0	0.0	1	0.8
内分泌障害	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
亜急性甲状腺炎	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
代謝および栄養障害	6	4.2	1	0.7	2	1.4	1	0.7	0	0.0	0	0.0	1	0.7	1	0.8
食欲減退	2	1.4	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0
脱水	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
糖尿病	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.8
脂質異常症	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
２型糖尿病	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
精神障害	15	10.4	5	3.5	5	3.5	5	3.5	1	0.7	1	0.7	0	0.0	1	0.8
不眠症	6	4.2	2	1.4	1	0.7	2	1.4	1	0.7	0	0.0	0	0.0	0	0.0
抑うつ気分	2	1.4	1	0.7	2	1.4	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
易刺激性	2	1.4	0	0.0	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: KLH2301
Group: Leuprorelin

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
アルコールによる宿酔	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
うつ病	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
睡眠障害	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
抑うつ症状	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.8
感情不安定	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
気分の落ち込み	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
神経系障害	28	19.4	12	8.3	5	3.5	4	2.8	7	5.0	4	2.9	1	0.7	2	1.5
頭痛	15	10.4	6	4.2	5	3.5	2	1.4	2	1.4	1	0.7	0	0.0	1	0.8
浮動性めまい	4	2.8	2	1.4	0	0.0	0	0.0	1	0.7	1	0.7	0	0.0	0	0.0
傾眠	4	2.8	3	2.1	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
感覚鈍麻	2	1.4	0	0.0	0	0.0	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0
手根管症候群	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
頚腕症候群	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
体位性めまい	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
片頭痛	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
神経痛	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	1	0.7	0	0.0
緊張性頭痛	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
肋間神経痛	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.8
起立不耐性	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
眼障害	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
緑内障	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
耳および迷路障害	6	4.2	1	0.7	0	0.0	0	0.0	0	0.0	2	1.5	0	0.0	3	2.3
耳鳴	2	1.4	0	0.0	0	0.0	0	0.0	0	0.0	2	1.5	0	0.0	0	0.0
回転性めまい	2	1.4	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.8
耳痛	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.8
耳そう痒症	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.8

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: KLH2301
Group: Leuprorelin

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
心臓障害	6	4.2	2	1.4	2	1.4	0	0.0	1	0.7	0	0.0	1	0.7	0	0.0
動悸	2	1.4	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
心房細動	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0
洞性不整脈	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
洞性徐脈	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
心室性期外収縮	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血管障害	78	54.2	17	11.8	39	27.1	13	9.2	9	6.4	3	2.2	2	1.5	2	1.5
ほてり	77	53.5	17	11.8	38	26.4	13	9.2	8	5.7	2	1.5	2	1.5	2	1.5
高血圧	3	2.1	0	0.0	1	0.7	0	0.0	1	0.7	1	0.7	0	0.0	0	0.0
呼吸器、胸郭および縦隔障害	8	5.6	1	0.7	2	1.4	1	0.7	1	0.7	2	1.5	0	0.0	1	0.8
口腔咽頭痛	3	2.1	0	0.0	0	0.0	0	0.0	1	0.7	1	0.7	0	0.0	1	0.8
呼吸困難	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
鼻出血	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
鼻閉	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
アレルギー性副鼻腔炎	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
口腔咽頭不快感	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
胃腸障害	26	18.1	7	4.9	5	3.5	10	7.0	2	1.4	2	1.5	2	1.5	3	2.3
下痢	3	2.1	2	1.4	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
悪心	3	2.1	0	0.0	2	1.4	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
歯痛	3	2.1	0	0.0	0	0.0	2	1.4	1	0.7	0	0.0	0	0.0	2	1.5
嘔吐	3	2.1	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	2	1.5	0	0.0
腹部不快感	2	1.4	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
下腹部痛	2	1.4	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
上腹部痛	2	1.4	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	1	0.8
便秘	2	1.4	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
齲歯	2	1.4	0	0.0	0	0.0	2	1.4	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: KLH2301
Group: Leuprorelin

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
腹部膨満	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
消化不良	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胃食道逆流性疾患	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
痔核	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
直腸ポリープ	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
大腸ポリープ	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
歯周の炎症	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
軟便	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
肝胆道系障害	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0
肝機能異常	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0
皮膚および皮下組織障害	36	25.0	13	9.0	10	6.9	6	4.2	6	4.3	2	1.5	0	0.0	3	2.3
多汗症	17	11.8	5	3.5	5	3.5	4	2.8	2	1.4	1	0.7	0	0.0	0	0.0
ざ瘡	5	3.5	4	2.8	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
皮膚炎	3	2.1	1	0.7	0	0.0	1	0.7	1	0.7	0	0.0	0	0.0	1	0.8
寝汗	2	1.4	0	0.0	2	1.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
脱毛症	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
寒冷蕁麻疹	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
アレルギー性皮膚炎	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
皮膚乾燥	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
湿疹	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
陥入爪	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.8
発疹	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
脂漏性皮膚炎	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
皮下気腫	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
蕁麻疹	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
瘢痕そう痒感	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: KLH2301
Group: Leuprorelin

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
皮膚硬結	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
手皮膚炎	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.8
筋骨格系および結合組織障害	36	25.0	4	2.8	10	6.9	8	5.6	7	5.0	6	4.4	5	3.7	2	1.5
関節痛	14	9.7	1	0.7	3	2.1	3	2.1	2	1.4	3	2.2	1	0.7	1	0.8
背部痛	7	4.9	2	1.4	3	2.1	2	1.4	0	0.0	1	0.7	0	0.0	0	0.0
筋骨格硬直	5	3.5	1	0.7	1	0.7	1	0.7	1	0.7	1	0.7	1	0.7	0	0.0
関節周囲炎	3	2.1	0	0.0	1	0.7	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0
足底筋膜炎	3	2.1	0	0.0	0	0.0	1	0.7	1	0.7	0	0.0	1	0.7	0	0.0
変形性関節症	2	1.4	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0
筋痙縮	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
筋肉痛	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
骨吸収亢進	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
腱鞘炎	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
弾発指	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
骨減少症	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0
椎間板突出	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
足根洞症候群	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
椎間板障害	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.8
生殖系および乳房障害	107	74.3	99	68.8	19	13.2	12	8.5	7	5.0	5	3.6	4	3.0	2	1.5
月経中間期出血	80	55.6	74	51.4	12	8.3	7	4.9	5	3.6	4	2.9	4	3.0	1	0.8
異常子宮出血	12	8.3	10	6.9	3	2.1	2	1.4	0	0.0	0	0.0	0	0.0	0	0.0
子宮出血	6	4.2	6	4.2	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
閉経期症状	4	2.8	4	2.8	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
重度月経出血	4	2.8	3	2.1	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
乳房不快感	3	2.1	2	1.4	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
卵巣嚢胞	2	1.4	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.8

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: KLH2301
Group: Leuprorelin

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
腟分泌物	2	1.4	2	1.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
腟出血	2	1.4	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
性器出血	2	1.4	1	0.7	1	0.7	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0
乳汁漏出症	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
月経障害	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
不規則月経	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
外陰腟そう痒症	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
外陰腟痛	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
一般・全身障害および投与部位の状態	30	20.8	9	6.3	12	8.3	4	2.8	2	1.4	3	2.2	4	3.0	1	0.8
倦怠感	9	6.3	4	2.8	3	2.1	2	1.4	0	0.0	0	0.0	0	0.0	0	0.0
浮腫	4	2.8	4	2.8	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
発熱	4	2.8	0	0.0	0	0.0	1	0.7	0	0.0	1	0.7	2	1.5	0	0.0
注射部位内出血	3	2.1	0	0.0	2	1.4	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
注射部位硬結	3	2.1	1	0.7	2	1.4	0	0.0	1	0.7	1	0.7	0	0.0	0	0.0
冷感	2	1.4	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	1	0.8
投与部位硬結	2	1.4	0	0.0	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
胸部不快感	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
疲労	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
注射部位疼痛	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
注射部位反応	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
末梢性浮腫	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0
腋窩痛	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0
末梢腫脹	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
投与部位疼痛	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
ワクチン接種部位関節痛	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
臨床検査	34	23.6	1	0.7	3	2.1	9	6.3	12	8.6	5	3.6	6	4.4	7	5.3

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: KLH2301
Group: Leuprorelin

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
酒石酸抵抗性酸ホスファターゼ増加	9	6.3	0	0.0	0	0.0	1	0.7	3	2.1	0	0.0	3	2.2	2	1.5
生化学的骨代謝マーカー上昇	6	4.2	0	0.0	0	0.0	2	1.4	3	2.1	0	0.0	0	0.0	1	0.8
血中トリグリセリド増加	5	3.5	0	0.0	0	0.0	3	2.1	1	0.7	1	0.7	0	0.0	0	0.0
γ－グルタミルトランスフェラーゼ増加	5	3.5	0	0.0	1	0.7	2	1.4	0	0.0	1	0.7	0	0.0	1	0.8
血中コレステロール増加	4	2.8	0	0.0	2	1.4	0	0.0	2	1.4	0	0.0	0	0.0	0	0.0
低比重リポ蛋白増加	4	2.8	0	0.0	1	0.7	0	0.0	1	0.7	1	0.7	1	0.7	0	0.0
骨密度減少	4	2.8	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	1	0.7	2	1.5
アラニンアミノトランスフェラーゼ増加	2	1.4	0	0.0	0	0.0	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0
血中アルカリホスファターゼ増加	2	1.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	1	0.8
活性化部分トロンボプラスチン時間延長	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
心電図ＱＴ延長	1	0.7	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
眼圧上昇	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
体重増加	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
Ａ型インフルエンザウイルス検査陽性	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
肝機能検査値上昇	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
ＳＡＲＳ－ＣｏＶ－２検査陽性	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
傷害、中毒および処置合併症	5	3.5	1	0.7	0	0.0	2	1.4	1	0.7	0	0.0	0	0.0	1	0.8
節足動物刺傷	2	1.4	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
足骨折	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
挫傷	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.8
剥離骨折	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
熱中症	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: KLH2302
Group: KLH-2109 200 mg

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
N	48	---	48	---	48	---	48	---	47	---	27	---	0	---	0	---
Any AEs	44	91.7	35	72.9	21	43.8	8	16.7	8	17.0	0	0.0	0	0.0	0	0.0
Leading to Death	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Other Serious Events	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Leading to Discontinuation	1	2.1	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Leading to Interruption	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
感染症および寄生虫症	13	27.1	4	8.3	3	6.3	3	6.3	4	8.5	0	0.0	0	0.0	0	0.0
ＣＯＶＩＤ－１９	5	10.4	1	2.1	1	2.1	1	2.1	2	4.3	0	0.0	0	0.0	0	0.0
上咽頭炎	4	8.3	2	4.2	1	2.1	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0
毛包炎	1	2.1	0	0.0	0	0.0	0	0.0	1	2.1	0	0.0	0	0.0	0	0.0
歯肉炎	1	2.1	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
インフルエンザ	1	2.1	0	0.0	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
歯周炎	1	2.1	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
副鼻腔炎	1	2.1	0	0.0	0	0.0	0	0.0	1	2.1	0	0.0	0	0.0	0	0.0
外陰部膣カンジダ症	1	2.1	0	0.0	0	0.0	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0
緑色爪症候群	1	2.1	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
代謝および栄養障害	1	2.1	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
食欲減退	1	2.1	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
精神障害	1	2.1	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
中期不眠症	1	2.1	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
神経系障害	6	12.5	2	4.2	4	8.3	1	2.1	1	2.1	0	0.0	0	0.0	0	0.0
頭痛	3	6.3	2	4.2	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
浮動性めまい	2	4.2	0	0.0	2	4.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
味覚不全	1	2.1	0	0.0	0	0.0	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0
顔面麻痺	1	2.1	0	0.0	0	0.0	0	0.0	1	2.1	0	0.0	0	0.0	0	0.0
嗅覚錯誤	1	2.1	0	0.0	0	0.0	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0
傾眠	1	2.1	0	0.0	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: KLH2302
Group: KLH-2109 200 mg

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
眼障害	1	2.1	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
アレルギー性結膜炎	1	2.1	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
耳および迷路障害	1	2.1	0	0.0	0	0.0	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0
耳鳴	1	2.1	0	0.0	0	0.0	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0
血管障害	23	47.9	9	18.8	14	29.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
ほてり	23	47.9	9	18.8	14	29.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
呼吸器、胸郭および縦隔障害	3	6.3	2	4.2	0	0.0	0	0.0	1	2.1	0	0.0	0	0.0	0	0.0
咳嗽	1	2.1	0	0.0	0	0.0	0	0.0	1	2.1	0	0.0	0	0.0	0	0.0
アレルギー性鼻炎	1	2.1	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
上気道の炎症	1	2.1	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胃腸障害	7	14.6	5	10.4	1	2.1	0	0.0	1	2.1	0	0.0	0	0.0	0	0.0
痔核	2	4.2	1	2.1	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
上腹部痛	1	2.1	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
便秘	1	2.1	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
齲歯	1	2.1	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
悪心	1	2.1	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
歯痛	1	2.1	0	0.0	0	0.0	0	0.0	1	2.1	0	0.0	0	0.0	0	0.0
肝胆道系障害	1	2.1	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
肝機能異常	1	2.1	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
皮膚および皮下組織障害	8	16.7	4	8.3	3	6.3	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0
多汗症	6	12.5	4	8.3	2	4.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
汗疹	1	2.1	0	0.0	0	0.0	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0
爪甲剥離症	1	2.1	0	0.0	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
筋骨格系および結合組織障害	2	4.2	1	2.1	0	0.0	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0
筋膜炎	1	2.1	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
筋肉痛	1	2.1	0	0.0	0	0.0	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: KLH2302
Group: KLH-2109 200 mg

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
生殖系および乳房障害	26	54.2	26	54.2	1	2.1	2	4.2	0	0.0	0	0.0	0	0.0	0	0.0
月経中間期出血	20	41.7	20	41.7	1	2.1	2	4.2	0	0.0	0	0.0	0	0.0	0	0.0
異常子宮出血	4	8.3	4	8.3	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
性器出血	2	4.2	2	4.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
重度月経出血	1	2.1	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
一般・全身障害および投与部位の状態	4	8.3	0	0.0	3	6.3	0	0.0	1	2.1	0	0.0	0	0.0	0	0.0
倦怠感	2	4.2	0	0.0	2	4.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
熱感	1	2.1	0	0.0	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
発熱	1	2.1	0	0.0	0	0.0	0	0.0	1	2.1	0	0.0	0	0.0	0	0.0
臨床検査	4	8.3	0	0.0	3	6.3	0	0.0	1	2.1	0	0.0	0	0.0	0	0.0
血中コレステロール増加	2	4.2	0	0.0	2	4.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
低比重リポ蛋白増加	2	4.2	0	0.0	2	4.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血中クレアチンホスホキナーゼ増加	1	2.1	0	0.0	0	0.0	0	0.0	1	2.1	0	0.0	0	0.0	0	0.0
γ－グルタミルトランスフェラーゼ増加	1	2.1	0	0.0	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
傷害、中毒および処置合併症	1	2.1	0	0.0	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
ワクチン接種合併症	1	2.1	0	0.0	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: KLH2302
Group: Placebo

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
N	41	---	41	---	41	---	40	---	40	---	17	---	0	---	0	---
Any AEs	31	75.6	19	46.3	16	39.0	18	45.0	5	12.5	0	0.0	0	0.0	0	0.0
Leading to Death	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Other Serious Events	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Leading to Discontinuation	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Leading to Interruption	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
感染症および寄生虫症	13	31.7	3	7.3	2	4.9	7	17.5	1	2.5	0	0.0	0	0.0	0	0.0
上咽頭炎	5	12.2	1	2.4	1	2.4	3	7.5	0	0.0	0	0.0	0	0.0	0	0.0
口腔ヘルペス	2	4.9	1	2.4	0	0.0	1	2.5	0	0.0	0	0.0	0	0.0	0	0.0
ＣＯＶＩＤ－１９	2	4.9	1	2.4	0	0.0	1	2.5	0	0.0	0	0.0	0	0.0	0	0.0
気管支炎	1	2.4	1	2.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
副鼻腔炎	1	2.4	0	0.0	0	0.0	1	2.5	0	0.0	0	0.0	0	0.0	0	0.0
皮膚感染	1	2.4	0	0.0	0	0.0	1	2.5	0	0.0	0	0.0	0	0.0	0	0.0
扁桃炎	1	2.4	0	0.0	0	0.0	0	0.0	1	2.5	0	0.0	0	0.0	0	0.0
外陰部腟カンジダ症	1	2.4	0	0.0	1	2.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
コロナウイルス感染	1	2.4	0	0.0	0	0.0	1	2.5	0	0.0	0	0.0	0	0.0	0	0.0
細菌性外陰腟炎	1	2.4	0	0.0	1	2.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血液およびリンパ系障害	1	2.4	0	0.0	1	2.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
鉄欠乏性貧血	1	2.4	0	0.0	1	2.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
免疫系障害	1	2.4	1	2.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
免疫反応	1	2.4	1	2.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
神経系障害	2	4.9	0	0.0	1	2.4	1	2.5	0	0.0	0	0.0	0	0.0	0	0.0
頭痛	1	2.4	0	0.0	1	2.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
片頭痛	1	2.4	0	0.0	0	0.0	1	2.5	0	0.0	0	0.0	0	0.0	0	0.0
眼障害	3	7.3	1	2.4	0	0.0	2	5.0	0	0.0	0	0.0	0	0.0	0	0.0
眼瞼炎	1	2.4	0	0.0	0	0.0	1	2.5	0	0.0	0	0.0	0	0.0	0	0.0
霰粒腫	1	2.4	0	0.0	0	0.0	1	2.5	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: KLH2302
Group: Placebo

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
ドライアイ	1	2.4	1	2.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
耳および迷路障害	2	4.9	1	2.4	1	2.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
耳管開放	1	2.4	1	2.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
回転性めまい	1	2.4	0	0.0	1	2.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
呼吸器、胸郭および縦隔障害	1	2.4	0	0.0	1	2.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
口腔咽頭痛	1	2.4	0	0.0	1	2.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胃腸障害	4	9.8	3	7.3	1	2.4	1	2.5	0	0.0	0	0.0	0	0.0	0	0.0
腹部不快感	1	2.4	1	2.4	1	2.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
下痢	1	2.4	1	2.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
悪心	1	2.4	0	0.0	0	0.0	1	2.5	0	0.0	0	0.0	0	0.0	0	0.0
嘔吐	1	2.4	0	0.0	0	0.0	1	2.5	0	0.0	0	0.0	0	0.0	0	0.0
軟便	1	2.4	1	2.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
肝胆道系障害	1	2.4	1	2.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
非アルコール性脂肪肝	1	2.4	1	2.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
皮膚および皮下組織障害	2	4.9	0	0.0	1	2.4	1	2.5	0	0.0	0	0.0	0	0.0	0	0.0
皮膚炎	1	2.4	0	0.0	0	0.0	1	2.5	0	0.0	0	0.0	0	0.0	0	0.0
多汗症	1	2.4	0	0.0	1	2.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
筋骨格系および結合組織障害	3	7.3	2	4.9	0	0.0	2	5.0	0	0.0	0	0.0	0	0.0	0	0.0
背部痛	2	4.9	2	4.9	0	0.0	1	2.5	0	0.0	0	0.0	0	0.0	0	0.0
関節痛	1	2.4	0	0.0	0	0.0	1	2.5	0	0.0	0	0.0	0	0.0	0	0.0
生殖系および乳房障害	15	36.6	9	22.0	8	19.5	11	27.5	2	5.0	0	0.0	0	0.0	0	0.0
月経中間期出血	13	31.7	9	22.0	8	19.5	9	22.5	2	5.0	0	0.0	0	0.0	0	0.0
不規則月経	2	4.9	0	0.0	0	0.0	2	5.0	0	0.0	0	0.0	0	0.0	0	0.0
外陰膣そう痒症	1	2.4	0	0.0	1	2.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
一般・全身障害および投与部位の状態	3	7.3	2	4.9	0	0.0	1	2.5	0	0.0	0	0.0	0	0.0	0	0.0
倦怠感	1	2.4	1	2.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: KLH2302
Group: Placebo

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
発熱	1	2.4	0	0.0	0	0.0	1	2.5	0	0.0	0	0.0	0	0.0	0	0.0
ワクチン接種部位疼痛	1	2.4	1	2.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
臨床検査	1	2.4	0	0.0	0	0.0	0	0.0	1	2.5	0	0.0	0	0.0	0	0.0
血中トリグリセリド増加	1	2.4	0	0.0	0	0.0	0	0.0	1	2.5	0	0.0	0	0.0	0	0.0
傷害、中毒および処置合併症	1	2.4	0	0.0	0	0.0	0	0.0	1	2.5	0	0.0	0	0.0	0	0.0
皮膚擦過傷	1	2.4	0	0.0	0	0.0	0	0.0	1	2.5	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 200 mg

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
N	498	---	498	---	483	---	471	---	460	---	411	---	357	---	297	---
Any AEs	400	80.3	290	58.2	178	36.9	139	29.5	102	22.2	65	15.8	55	15.4	41	13.8
Leading to Death	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Other Serious Events	4	0.8	1	0.2	1	0.2	0	0.0	0	0.0	1	0.2	1	0.3	0	0.0
Leading to Discontinuation	41	8.2	22	4.4	8	1.7	6	1.3	3	0.7	0	0.0	4	1.1	1	0.3
Leading to Interruption	9	1.8	5	1.0	1	0.2	1	0.2	1	0.2	1	0.2	0	0.0	0	0.0
感染症および寄生虫症	133	26.7	37	7.4	25	5.2	32	6.8	25	5.4	15	3.6	17	4.8	14	4.7
上咽頭炎	52	10.4	14	2.8	9	1.9	14	3.0	8	1.7	7	1.7	5	1.4	5	1.7
ＣＯＶＩＤ－１９	12	2.4	2	0.4	1	0.2	2	0.4	3	0.7	2	0.5	2	0.6	0	0.0
インフルエンザ	9	1.8	0	0.0	1	0.2	1	0.2	1	0.2	1	0.2	3	0.8	3	1.0
気管支炎	8	1.6	3	0.6	2	0.4	1	0.2	0	0.0	1	0.2	0	0.0	1	0.3
膀胱炎	6	1.2	1	0.2	0	0.0	2	0.4	2	0.4	1	0.2	1	0.3	0	0.0
副鼻腔炎	6	1.2	3	0.6	0	0.0	0	0.0	2	0.4	0	0.0	1	0.3	0	0.0
尿路感染	6	1.2	1	0.2	4	0.8	1	0.2	3	0.7	0	0.0	0	0.0	0	0.0
外陰部腟カンジダ症	5	1.0	1	0.2	0	0.0	1	0.2	0	0.0	1	0.2	1	0.3	1	0.3
歯周炎	4	0.8	2	0.4	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
外陰腟真菌感染	4	0.8	0	0.0	0	0.0	3	0.6	0	0.0	0	0.0	1	0.3	0	0.0
胃腸炎	3	0.6	0	0.0	0	0.0	1	0.2	1	0.2	0	0.0	0	0.0	1	0.3
上気道感染	3	0.6	2	0.4	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
腟感染	3	0.6	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	1	0.3	0	0.0
ウイルス性気道感染	3	0.6	0	0.0	1	0.2	0	0.0	0	0.0	1	0.2	0	0.0	1	0.3
細菌性外陰腟炎	3	0.6	1	0.2	0	0.0	0	0.0	2	0.4	0	0.0	0	0.0	0	0.0
帯状疱疹	2	0.4	0	0.0	0	0.0	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0
中耳炎	2	0.4	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	1	0.3	0	0.0
咽頭炎	2	0.4	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
コロナウイルス感染	2	0.4	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	1	0.3
気道感染	2	0.4	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 200 mg

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
急性副鼻腔炎	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
細菌性膣症	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
バルトリン腺膿瘍	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
結膜炎	1	0.2	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
爪の皮膚糸状菌症	1	0.2	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
毛包炎	1	0.2	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
歯肉炎	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Ｃ型肝炎	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
麦粒腫	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0
急性中耳炎	1	0.2	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
爪囲炎	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
レンサ球菌性咽頭炎	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
鼻炎	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
皮膚感染	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.3
扁桃炎	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.3	0	0.0
尿道膿瘍	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	1	0.3	0	0.0
細菌性膀胱炎	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
カンジダ感染	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
緑色爪症候群	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	3	0.6	0	0.0	0	0.0	1	0.2	1	0.2	0	0.0	1	0.3	0	0.0
乳癌	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.3	0	0.0
皮膚乳頭腫	1	0.2	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
子宮平滑筋腫	1	0.2	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
血液およびリンパ系障害	8	1.6	6	1.2	0	0.0	0	0.0	0	0.0	0	0.0	2	0.6	0	0.0
貧血	6	1.2	5	1.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.3	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 200 mg

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
鉄欠乏性貧血	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
リンパ節症	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.3	0	0.0
免疫系障害	2	0.4	0	0.0	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
季節性アレルギー	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
節足動物咬傷アレルギー	1	0.2	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
代謝および栄養障害	12	2.4	3	0.6	5	1.0	2	0.4	1	0.2	0	0.0	0	0.0	1	0.3
脂質異常症	5	1.0	0	0.0	3	0.6	2	0.4	0	0.0	0	0.0	0	0.0	0	0.0
食欲減退	4	0.8	2	0.4	2	0.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
食欲亢進	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
高脂血症	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.3
２型糖尿病	1	0.2	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
精神障害	41	8.2	23	4.6	11	2.3	6	1.3	2	0.4	2	0.5	0	0.0	0	0.0
不眠症	9	1.8	3	0.6	3	0.6	2	0.4	1	0.2	1	0.2	0	0.0	0	0.0
リビドー減退	7	1.4	3	0.6	2	0.4	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0
不安	6	1.2	4	0.8	2	0.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
気分動揺	5	1.0	3	0.6	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
うつ病	3	0.6	1	0.2	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
睡眠障害	3	0.6	2	0.4	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
感情不安定	3	0.6	2	0.4	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
易刺激性	2	0.4	1	0.2	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
中期不眠症	2	0.4	2	0.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
錯乱状態	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
リビドー亢進	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
神経過敏	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
睡眠の質低下	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
神経系障害	94	18.9	55	11.0	34	7.0	11	2.3	13	2.8	5	1.2	6	1.7	1	0.3

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 200 mg

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
頭痛	67	13.5	40	8.0	22	4.6	8	1.7	9	2.0	5	1.2	4	1.1	1	0.3
浮動性めまい	15	3.0	9	1.8	5	1.0	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0
傾眠	7	1.4	4	0.8	3	0.6	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
片頭痛	5	1.0	3	0.6	1	0.2	0	0.0	1	0.2	0	0.0	1	0.3	0	0.0
記憶障害	3	0.6	1	0.2	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
構語障害	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
味覚不全	1	0.2	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
顔面麻痺	1	0.2	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
感覚鈍麻	1	0.2	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
嗜眠	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
錯感覚	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
嗅覚錯誤	1	0.2	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
鎮静	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
くも膜下出血	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
緊張性頭痛	1	0.2	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
振戦	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
認知障害	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
眼障害	9	1.8	2	0.4	5	1.0	0	0.0	1	0.2	0	0.0	0	0.0	1	0.3
ドライアイ	2	0.4	0	0.0	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
霧視	2	0.4	0	0.0	2	0.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
眼瞼炎	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.3
アレルギー性結膜炎	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
眼部腫脹	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
眼そう痒症	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
マイボーム腺機能不全	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
耳および迷路障害	7	1.4	2	0.4	1	0.2	1	0.2	3	0.7	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 200 mg

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
耳痛	3	0.6	1	0.2	0	0.0	0	0.0	2	0.4	0	0.0	0	0.0	0	0.0
回転性めまい	2	0.4	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
耳鳴	1	0.2	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
耳不快感	1	0.2	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
心臓障害	11	2.2	6	1.2	2	0.4	2	0.4	1	0.2	0	0.0	0	0.0	1	0.3
動悸	8	1.6	5	1.0	2	0.4	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0
頻脈	2	0.4	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
洞性不整脈	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.3
血管障害	227	45.6	123	24.7	74	15.3	25	5.3	11	2.4	5	1.2	0	0.0	2	0.7
ほてり	220	44.2	122	24.5	72	14.9	23	4.9	9	2.0	4	1.0	0	0.0	0	0.0
高血圧	9	1.8	1	0.2	3	0.6	1	0.2	2	0.4	1	0.2	0	0.0	2	0.7
潮紅	1	0.2	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
呼吸器、胸郭および縦隔障害	29	5.8	8	1.6	6	1.2	5	1.1	2	0.4	5	1.2	2	0.6	3	1.0
咳嗽	9	1.8	2	0.4	1	0.2	2	0.4	2	0.4	2	0.5	1	0.3	0	0.0
口腔咽頭痛	5	1.0	0	0.0	0	0.0	1	0.2	0	0.0	2	0.5	1	0.3	2	0.7
鼻閉	2	0.4	1	0.2	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0
アレルギー性鼻炎	2	0.4	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
副鼻腔うっ血	2	0.4	0	0.0	0	0.0	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0
咽喉絞扼感	2	0.4	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
喘息	1	0.2	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
発声障害	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
呼吸困難	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
肺塞栓症	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
喘鳴	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.3
上気道の炎症	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
副鼻腔不快感	1	0.2	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 200 mg

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
アレルギー性咳嗽	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
アレルギー性呼吸器疾患	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胃腸障害	85	17.1	40	8.0	17	3.5	7	1.5	12	2.6	9	2.2	3	0.8	4	1.3
悪心	27	5.4	23	4.6	4	0.8	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
下痢	10	2.0	3	0.6	3	0.6	2	0.4	1	0.2	1	0.2	0	0.0	1	0.3
上腹部痛	9	1.8	2	0.4	1	0.2	0	0.0	2	0.4	2	0.5	1	0.3	1	0.3
腹痛	7	1.4	1	0.2	0	0.0	1	0.2	2	0.4	2	0.5	0	0.0	1	0.3
便秘	7	1.4	2	0.4	2	0.4	1	0.2	1	0.2	1	0.2	0	0.0	0	0.0
腹部不快感	5	1.0	2	0.4	2	0.4	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0
歯痛	5	1.0	1	0.2	1	0.2	1	0.2	1	0.2	1	0.2	0	0.0	0	0.0
嘔吐	4	0.8	2	0.4	0	0.0	0	0.0	2	0.4	0	0.0	0	0.0	0	0.0
腹部膨満	3	0.6	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	1	0.3	1	0.3
齲歯	3	0.6	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0
胃炎	3	0.6	2	0.4	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
痔核	3	0.6	1	0.2	2	0.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
下腹部痛	2	0.4	0	0.0	0	0.0	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0
消化不良	2	0.4	2	0.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
口角口唇炎	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
慢性胃炎	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
鼓腸	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
歯肉出血	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
排便困難	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0
閉塞性膵炎	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
肝胆道系障害	8	1.6	2	0.4	0	0.0	2	0.4	2	0.4	1	0.2	0	0.0	1	0.3
肝機能異常	6	1.2	1	0.2	0	0.0	1	0.2	2	0.4	1	0.2	0	0.0	1	0.3
脂肪肝	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 200 mg

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
非アルコール性脂肪肝	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胆嚢摘出術後症候群	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
高トランスアミナーゼ血症	1	0.2	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
皮膚および皮下組織障害	74	14.9	29	5.8	22	4.6	12	2.5	8	1.7	4	1.0	3	0.8	2	0.7
多汗症	36	7.2	15	3.0	13	2.7	4	0.8	2	0.4	2	0.5	0	0.0	0	0.0
脱毛症	7	1.4	3	0.6	2	0.4	0	0.0	2	0.4	0	0.0	0	0.0	0	0.0
湿疹	6	1.2	2	0.4	1	0.2	3	0.6	0	0.0	0	0.0	0	0.0	0	0.0
発疹	5	1.0	2	0.4	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	1	0.3
寝汗	4	0.8	2	0.4	2	0.4	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
ざ瘡	3	0.6	2	0.4	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
接触皮膚炎	3	0.6	2	0.4	1	0.2	0	0.0	0	0.0	0	0.0	1	0.3	0	0.0
そう痒症	3	0.6	2	0.4	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
蕁麻疹	3	0.6	1	0.2	0	0.0	0	0.0	1	0.2	1	0.2	0	0.0	0	0.0
皮膚嚢腫	2	0.4	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	1	0.3
汗疹	2	0.4	0	0.0	0	0.0	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0
円形脱毛症	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
冷汗	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
皮膚炎	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.3	0	0.0
アレルギー性皮膚炎	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
貨幣状湿疹	1	0.2	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
陥入爪	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.3	0	0.0
爪甲剥離症	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
皮膚剥脱	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
皮膚硬結	1	0.2	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
手皮膚炎	1	0.2	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
筋骨格系および結合組織障害	78	15.7	17	3.4	15	3.1	18	3.8	13	2.8	12	2.9	12	3.4	2	0.7

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 200 mg

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
関節痛	33	6.6	5	1.0	3	0.6	5	1.1	6	1.3	9	2.2	4	1.1	1	0.3
背部痛	20	4.0	5	1.0	4	0.8	4	0.8	2	0.4	1	0.2	5	1.4	0	0.0
筋骨格硬直	15	3.0	5	1.0	3	0.6	2	0.4	3	0.7	1	0.2	1	0.3	0	0.0
四肢痛	6	1.2	1	0.2	3	0.6	2	0.4	0	0.0	0	0.0	0	0.0	0	0.0
筋痙縮	2	0.4	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
筋肉痛	2	0.4	0	0.0	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
骨吸収亢進	2	0.4	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	1	0.3
腱鞘炎	2	0.4	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	1	0.3	0	0.0
関節炎	1	0.2	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
筋膜炎	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
側腹部痛	1	0.2	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
筋骨格痛	1	0.2	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
顎痛	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
足底筋膜炎	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0
変形性脊椎症	1	0.2	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
仙骨痛	1	0.2	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
椎間板突出	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.3	0	0.0
骨喪失	1	0.2	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
半月板変性	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
腎および尿路障害	8	1.6	3	0.6	0	0.0	3	0.6	2	0.4	0	0.0	0	0.0	0	0.0
頻尿	5	1.0	2	0.4	0	0.0	3	0.6	0	0.0	0	0.0	0	0.0	0	0.0
排尿困難	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
緊張性膀胱	1	0.2	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
夜間頻尿	1	0.2	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
生殖系および乳房障害	158	31.7	131	26.3	27	5.6	16	3.4	10	2.2	9	2.2	8	2.2	6	2.0
月経中間期出血	99	19.9	87	17.5	14	2.9	8	1.7	4	0.9	6	1.5	4	1.1	4	1.3

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 200 mg

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
重度月経出血	14	2.8	13	2.6	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
異常子宮出血	10	2.0	8	1.6	3	0.6	1	0.2	1	0.2	1	0.2	2	0.6	1	0.3
閉経期症状	8	1.6	4	0.8	2	0.4	2	0.4	0	0.0	0	0.0	0	0.0	0	0.0
外陰腟乾燥	8	1.6	4	0.8	3	0.6	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
骨盤痛	7	1.4	2	0.4	2	0.4	2	0.4	0	0.0	0	0.0	1	0.3	0	0.0
子宮出血	6	1.2	6	1.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
腟出血	6	1.2	5	1.0	0	0.0	0	0.0	0	0.0	2	0.5	1	0.3	0	0.0
乳房圧痛	4	0.8	1	0.2	2	0.4	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
不規則月経	3	0.6	2	0.4	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
腟分泌物	3	0.6	2	0.4	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
性器出血	3	0.6	3	0.6	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
無月経	2	0.4	2	0.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
子宮内膜増殖症	2	0.4	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	1	0.3
乳房不快感	2	0.4	2	0.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
萎縮性外陰腟炎	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
乳房分泌	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
月経困難症	1	0.2	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
乳汁漏出症	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
月経遅延	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
外陰腟不快感	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
外陰腟そう痒症	1	0.2	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
外陰部湿疹	1	0.2	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
外陰腟灼熱感	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
一般・全身障害および投与部位の状態	46	9.2	18	3.6	15	3.1	8	1.7	6	1.3	1	0.2	2	0.6	0	0.0
倦怠感	18	3.6	7	1.4	7	1.4	3	0.6	2	0.4	1	0.2	0	0.0	0	0.0
疲労	8	1.6	4	0.8	3	0.6	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 200 mg

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
発熱	7	1.4	3	0.6	0	0.0	1	0.2	3	0.7	0	0.0	0	0.0	0	0.0
浮腫	4	0.8	1	0.2	1	0.2	0	0.0	2	0.4	0	0.0	1	0.3	0	0.0
疼痛	4	0.8	2	0.4	2	0.4	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
無力症	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胸痛	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
異常感	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
熱感	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
びくびく感	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
インフルエンザ様疾患	1	0.2	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
注射部位疼痛	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
顔面腫脹	1	0.2	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
末梢腫脹	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.3	0	0.0
臨床検査	99	19.9	23	4.6	27	5.6	26	5.5	18	3.9	8	1.9	8	2.2	8	2.7
アラニンアミノトランスフェラーゼ増加	24	4.8	7	1.4	6	1.2	3	0.6	5	1.1	2	0.5	1	0.3	0	0.0
γ－グルタミルトランスフェラーゼ増加	17	3.4	4	0.8	9	1.9	2	0.4	1	0.2	0	0.0	0	0.0	1	0.3
アスパラギン酸アミノトランスフェラーゼ増加	15	3.0	5	1.0	4	0.8	2	0.4	3	0.7	1	0.2	0	0.0	0	0.0
骨密度減少	13	2.6	0	0.0	0	0.0	0	0.0	3	0.7	0	0.0	6	1.7	4	1.3
血中コレステロール増加	12	2.4	4	0.8	4	0.8	2	0.4	2	0.4	0	0.0	0	0.0	0	0.0
低比重リポ蛋白増加	10	2.0	5	1.0	3	0.6	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0
生化学的骨代謝マーカー上昇	10	2.0	0	0.0	0	0.0	8	1.7	1	0.2	1	0.2	0	0.0	0	0.0
血中クレアチンホスホキナーゼ増加	9	1.8	1	0.2	3	0.6	3	0.6	1	0.2	1	0.2	0	0.0	0	0.0
酒石酸抵抗性酸ホスファターゼ増加	7	1.4	0	0.0	0	0.0	2	0.4	2	0.4	0	0.0	2	0.6	1	0.3
グアナーゼ増加	6	1.2	3	0.6	1	0.2	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0
血中トリグリセリド増加	5	1.0	1	0.2	2	0.4	2	0.4	1	0.2	0	0.0	0	0.0	0	0.0
血圧上昇	4	0.8	2	0.4	2	0.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 200 mg

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
活性化部分トロンボプラスチン時間延長	3	0.6	2	0.4	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
血中尿酸増加	3	0.6	1	0.2	2	0.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
体重増加	3	0.6	1	0.2	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	1	0.3
肝機能検査値上昇	3	0.6	0	0.0	2	0.4	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
血中乳酸脱水素酵素増加	2	0.4	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
遊離脂肪酸増加	2	0.4	2	0.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
体重減少	2	0.4	2	0.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血中アルカリホスファターゼ増加	2	0.4	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	1	0.3
肝酵素上昇	2	0.4	0	0.0	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
血中ビリルビン増加	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0
血中クレアチニン増加	1	0.2	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
血中ブドウ糖異常	1	0.2	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
血中鉄減少	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
心電図異常	1	0.2	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
心電図ＱＴ延長	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
心電図Ｔ波逆転	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
尿中ブドウ糖陽性	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
高比重リポ蛋白増加	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
平均赤血球容積異常	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.3
プロトロンビン時間短縮	1	0.2	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
白血球数増加	1	0.2	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
糖鎖抗原１９－９増加	1	0.2	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
トランスアミナーゼ上昇	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
尿中ケトン体陽性	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0
ＳＡＲＳ－ＣｏＶ－２検査陽性	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0
傷害、中毒および処置合併症	15	3.0	2	0.4	4	0.8	3	0.6	1	0.2	3	0.7	1	0.3	1	0.3

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 200 mg

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
靱帯捻挫	3	0.6	0	0.0	1	0.2	0	0.0	1	0.2	1	0.2	0	0.0	0	0.0
転倒	2	0.4	0	0.0	0	0.0	0	0.0	0	0.0	2	0.5	0	0.0	0	0.0
ワクチン接種合併症	2	0.4	0	0.0	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
挫傷	2	0.4	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	1	0.3	0	0.0
足関節部骨折	1	0.2	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
節足動物刺傷	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
背部損傷	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
足骨折	1	0.2	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
肋骨骨折	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.3
熱傷	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
処置による疼痛	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
外科および内科処置	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0
大腸ポリープ切除	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 ALL

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
N	1452	---	1452	---	1416	---	1385	---	1334	---	1182	---	1016	---	843	---
Any AEs	1081	74.4	675	46.5	454	32.1	369	26.6	279	20.9	187	15.8	175	17.2	111	13.2
Leading to Death	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Other Serious Events	20	1.4	2	0.1	5	0.4	3	0.2	0	0.0	7	0.6	4	0.4	0	0.0
Leading to Discontinuation	90	6.2	45	3.1	21	1.5	10	0.7	6	0.4	6	0.5	5	0.5	2	0.2
Leading to Interruption	21	1.4	8	0.6	3	0.2	2	0.1	2	0.1	4	0.3	1	0.1	1	0.1
感染症および寄生虫症	400	27.5	116	8.0	100	7.1	94	6.8	74	5.5	47	4.0	58	5.7	37	4.4
上咽頭炎	186	12.8	46	3.2	50	3.5	41	3.0	30	2.2	22	1.9	23	2.3	15	1.8
インフルエンザ	29	2.0	7	0.5	5	0.4	4	0.3	3	0.2	1	0.1	6	0.6	4	0.5
尿路感染	21	1.4	5	0.3	8	0.6	2	0.1	7	0.5	1	0.1	1	0.1	1	0.1
副鼻腔炎	20	1.4	4	0.3	2	0.1	6	0.4	2	0.1	1	0.1	5	0.5	0	0.0
外陰部腟カンジダ症	16	1.1	3	0.2	3	0.2	3	0.2	1	0.1	2	0.2	1	0.1	3	0.4
膀胱炎	13	0.9	1	0.1	2	0.1	2	0.1	3	0.2	3	0.3	2	0.2	1	0.1
気管支炎	12	0.8	4	0.3	3	0.2	1	0.1	1	0.1	1	0.1	2	0.2	1	0.1
胃腸炎	12	0.8	2	0.1	2	0.1	1	0.1	4	0.3	1	0.1	1	0.1	1	0.1
ＣＯＶＩＤ－１９	12	0.8	2	0.1	1	0.1	2	0.1	3	0.2	2	0.2	2	0.2	0	0.0
咽頭炎	11	0.8	4	0.3	1	0.1	1	0.1	1	0.1	0	0.0	3	0.3	1	0.1
上気道感染	10	0.7	4	0.3	1	0.1	4	0.3	0	0.0	1	0.1	0	0.0	0	0.0
扁桃炎	9	0.6	4	0.3	0	0.0	0	0.0	0	0.0	3	0.3	2	0.2	0	0.0
ウイルス性気道感染	9	0.6	2	0.1	2	0.1	2	0.1	1	0.1	2	0.2	0	0.0	1	0.1
細菌性外陰腟炎	8	0.6	1	0.1	1	0.1	2	0.1	4	0.3	0	0.0	1	0.1	0	0.0
歯周炎	7	0.5	3	0.2	1	0.1	2	0.1	1	0.1	0	0.0	0	0.0	0	0.0
腟感染	7	0.5	2	0.1	2	0.1	1	0.1	2	0.1	0	0.0	1	0.1	0	0.0
レンサ球菌性咽頭炎	6	0.4	2	0.1	1	0.1	1	0.1	0	0.0	1	0.1	1	0.1	0	0.0
外陰腟真菌感染	6	0.4	1	0.1	0	0.0	3	0.2	1	0.1	0	0.0	2	0.2	0	0.0
細菌性腟症	5	0.3	3	0.2	0	0.0	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0
歯肉炎	5	0.3	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	2	0.2

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 ALL

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
結膜炎	4	0.3	0	0.0	2	0.1	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0
歯膿瘍	4	0.3	1	0.1	2	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
外陰部炎	4	0.3	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	2	0.2	0	0.0
急性副鼻腔炎	3	0.2	1	0.1	0	0.0	0	0.0	1	0.1	1	0.1	0	0.0	0	0.0
真菌感染	3	0.2	2	0.1	0	0.0	1	0.1	1	0.1	0	0.0	0	0.0	1	0.1
陰部ヘルペス	3	0.2	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	2	0.2	0	0.0
帯状疱疹	3	0.2	0	0.0	1	0.1	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0
麦粒腫	3	0.2	0	0.0	0	0.0	0	0.0	1	0.1	1	0.1	0	0.0	1	0.1
中耳炎	3	0.2	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	1	0.1	0	0.0
肺炎	3	0.2	1	0.1	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
鼻炎	3	0.2	0	0.0	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1
気道感染	3	0.2	2	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
口腔ヘルペス	3	0.2	0	0.0	0	0.0	1	0.1	0	0.0	1	0.1	1	0.1	0	0.0
毛包炎	2	0.1	0	0.0	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
ウイルス性胃腸炎	2	0.1	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
膿痂疹	2	0.1	0	0.0	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
急性中耳炎	2	0.1	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
爪囲炎	2	0.1	0	0.0	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
皮膚感染	2	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1
外陰部膿瘍	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	1	0.1
トリコモナス外陰腟炎	2	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0
コロナウイルス感染	2	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	1	0.1
白癬感染	2	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1
レンサ球菌感染	2	0.1	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
カンジダ感染	2	0.1	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
膿疱性ざ瘡	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 ALL

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
バルトリン腺膿瘍	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
ウイルス性結膜炎	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
爪の皮膚糸状菌症	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
憩室炎	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
Ｃ型肝炎	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
ヘルペスウイルス感染	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
喉頭炎	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
腹膜炎	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
扁桃周囲膿瘍	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
腎盂腎炎	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
急性腎盂腎炎	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
風疹	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
敗血症	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
足部白癬	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
気管炎	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
尿道膿瘍	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
ウイルス感染	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
外陰腟炎	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
歯感染	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
ヘリコバクター感染	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
ヘリコバクター性胃炎	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
癜風	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
感染性腸炎	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
細菌性気道感染	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
アデノウイルス感染	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
爪感染	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 ALL

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
ダニ皮膚炎	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
細菌性膀胱炎	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
真菌性乳腺炎	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
ウイルス性耳下腺炎	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
緑色爪症候群	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	11	0.8	1	0.1	1	0.1	5	0.4	1	0.1	0	0.0	1	0.1	2	0.2
子宮平滑筋腫	3	0.2	0	0.0	0	0.0	1	0.1	1	0.1	0	0.0	0	0.0	1	0.1
乳癌	2	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0
乳腺線維腺腫	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血管腫	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
肝臓血管腫	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
悪性黒色腫	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
皮膚乳頭腫	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
肛門性器疣贅	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1
血液およびリンパ系障害	39	2.7	18	1.2	6	0.4	3	0.2	6	0.4	2	0.2	3	0.3	2	0.2
貧血	31	2.1	14	1.0	5	0.4	3	0.2	5	0.4	2	0.2	1	0.1	2	0.2
鉄欠乏性貧血	3	0.2	2	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
リンパ節症	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	2	0.2	0	0.0
好中球減少症	2	0.1	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血小板減少症	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
免疫系障害	11	0.8	4	0.3	1	0.1	2	0.1	0	0.0	2	0.2	2	0.2	0	0.0
季節性アレルギー	6	0.4	2	0.1	1	0.1	1	0.1	0	0.0	2	0.2	0	0.0	0	0.0
アナフィラキシー反応	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
薬物過敏症	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
過敏症	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 ALL

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
節足動物刺傷アレルギー	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
節足動物咬傷アレルギー	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
内分泌障害	2	0.1	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
甲状腺腫	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
甲状腺機能亢進症	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
代謝および栄養障害	29	2.0	12	0.8	6	0.4	3	0.2	5	0.4	1	0.1	0	0.0	4	0.5
脂質異常症	10	0.7	3	0.2	3	0.2	3	0.2	1	0.1	0	0.0	0	0.0	1	0.1
食欲減退	6	0.4	4	0.3	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
高コレステロール血症	2	0.1	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
食欲亢進	2	0.1	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
鉄欠乏	2	0.1	0	0.0	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
高脂血症	2	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1
体液貯留	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1
過食	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
高トリグリセリド血症	1	0.1	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
低カルシウム血症	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
低カリウム血症	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
肥満	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1
ビタミンD欠乏	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
２型糖尿病	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
精神障害	82	5.6	41	2.8	18	1.3	13	0.9	7	0.5	5	0.4	1	0.1	0	0.0
気分動揺	19	1.3	10	0.7	2	0.1	4	0.3	2	0.1	1	0.1	0	0.0	0	0.0
不眠症	14	1.0	3	0.2	6	0.4	3	0.2	2	0.1	1	0.1	0	0.0	0	0.0
不安	10	0.7	6	0.4	3	0.2	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
リビドー減退	10	0.7	5	0.3	3	0.2	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0
感情不安定	9	0.6	5	0.3	1	0.1	1	0.1	1	0.1	1	0.1	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 ALL

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
うつ病	7	0.5	4	0.3	1	0.1	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0
易刺激性	6	0.4	1	0.1	2	0.1	1	0.1	2	0.1	0	0.0	0	0.0	0	0.0
睡眠障害	4	0.3	2	0.1	0	0.0	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0
中期不眠症	2	0.1	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
気分変化	2	0.1	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
抑うつ気分を伴う適応障害	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
錯乱状態	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
抑うつ気分	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
薬物乱用	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
リビドー亢進	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
リビドー消失	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
神経過敏	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
睡眠の質低下	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
注意欠如・多動性障害	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
神経系障害	247	17.0	150	10.3	73	5.2	42	3.0	29	2.2	15	1.3	16	1.6	5	0.6
頭痛	172	11.8	106	7.3	50	3.5	31	2.2	22	1.6	13	1.1	11	1.1	5	0.6
浮動性めまい	43	3.0	25	1.7	11	0.8	5	0.4	2	0.1	0	0.0	1	0.1	0	0.0
片頭痛	17	1.2	6	0.4	6	0.4	2	0.1	1	0.1	1	0.1	2	0.2	0	0.0
傾眠	16	1.1	12	0.8	3	0.2	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
体位性めまい	3	0.2	2	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
記憶障害	3	0.2	1	0.1	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
緊張性頭痛	3	0.2	2	0.1	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
味覚不全	2	0.1	0	0.0	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
感覚鈍麻	2	0.1	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
嗜眠	2	0.1	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
坐骨神経痛	2	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 ALL

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
くも膜下出血	2	0.1	0	0.0	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
振戦	2	0.1	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
認知障害	2	0.1	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
構語障害	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
顔面麻痺	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
神経炎	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
末梢性ニューロパチー	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
眼振	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
錯感覚	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
嗅覚錯誤	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
鎮静	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
副鼻腔炎に伴う頭痛	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
失神	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
肋間神経痛	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
顔面痙攣	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
眼障害	16	1.1	4	0.3	6	0.4	1	0.1	2	0.1	0	0.0	1	0.1	2	0.2
ドライアイ	3	0.2	1	0.1	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
眼瞼炎	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	1	0.1
アレルギー性結膜炎	2	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1
霧視	2	0.1	0	0.0	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
眼のアレルギー	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
眼の炎症	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
眼部腫脹	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
角膜炎	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
眼瞼腫脹	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
眼そう痒症	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 ALL

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
マイボーム腺機能不全	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
耳および迷路障害	19	1.3	4	0.3	6	0.4	2	0.1	6	0.4	0	0.0	1	0.1	0	0.0
回転性めまい	10	0.7	3	0.2	4	0.3	1	0.1	1	0.1	0	0.0	1	0.1	0	0.0
耳痛	4	0.3	1	0.1	1	0.1	0	0.0	2	0.1	0	0.0	0	0.0	0	0.0
耳鳴	3	0.2	0	0.0	1	0.1	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0
難聴	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
メニエール病	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
耳不快感	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
心臓障害	26	1.8	11	0.8	8	0.6	6	0.4	1	0.1	1	0.1	0	0.0	2	0.2
動悸	14	1.0	8	0.6	4	0.3	4	0.3	1	0.1	0	0.0	0	0.0	0	0.0
頻脈	4	0.3	2	0.1	0	0.0	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0
狭心症	3	0.2	1	0.1	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
洞性不整脈	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1
洞性徐脈	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
上室性期外収縮	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
心室性期外収縮	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1
心粗動	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血管障害	382	26.3	210	14.5	110	7.8	42	3.0	22	1.6	12	1.0	6	0.6	3	0.4
ほてり	365	25.1	207	14.3	106	7.5	38	2.7	20	1.5	8	0.7	5	0.5	0	0.0
高血圧	15	1.0	3	0.2	4	0.3	2	0.1	2	0.1	3	0.3	0	0.0	2	0.2
血腫	2	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1
潮紅	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
低血圧	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
高血圧切迫症	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
末梢静脈疾患	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
呼吸器、胸郭および縦隔障害	59	4.1	18	1.2	12	0.8	8	0.6	7	0.5	8	0.7	5	0.5	5	0.6

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 ALL

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
咳嗽	12	0.8	2	0.1	2	0.1	3	0.2	3	0.2	2	0.2	1	0.1	0	0.0
口腔咽頭痛	9	0.6	2	0.1	0	0.0	3	0.2	0	0.0	2	0.2	1	0.1	2	0.2
アレルギー性鼻炎	6	0.4	2	0.1	2	0.1	0	0.0	1	0.1	0	0.0	1	0.1	0	0.0
上気道の炎症	6	0.4	3	0.2	0	0.0	0	0.0	1	0.1	2	0.2	1	0.1	0	0.0
鼻出血	3	0.2	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1
副鼻腔うっ血	3	0.2	0	0.0	1	0.1	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0
咽喉絞扼感	3	0.2	1	0.1	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
咳喘息	3	0.2	0	0.0	0	0.0	1	0.1	1	0.1	0	0.0	0	0.0	1	0.1
喘息	2	0.1	0	0.0	0	0.0	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0
発声障害	2	0.1	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
鼻閉	2	0.1	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
肺塞栓症	2	0.1	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
副鼻腔不快感	2	0.1	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
呼吸困難	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
咽頭潰瘍	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胸水	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胸膜炎	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
肺うっ血	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
喘鳴	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1
アレルギー性咳嗽	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
アレルギー性呼吸器疾患	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胃腸障害	219	15.1	94	6.5	44	3.1	20	1.4	32	2.4	30	2.5	16	1.6	9	1.1
悪心	57	3.9	40	2.8	13	0.9	2	0.1	5	0.4	2	0.2	1	0.1	0	0.0
上腹部痛	25	1.7	7	0.5	5	0.4	0	0.0	3	0.2	8	0.7	1	0.1	1	0.1
下痢	25	1.7	11	0.8	4	0.3	3	0.2	4	0.3	2	0.2	1	0.1	1	0.1
便秘	20	1.4	4	0.3	6	0.4	3	0.2	4	0.3	1	0.1	1	0.1	1	0.1

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 ALL

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
腹痛	17	1.2	5	0.3	2	0.1	1	0.1	3	0.2	3	0.3	1	0.1	2	0.2
腹部不快感	16	1.1	7	0.5	4	0.3	0	0.0	2	0.1	3	0.3	0	0.0	0	0.0
歯痛	15	1.0	3	0.2	1	0.1	3	0.2	1	0.1	4	0.3	2	0.2	1	0.1
嘔吐	13	0.9	7	0.5	2	0.1	2	0.1	4	0.3	0	0.0	1	0.1	0	0.0
腹部膨満	8	0.6	5	0.3	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	1	0.1
痔核	8	0.6	1	0.1	3	0.2	1	0.1	1	0.1	1	0.1	1	0.1	0	0.0
下腹部痛	6	0.4	1	0.1	1	0.1	1	0.1	2	0.1	1	0.1	0	0.0	0	0.0
胃炎	6	0.4	2	0.1	0	0.0	1	0.1	2	0.1	1	0.1	0	0.0	0	0.0
裂肛	4	0.3	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	2	0.2	0	0.0
齲歯	4	0.3	1	0.1	0	0.0	2	0.1	0	0.0	0	0.0	1	0.1	0	0.0
口角口唇炎	3	0.2	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	1	0.1	0	0.0
消化不良	3	0.2	3	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
鼓腸	3	0.2	1	0.1	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
食中毒	3	0.2	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1
虚血性大腸炎	2	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	1	0.1
腸炎	2	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0
胃食道逆流性疾患	2	0.1	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
歯肉出血	2	0.1	0	0.0	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
慢性胃炎	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
大腸炎	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
口内乾燥	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胃酸過多	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
口唇腫脹	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
食道痙攣	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
耳下腺腫大	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
歯周病	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 ALL

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
口内炎	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
歯の障害	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
肛門出血	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
排便困難	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
大腸ポリープ	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
閉塞性膵炎	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
肝胆道系障害	11	0.8	2	0.1	2	0.1	2	0.1	2	0.1	1	0.1	1	0.1	1	0.1
肝機能異常	6	0.4	1	0.1	0	0.0	1	0.1	2	0.1	1	0.1	0	0.0	1	0.1
脂肪肝	3	0.2	0	0.0	2	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
肝腫大	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
非アルコール性脂肪肝	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胆嚢摘出術後症候群	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
高トランスアミナーゼ血症	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
皮膚および皮下組織障害	152	10.5	50	3.4	43	3.0	28	2.0	18	1.3	13	1.1	9	0.9	3	0.4
多汗症	48	3.3	20	1.4	15	1.1	8	0.6	3	0.2	2	0.2	0	0.0	0	0.0
ざ瘡	15	1.0	4	0.3	4	0.3	6	0.4	1	0.1	1	0.1	0	0.0	0	0.0
脱毛症	14	1.0	6	0.4	5	0.4	0	0.0	2	0.1	1	0.1	0	0.0	0	0.0
湿疹	13	0.9	4	0.3	1	0.1	4	0.3	1	0.1	2	0.2	1	0.1	0	0.0
蕁麻疹	13	0.9	3	0.2	4	0.3	1	0.1	4	0.3	2	0.2	1	0.1	0	0.0
発疹	9	0.6	4	0.3	2	0.1	1	0.1	0	0.0	1	0.1	0	0.0	1	0.1
接触皮膚炎	8	0.6	2	0.1	2	0.1	0	0.0	2	0.1	1	0.1	2	0.2	0	0.0
寝汗	8	0.6	3	0.2	3	0.2	2	0.1	1	0.1	0	0.0	0	0.0	0	0.0
皮膚嚢腫	5	0.3	0	0.0	1	0.1	0	0.0	1	0.1	1	0.1	1	0.1	1	0.1
そう痒症	5	0.3	4	0.3	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
アレルギー性皮膚炎	3	0.2	1	0.1	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
円形脱毛症	2	0.1	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 ALL

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
皮膚炎	2	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
薬疹	2	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0
皮膚乾燥	2	0.1	0	0.0	0	0.0	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0
男性型多毛症	2	0.1	0	0.0	0	0.0	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0
汗疹	2	0.1	0	0.0	0	0.0	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0
嚢胞性ざ瘡	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
冷汗	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
斑状出血	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
貨幣状湿疹	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
紅斑	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
過角化	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
陥入爪	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
間擦疹	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1
爪甲剥離症	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
ばら色粃糠疹	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
酒さ	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
脂漏性皮膚炎	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
皮膚剥脱	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
瘢痕痛	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
皮膚硬結	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
手皮膚炎	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
色素沈着障害	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
皮膚過形成	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
筋骨格系および結合組織障害	149	10.3	34	2.3	34	2.4	26	1.9	26	1.9	21	1.8	21	2.1	5	0.6
関節痛	52	3.6	8	0.6	9	0.6	6	0.4	11	0.8	13	1.1	5	0.5	2	0.2
背部痛	39	2.7	9	0.6	8	0.6	6	0.4	5	0.4	2	0.2	11	1.1	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 ALL

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
筋骨格硬直	22	1.5	8	0.6	4	0.3	3	0.2	5	0.4	1	0.1	1	0.1	0	0.0
四肢痛	10	0.7	3	0.2	3	0.2	2	0.1	0	0.0	0	0.0	1	0.1	1	0.1
筋肉痛	6	0.4	1	0.1	2	0.1	1	0.1	0	0.0	2	0.2	0	0.0	0	0.0
関節炎	5	0.3	0	0.0	1	0.1	0	0.0	2	0.1	1	0.1	1	0.1	0	0.0
筋痙縮	5	0.3	1	0.1	2	0.1	0	0.0	0	0.0	0	0.0	1	0.1	1	0.1
腱鞘炎	3	0.2	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0
側腹部痛	2	0.1	0	0.0	0	0.0	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0
頚部痛	2	0.1	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
足底筋膜炎	2	0.1	0	0.0	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
骨吸収亢進	2	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1
骨喪失	2	0.1	0	0.0	0	0.0	0	0.0	1	0.1	1	0.1	0	0.0	0	0.0
骨痛	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
滑液包炎	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
外骨腫	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
筋膜炎	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
筋骨格痛	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
骨粗鬆症	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
顎痛	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
関節周囲炎	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
仙腸骨炎	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
変形性脊椎症	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
滑膜炎	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
顎関節症候群	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
腱炎	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
仙骨痛	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
骨減少症	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 ALL

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
膝蓋大腿関節痛症候群	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
筋緊張	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
椎間板突出	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
半月板変性	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
脊椎痛	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
大転子疼痛症候群	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
腎および尿路障害	16	1.1	5	0.3	3	0.2	4	0.3	2	0.1	1	0.1	0	0.0	1	0.1
頻尿	7	0.5	3	0.2	1	0.1	3	0.2	0	0.0	0	0.0	0	0.0	0	0.0
排尿困難	2	0.1	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
膀胱痛	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
尿路結石	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血尿	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
緊張性膀胱	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
腎結石症	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
腎下垂症	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
夜間頻尿	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
腎嚢胞	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1
尿管結石症	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
妊娠、産褥および周産期の状態	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
異所性妊娠	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
生殖系および乳房障害	379	26.1	256	17.6	86	6.1	77	5.6	45	3.4	38	3.2	32	3.1	26	3.1
月経中間期出血	247	17.0	174	12.0	64	4.5	57	4.1	26	1.9	24	2.0	20	2.0	13	1.5
重度月経出血	61	4.2	41	2.8	4	0.3	3	0.2	6	0.4	3	0.3	5	0.5	5	0.6
骨盤痛	14	1.0	4	0.3	3	0.2	3	0.2	1	0.1	1	0.1	2	0.2	0	0.0
外陰腟乾燥	13	0.9	7	0.5	3	0.2	3	0.2	0	0.0	0	0.0	0	0.0	0	0.0
閉経期症状	12	0.8	5	0.3	3	0.2	3	0.2	1	0.1	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 ALL

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
異常子宮出血	10	0.7	8	0.6	3	0.2	1	0.1	1	0.1	1	0.1	2	0.2	1	0.1
腟分泌物	9	0.6	3	0.2	1	0.1	1	0.1	3	0.2	1	0.1	0	0.0	0	0.0
腟出血	9	0.6	6	0.4	0	0.0	2	0.1	0	0.0	2	0.2	1	0.1	0	0.0
無月経	8	0.6	6	0.4	0	0.0	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0
子宮出血	7	0.5	7	0.5	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
乳房圧痛	6	0.4	1	0.1	2	0.1	0	0.0	1	0.1	0	0.0	0	0.0	2	0.2
外陰腟そう痒症	6	0.4	1	0.1	1	0.1	2	0.1	1	0.1	1	0.1	0	0.0	0	0.0
子宮頚管ポリープ	3	0.2	0	0.0	0	0.0	0	0.0	1	0.1	1	0.1	0	0.0	1	0.1
子宮内膜症	3	0.2	0	0.0	0	0.0	1	0.1	1	0.1	0	0.0	1	0.1	0	0.0
不規則月経	3	0.2	2	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
卵巣嚢胞	3	0.2	0	0.0	0	0.0	0	0.0	1	0.1	1	0.1	0	0.0	1	0.1
乳房不快感	3	0.2	3	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
性器出血	3	0.2	3	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
月経困難症	2	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	1	0.1
子宮内膜増殖症	2	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	1	0.1
月経障害	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0	2	0.2	0	0.0	0	0.0
子宮ポリープ	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	1	0.1
外陰部湿疹	2	0.1	0	0.0	0	0.0	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0
外陰腟灼熱感	2	0.1	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
萎縮性外陰腟炎	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
乳房分泌	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
乳房変色	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
乳房腫大	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1
乳房痛	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
乳汁漏出症	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
過長過多不規則月経	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 ALL

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
月経遅延	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
希発月経	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
月経前症候群	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
外陰腟不快感	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
性交出血	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
卵巣出血	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
外陰腟痛	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
一般・全身障害および投与部位の状態	93	6.4	35	2.4	27	1.9	15	1.1	16	1.2	4	0.3	2	0.2	0	0.0
倦怠感	25	1.7	10	0.7	9	0.6	4	0.3	3	0.2	2	0.2	0	0.0	0	0.0
疲労	14	1.0	6	0.4	4	0.3	1	0.1	3	0.2	0	0.0	0	0.0	0	0.0
発熱	13	0.9	4	0.3	1	0.1	2	0.1	5	0.4	1	0.1	0	0.0	0	0.0
異常感	7	0.5	3	0.2	2	0.1	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0
浮腫	7	0.5	2	0.1	3	0.2	0	0.0	2	0.1	0	0.0	1	0.1	0	0.0
無力症	4	0.3	1	0.1	1	0.1	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0
末梢性浮腫	4	0.3	1	0.1	1	0.1	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0
疼痛	4	0.3	2	0.1	2	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
末梢腫脹	3	0.2	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
熱感	2	0.1	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
顔面腫脹	2	0.1	0	0.0	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
非心臓性胸痛	2	0.1	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胸部不快感	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
胸痛	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
悪寒	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
泣き	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
嚢胞	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
びくびく感	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 ALL

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
インフルエンザ様疾患	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
注射部位疼痛	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
口渇	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
炎症	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
血管穿刺部位内出血	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
血管穿刺部位疼痛	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血管穿刺部位知覚低下	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
臨床検査	226	15.6	49	3.4	57	4.0	65	4.7	44	3.3	17	1.4	23	2.3	19	2.3
アラニンアミノトランスフェラーゼ増加	59	4.1	7	0.5	19	1.3	13	0.9	12	0.9	4	0.3	6	0.6	2	0.2
アスパラギン酸アミノトランスフェラーゼ増加	46	3.2	6	0.4	13	0.9	13	0.9	9	0.7	3	0.3	1	0.1	2	0.2
γーグルタミルトランスフェラーゼ増加	39	2.7	8	0.6	18	1.3	6	0.4	6	0.4	0	0.0	0	0.0	1	0.1
血中クレアチンホスホキナーゼ増加	31	2.1	4	0.3	4	0.3	9	0.6	8	0.6	2	0.2	2	0.2	3	0.4
血中コレステロール増加	23	1.6	5	0.3	7	0.5	7	0.5	4	0.3	0	0.0	0	0.0	0	0.0
骨密度減少	22	1.5	2	0.1	0	0.0	1	0.1	4	0.3	0	0.0	10	1.0	5	0.6
低比重リポ蛋白増加	17	1.2	5	0.3	4	0.3	4	0.3	3	0.2	1	0.1	0	0.0	0	0.0
体重増加	14	1.0	4	0.3	0	0.0	2	0.1	1	0.1	1	0.1	1	0.1	5	0.6
グアナーゼ増加	14	1.0	5	0.3	4	0.3	3	0.2	2	0.1	0	0.0	0	0.0	0	0.0
血圧上昇	12	0.8	5	0.3	6	0.4	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
血中トリグリセリド増加	10	0.7	1	0.1	4	0.3	4	0.3	2	0.1	0	0.0	1	0.1	0	0.0
生化学的骨代謝マーカー上昇	10	0.7	0	0.0	0	0.0	8	0.6	1	0.1	1	0.1	0	0.0	0	0.0
活性化部分トロンボプラスチン時間延長	8	0.6	2	0.1	1	0.1	2	0.1	2	0.1	0	0.0	1	0.1	0	0.0
血中ビリルビン増加	8	0.6	1	0.1	2	0.1	1	0.1	1	0.1	3	0.3	0	0.0	1	0.1
酒石酸抵抗性酸ホスファターゼ増加	7	0.5	0	0.0	0	0.0	2	0.1	2	0.1	0	0.0	2	0.2	1	0.1
血中乳酸脱水素酵素増加	6	0.4	1	0.1	3	0.2	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0
体重減少	5	0.3	3	0.2	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 ALL

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
高比重リポ蛋白増加	4	0.3	2	0.1	0	0.0	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0
血中アルカリホスファターゼ増加	4	0.3	0	0.0	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	2	0.2
肝酵素上昇	4	0.3	1	0.1	1	0.1	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0
血中尿酸増加	3	0.2	1	0.1	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
尿中ケトン体陽性	3	0.2	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	1	0.1
肝機能検査値上昇	3	0.2	0	0.0	2	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
血中クレアチニン増加	2	0.1	0	0.0	0	0.0	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0
Ｃ－反応性蛋白増加	2	0.1	0	0.0	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
心電図ＱＴ延長	2	0.1	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
遊離脂肪酸増加	2	0.1	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
脂質増加	2	0.1	0	0.0	0	0.0	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0
血小板数減少	2	0.1	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
プロトロンビン時間短縮	2	0.1	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
血清フェリチン減少	2	0.1	0	0.0	0	0.0	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0
血中リン増加	2	0.1	0	0.0	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
Ｎ－テロペプチド	2	0.1	0	0.0	0	0.0	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0
血中ブドウ糖異常	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
血中鉄減少	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血中カリウム減少	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1
血中ナトリウム増加	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
血中尿素減少	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
体温低下	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
心電図異常	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
心電図Ｔ波逆転	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
尿中ブドウ糖陽性	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
平均赤血球容積異常	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 ALL

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
血中ミオグロビン増加	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
総蛋白増加	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
白血球数減少	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
白血球数増加	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
糖鎖抗原１９－９増加	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
血小板数増加	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
尿中蛋白陽性	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
トランスアミナーゼ上昇	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
便潜血陽性	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
ＳＡＲＳ－ＣｏＶ－２検査陽性	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
傷害、中毒および処置合併症	48	3.3	4	0.3	11	0.8	9	0.6	4	0.3	11	0.9	8	0.8	3	0.4
靱帯捻挫	8	0.6	0	0.0	1	0.1	1	0.1	2	0.1	3	0.3	0	0.0	1	0.1
挫傷	7	0.5	1	0.1	0	0.0	0	0.0	1	0.1	2	0.2	3	0.3	0	0.0
節足動物刺傷	3	0.2	1	0.1	0	0.0	0	0.0	1	0.1	1	0.1	0	0.0	0	0.0
転倒	3	0.2	0	0.0	0	0.0	1	0.1	0	0.0	2	0.2	0	0.0	0	0.0
処置による疼痛	3	0.2	0	0.0	1	0.1	0	0.0	0	0.0	1	0.1	1	0.1	0	0.0
足骨折	2	0.1	0	0.0	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
ワクチン接種合併症	2	0.1	0	0.0	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
肉離れ	2	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
熱傷	2	0.1	0	0.0	2	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
足関節部骨折	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
節足動物咬傷	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
背部損傷	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
第２度熱傷	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
凍瘡	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
上顎炎	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 ALL

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
人による咬傷	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
筋断裂	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
橈骨骨折	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1
肋骨骨折	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1
サンバーン	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
創傷	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
切開部位痛	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
四肢損傷	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
骨亀裂	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
皮膚擦過傷	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
熱中症	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
脊柱損傷	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
半月板損傷	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
外科および内科処置	2	0.1	0	0.0	0	0.0	0	0.0	1	0.1	1	0.1	0	0.0	0	0.0
人工流産	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
大腸ポリープ切除	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: Placebo

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
N	415	---	415	---	405	---	397	---	355	---	219	---	173	---	110	---
Any AEs	224	54.0	118	28.4	80	19.8	95	23.9	36	10.1	8	3.7	16	9.2	6	5.5
Leading to Death	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Other Serious Events	6	1.4	2	0.5	1	0.2	1	0.3	1	0.3	0	0.0	1	0.6	0	0.0
Leading to Discontinuation	20	4.8	9	2.2	2	0.5	5	1.3	3	0.8	1	0.5	1	0.6	0	0.0
Leading to Interruption	5	1.2	3	0.7	0	0.0	2	0.5	0	0.0	0	0.0	1	0.6	0	0.0
感染症および寄生虫症	71	17.1	19	4.6	19	4.7	33	8.3	8	2.3	4	1.8	3	1.7	1	0.9
上咽頭炎	35	8.4	11	2.7	8	2.0	17	4.3	2	0.6	1	0.5	0	0.0	0	0.0
副鼻腔炎	5	1.2	0	0.0	1	0.2	3	0.8	0	0.0	0	0.0	1	0.6	0	0.0
ウイルス性胃腸炎	4	1.0	0	0.0	2	0.5	2	0.5	0	0.0	0	0.0	0	0.0	0	0.0
インフルエンザ	4	1.0	0	0.0	1	0.2	2	0.5	0	0.0	1	0.5	0	0.0	1	0.9
扁桃炎	3	0.7	0	0.0	1	0.2	1	0.3	1	0.3	0	0.0	0	0.0	0	0.0
尿路感染	3	0.7	1	0.2	2	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
口腔ヘルペス	3	0.7	1	0.2	1	0.2	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
気管支炎	2	0.5	1	0.2	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
毛包炎	2	0.5	1	0.2	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
咽頭炎	2	0.5	0	0.0	1	0.2	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0
上気道感染	2	0.5	0	0.0	0	0.0	1	0.3	0	0.0	1	0.5	0	0.0	0	0.0
腟感染	2	0.5	0	0.0	0	0.0	0	0.0	2	0.6	0	0.0	0	0.0	0	0.0
外陰部腟カンジダ症	2	0.5	0	0.0	1	0.2	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
細菌性外陰腟炎	2	0.5	0	0.0	1	0.2	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
ＣＯＶＩＤ－１９	2	0.5	1	0.2	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
膀胱炎	1	0.2	0	0.0	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0
ヘルペスウイルス感染	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
下気道感染	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
外耳炎	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
歯周炎	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: Placebo

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
腎盂腎炎	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0
皮膚感染	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
歯膿瘍	1	0.2	0	0.0	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0
ウイルス性上気道感染	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
外陰部炎	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
ウイルス性下痢	1	0.2	0	0.0	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0
コロナウイルス感染	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
ヘリコバクター感染	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
癜風	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0
クラミジア感染	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
ウイルス性気道感染	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
乳房新生物	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
血液およびリンパ系障害	22	5.3	6	1.4	5	1.2	3	0.8	5	1.4	0	0.0	1	0.6	3	2.7
貧血	17	4.1	5	1.2	3	0.7	3	0.8	4	1.1	0	0.0	1	0.6	2	1.8
鉄欠乏性貧血	3	0.7	0	0.0	1	0.2	0	0.0	1	0.3	0	0.0	0	0.0	1	0.9
小球性貧血	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
失血性貧血	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
免疫系障害	3	0.7	3	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
季節性アレルギー	2	0.5	2	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
免疫反応	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
内分泌障害	2	0.5	1	0.2	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
高プロラクチン血症	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
甲状腺機能低下症	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
代謝および栄養障害	6	1.4	3	0.7	2	0.5	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: Placebo

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
高コレステロール血症	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
過食	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
高トリグリセリド血症	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
高尿酸血症	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
低カリウム血症	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
ビタミンD欠乏	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
食欲減退	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
精神障害	12	2.9	9	2.2	1	0.2	2	0.5	1	0.3	0	0.0	1	0.6	0	0.0
気分動揺	8	1.9	7	1.7	1	0.2	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
不眠症	3	0.7	1	0.2	0	0.0	1	0.3	1	0.3	0	0.0	0	0.0	0	0.0
不安	2	0.5	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0
易刺激性	2	0.5	1	0.2	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
うつ病	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
睡眠障害	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
睡眠の質低下	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
神経系障害	46	11.1	25	6.0	13	3.2	14	3.5	5	1.4	0	0.0	1	0.6	0	0.0
頭痛	30	7.2	16	3.9	10	2.5	10	2.5	5	1.4	0	0.0	0	0.0	0	0.0
浮動性めまい	5	1.2	1	0.2	2	0.5	1	0.3	0	0.0	0	0.0	1	0.6	0	0.0
片頭痛	5	1.2	2	0.5	1	0.2	2	0.5	0	0.0	0	0.0	0	0.0	0	0.0
傾眠	3	0.7	2	0.5	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
体位性めまい	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
感覚鈍麻	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
眼振	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
錯感覚	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
副鼻腔炎に伴う頭痛	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
眼障害	4	1.0	1	0.2	1	0.2	2	0.5	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: Placebo

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
眼瞼炎	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
霰粒腫	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
ドライアイ	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
強膜炎	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
耳および迷路障害	4	1.0	2	0.5	2	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
回転性めまい	2	0.5	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
耳管開放	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
頭位性回転性めまい	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
心臓障害	3	0.7	1	0.2	1	0.2	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
急性心筋梗塞	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
冠動脈疾患	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
動悸	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
上室性頻脈	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
虚血性心筋症	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
血管障害	26	6.3	12	2.9	6	1.5	5	1.3	1	0.3	1	0.5	0	0.0	1	0.9
ほてり	21	5.1	11	2.7	4	1.0	4	1.0	1	0.3	1	0.5	0	0.0	0	0.0
高血圧	4	1.0	1	0.2	1	0.2	1	0.3	0	0.0	0	0.0	0	0.0	1	0.9
静脈瘤	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
呼吸器、胸郭および縦隔障害	9	2.2	3	0.7	2	0.5	3	0.8	0	0.0	1	0.5	1	0.6	0	0.0
上気道の炎症	3	0.7	1	0.2	1	0.2	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
咳嗽	2	0.5	0	0.0	0	0.0	1	0.3	0	0.0	1	0.5	0	0.0	0	0.0
口腔咽頭痛	2	0.5	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0
喘息	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
労作性呼吸困難	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
鼻出血	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
胃腸障害	32	7.7	16	3.9	8	2.0	7	1.8	3	0.8	0	0.0	2	1.2	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: Placebo

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
歯痛	6	1.4	4	1.0	1	0.2	1	0.3	1	0.3	0	0.0	0	0.0	0	0.0
腹部膨満	5	1.2	2	0.5	1	0.2	1	0.3	1	0.3	0	0.0	0	0.0	0	0.0
腹痛	4	1.0	3	0.7	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
上腹部痛	4	1.0	1	0.2	1	0.2	2	0.5	0	0.0	0	0.0	1	0.6	0	0.0
悪心	4	1.0	1	0.2	2	0.5	1	0.3	0	0.0	0	0.0	1	0.6	0	0.0
下痢	3	0.7	3	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
嘔吐	3	0.7	0	0.0	1	0.2	2	0.5	0	0.0	0	0.0	0	0.0	0	0.0
腹部不快感	1	0.2	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
呼気臭	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
齲歯	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
口内乾燥	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
消化不良	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
鼓腸	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胃食道逆流性疾患	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
肛門周囲痛	1	0.2	0	0.0	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0
口内炎	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
軟便	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
歯嚢胞	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
肝胆道系障害	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
非アルコール性脂肪肝	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
皮膚および皮下組織障害	17	4.1	8	1.9	5	1.2	4	1.0	2	0.6	0	0.0	0	0.0	0	0.0
ざ瘡	6	1.4	4	1.0	0	0.0	0	0.0	2	0.6	0	0.0	0	0.0	0	0.0
脱毛症	2	0.5	2	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
接触皮膚炎	2	0.5	1	0.2	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
多汗症	2	0.5	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
皮膚炎	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: Placebo

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
アレルギー性皮膚炎	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
雀卵斑	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
紅斑	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
寝汗	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
発疹	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
丘疹性皮疹	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
皮膚色素過剰	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
皮膚局面	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
筋骨格系および結合組織障害	25	6.0	11	2.7	4	1.0	6	1.5	4	1.1	0	0.0	4	2.3	0	0.0
関節痛	9	2.2	3	0.7	1	0.2	2	0.5	1	0.3	0	0.0	2	1.2	0	0.0
背部痛	6	1.4	4	1.0	0	0.0	2	0.5	0	0.0	0	0.0	1	0.6	0	0.0
筋痙縮	3	0.7	1	0.2	0	0.0	1	0.3	1	0.3	0	0.0	0	0.0	0	0.0
四肢痛	2	0.5	2	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
側腹部痛	1	0.2	0	0.0	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0
関節腫脹	1	0.2	0	0.0	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0
筋肉痛	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
ミオキミア	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
頚部痛	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
変形性関節症	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
滑液嚢腫	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
骨減少症	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0
椎間板障害	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0
関節不安定	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
腎および尿路障害	5	1.2	0	0.0	1	0.2	2	0.5	1	0.3	0	0.0	0	0.0	1	0.9
排尿困難	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
糖尿	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: Placebo

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
頻尿	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
蛋白尿	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.9
腎臓痛	1	0.2	0	0.0	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0
生殖系および乳房障害	51	12.3	22	5.3	13	3.2	26	6.5	7	2.0	0	0.0	3	1.7	1	0.9
月経中間期出血	25	6.0	13	3.1	11	2.7	18	4.5	3	0.8	0	0.0	0	0.0	0	0.0
重度月経出血	6	1.4	1	0.2	0	0.0	3	0.8	2	0.6	0	0.0	0	0.0	0	0.0
骨盤痛	5	1.2	2	0.5	0	0.0	1	0.3	0	0.0	0	0.0	2	1.2	0	0.0
腟出血	4	1.0	2	0.5	1	0.2	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
乳房圧痛	2	0.5	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
不規則月経	2	0.5	0	0.0	0	0.0	2	0.5	0	0.0	0	0.0	0	0.0	0	0.0
外陰腟そう痒症	2	0.5	0	0.0	1	0.2	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0
乳房うっ滞	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
乳房痛	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
子宮頚管ポリープ	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0
月経困難症	1	0.2	0	0.0	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0
卵巣嚢胞	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
子宮ポリープ	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.9
子宮付属器痛	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
一般・全身障害および投与部位の状態	24	5.8	15	3.6	5	1.2	3	0.8	2	0.6	1	0.5	0	0.0	0	0.0
疲労	4	1.0	2	0.5	1	0.2	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
末梢性浮腫	4	1.0	2	0.5	1	0.2	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0
倦怠感	3	0.7	3	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胸部不快感	2	0.5	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胸痛	2	0.5	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
発熱	2	0.5	1	0.2	1	0.2	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
末梢腫脹	2	0.5	2	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: Placebo

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
顔面浮腫	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
熱感	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
空腹	1	0.2	0	0.0	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0
顔面腫脹	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
非心臓性胸痛	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
ワクチン接種部位疼痛	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
臨床検査	35	8.4	11	2.7	6	1.5	7	1.8	11	3.1	1	0.5	1	0.6	0	0.0
γ－グルタミルトランスフェラーゼ増加	6	1.4	5	1.2	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
血中クレアチンホスホキナーゼ増加	5	1.2	2	0.5	0	0.0	2	0.5	1	0.3	0	0.0	0	0.0	0	0.0
血清フェリチン減少	5	1.2	1	0.2	2	0.5	0	0.0	1	0.3	0	0.0	1	0.6	0	0.0
アラニンアミノトランスフェラーゼ増加	4	1.0	0	0.0	1	0.2	1	0.3	2	0.6	0	0.0	0	0.0	0	0.0
アスパラギン酸アミノトランスフェラーゼ増加	4	1.0	1	0.2	1	0.2	1	0.3	1	0.3	0	0.0	0	0.0	0	0.0
血中ビリルビン増加	2	0.5	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0
血中トリグリセリド増加	2	0.5	0	0.0	1	0.2	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0
ヘモグロビン減少	2	0.5	0	0.0	0	0.0	1	0.3	1	0.3	0	0.0	0	0.0	0	0.0
尿中ケトン体陽性	2	0.5	0	0.0	1	0.2	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0
活性化部分トロンボプラスチン時間延長	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血中コレステロール増加	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血中鉄減少	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
血中乳酸脱水素酵素増加	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
心電図異常	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
遊離脂肪酸増加	1	0.2	0	0.0	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0
尿中ブドウ糖	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
ヘマトクリット減少	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
国際標準比増加	1	0.2	0	0.0	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: Placebo

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
低比重リポ蛋白増加	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
プロトロンビン時間延長	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
体重増加	1	0.2	0	0.0	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0
白血球数増加	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
骨密度減少	1	0.2	0	0.0	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0
心電図異常T波	1	0.2	0	0.0	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0
血中アルカリホスファターゼ増加	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
肝酵素上昇	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
肝機能検査値上昇	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
傷害、中毒および処置合併症	10	2.4	2	0.5	3	0.7	2	0.5	2	0.6	1	0.5	0	0.0	0	0.0
靭帯捻挫	2	0.5	0	0.0	2	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
肉離れ	2	0.5	1	0.2	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
足関節部骨折	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
足骨折	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
刺創	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
熱傷	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
椎間板損傷	1	0.2	0	0.0	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0
皮膚擦過傷	1	0.2	0	0.0	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: Leuprorelin

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
N	187	---	187	---	187	---	185	---	182	---	179	---	176	---	174	---
Any AEs	181	96.8	151	80.7	100	53.5	84	45.4	76	41.8	56	31.3	42	23.9	42	24.1
Leading to Death	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Other Serious Events	2	1.1	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0
Leading to Discontinuation	9	4.8	5	2.7	1	0.5	2	1.1	0	0.0	1	0.6	0	0.0	0	0.0
Leading to Interruption	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
感染症および寄生虫症	86	46.0	15	8.0	8	4.3	20	10.8	18	9.9	20	11.2	16	9.1	13	7.5
上咽頭炎	37	19.8	7	3.7	4	2.1	7	3.8	9	4.9	6	3.4	5	2.8	7	4.0
ＣＯＶＩＤ－１９	11	5.9	3	1.6	0	0.0	2	1.1	3	1.6	2	1.1	1	0.6	0	0.0
コロナウイルス感染	8	4.3	1	0.5	1	0.5	1	0.5	2	1.1	0	0.0	1	0.6	2	1.1
インフルエンザ	5	2.7	0	0.0	0	0.0	0	0.0	1	0.5	3	1.7	0	0.0	1	0.6
副鼻腔炎	5	2.7	2	1.1	1	0.5	1	0.5	0	0.0	0	0.0	1	0.6	0	0.0
胃腸炎	4	2.1	1	0.5	0	0.0	0	0.0	0	0.0	1	0.6	2	1.1	0	0.0
扁桃炎	4	2.1	0	0.0	1	0.5	0	0.0	1	0.5	2	1.1	0	0.0	0	0.0
細菌性外陰膣炎	4	2.1	0	0.0	1	0.5	2	1.1	0	0.0	0	0.0	1	0.6	0	0.0
咽頭炎	3	1.6	0	0.0	0	0.0	0	0.0	0	0.0	2	1.1	1	0.6	0	0.0
外陰部膣カンジダ症	3	1.6	0	0.0	0	0.0	0	0.0	1	0.5	1	0.6	1	0.6	0	0.0
細菌性膣症	2	1.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	1	0.6
膀胱炎	2	1.1	0	0.0	0	0.0	2	1.1	0	0.0	0	0.0	0	0.0	0	0.0
陰部ヘルペス	2	1.1	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	1	0.6	0	0.0
口腔ヘルペス	2	1.1	0	0.0	0	0.0	2	1.1	0	0.0	0	0.0	0	0.0	0	0.0
結膜炎	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0	0	0.0
喉頭蓋炎	1	0.5	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
毛包炎	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0	0	0.0
歯肉炎	1	0.5	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
膿痂疹	1	0.5	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
爪囲炎	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: Leuprorelin

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
歯冠周囲炎	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0	0	0.0
歯髄炎	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
腎盂腎炎	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6
鼻炎	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0	0	0.0
上気道感染	1	0.5	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
前庭神経炎	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0
外陰部炎	1	0.5	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
ヘリコバクター性胃炎	1	0.5	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0
咽喉頭炎	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1	0.5	0	0.0	1	0.5	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0
メラノサイト性母斑	1	0.5	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
皮膚乳頭腫	1	0.5	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0
血液およびリンパ系障害	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0
リンパ節症	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0
免疫系障害	7	3.7	2	1.1	0	0.0	2	1.1	0	0.0	2	1.1	0	0.0	1	0.6
免疫反応	4	2.1	2	1.1	0	0.0	0	0.0	0	0.0	2	1.1	0	0.0	0	0.0
季節性アレルギー	3	1.6	0	0.0	0	0.0	2	1.1	0	0.0	0	0.0	0	0.0	1	0.6
内分泌障害	1	0.5	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
亜急性甲状腺炎	1	0.5	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
代謝および栄養障害	8	4.3	1	0.5	3	1.6	2	1.1	0	0.0	0	0.0	1	0.6	1	0.6
脂質異常症	3	1.6	0	0.0	2	1.1	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
食欲減退	2	1.1	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	1	0.6	0	0.0
脱水	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
糖尿病	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6
２型糖尿病	1	0.5	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: Leuprorelin

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
精神障害	19	10.2	5	2.7	6	3.2	7	3.8	1	0.5	1	0.6	0	0.0	2	1.1
不眠症	8	4.3	2	1.1	2	1.1	3	1.6	1	0.5	0	0.0	0	0.0	0	0.0
抑うつ気分	2	1.1	1	0.5	2	1.1	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
易刺激性	2	1.1	0	0.0	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
感情不安定	2	1.1	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0	1	0.6
アルコールによる宿酔	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
うつ病	1	0.5	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
中期不眠症	1	0.5	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
睡眠障害	1	0.5	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
抑うつ症状	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6
気分の落ち込み	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
神経系障害	37	19.8	13	7.0	10	5.3	4	2.2	8	4.4	5	2.8	3	1.7	3	1.7
頭痛	22	11.8	7	3.7	9	4.8	2	1.1	3	1.6	2	1.1	1	0.6	1	0.6
浮動性めまい	6	3.2	2	1.1	1	0.5	0	0.0	1	0.5	1	0.6	0	0.0	1	0.6
傾眠	5	2.7	3	1.6	0	0.0	0	0.0	1	0.5	1	0.6	0	0.0	0	0.0
手根管症候群	2	1.1	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	1	0.6	0	0.0
感覚鈍麻	2	1.1	0	0.0	0	0.0	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0
頚腕症候群	1	0.5	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
体位性めまい	1	0.5	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0
片頭痛	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
神経痛	1	0.5	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	1	0.6	0	0.0
緊張性頭痛	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0	0	0.0
肋間神経痛	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6
起立不耐性	1	0.5	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
眼障害	2	1.1	0	0.0	0	0.0	2	1.1	0	0.0	0	0.0	0	0.0	0	0.0
眼瞼炎	1	0.5	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: Leuprorelin

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
緑内障	1	0.5	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
耳および迷路障害	7	3.7	1	0.5	0	0.0	1	0.5	0	0.0	3	1.7	0	0.0	3	1.7
耳鳴	3	1.6	0	0.0	0	0.0	1	0.5	0	0.0	2	1.1	0	0.0	0	0.0
回転性めまい	2	1.1	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6
耳痛	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6
耳垢栓塞	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0	0	0.0
耳そう痒症	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6
心臓障害	9	4.8	3	1.6	3	1.6	0	0.0	2	1.1	0	0.0	1	0.6	0	0.0
動悸	5	2.7	2	1.1	1	0.5	0	0.0	2	1.1	0	0.0	0	0.0	0	0.0
心房細動	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0
洞性不整脈	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
洞性徐脈	1	0.5	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
心室性期外収縮	1	0.5	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血管障害	104	55.6	25	13.4	50	26.7	18	9.7	11	6.0	3	1.7	2	1.1	3	1.7
ほてり	103	55.1	25	13.4	49	26.2	18	9.7	10	5.5	2	1.1	2	1.1	3	1.7
高血圧	3	1.6	0	0.0	1	0.5	0	0.0	1	0.5	1	0.6	0	0.0	0	0.0
呼吸器、胸郭および縦隔障害	8	4.3	1	0.5	2	1.1	1	0.5	1	0.5	2	1.1	0	0.0	1	0.6
口腔咽頭痛	3	1.6	0	0.0	0	0.0	0	0.0	1	0.5	1	0.6	0	0.0	1	0.6
呼吸困難	1	0.5	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
鼻出血	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0	0	0.0
鼻閉	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
アレルギー性副鼻腔炎	1	0.5	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
口腔咽頭不快感	1	0.5	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
胃腸障害	33	17.6	8	4.3	6	3.2	10	5.4	6	3.3	3	1.7	2	1.1	4	2.3
便秘	5	2.7	1	0.5	1	0.5	0	0.0	3	1.6	0	0.0	0	0.0	0	0.0
下痢	4	2.1	3	1.6	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: Leuprorelin

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
嘔吐	4	2.1	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	2	1.1	1	0.6
悪心	3	1.6	0	0.0	2	1.1	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
歯痛	3	1.6	0	0.0	0	0.0	2	1.1	1	0.5	0	0.0	0	0.0	2	1.1
腹部不快感	2	1.1	1	0.5	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0	0	0.0
下腹部痛	2	1.1	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
上腹部痛	2	1.1	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	1	0.6
齲歯	2	1.1	0	0.0	0	0.0	2	1.1	0	0.0	0	0.0	0	0.0	0	0.0
腹部膨満	1	0.5	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
口角口唇炎	1	0.5	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
消化不良	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胃炎	1	0.5	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0
胃食道逆流性疾患	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
痔核	1	0.5	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
直腸ポリープ	1	0.5	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0
口内炎	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0	0	0.0
大腸ポリープ	1	0.5	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0
歯周の炎症	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0	0	0.0
軟便	1	0.5	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
肝胆道系障害	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0
肝機能異常	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0
皮膚および皮下組織障害	43	23.0	16	8.6	12	6.4	8	4.3	6	3.3	3	1.7	0	0.0	3	1.7
多汗症	22	11.8	7	3.7	7	3.7	5	2.7	2	1.1	1	0.6	0	0.0	0	0.0
ざ瘡	6	3.2	4	2.1	0	0.0	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0
皮膚炎	3	1.6	1	0.5	0	0.0	1	0.5	1	0.5	0	0.0	0	0.0	1	0.6
寝汗	2	1.1	0	0.0	2	1.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
手皮膚炎	2	1.1	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	1	0.6

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: Leuprorelin

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
脱毛症	1	0.5	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
寒冷蕁麻疹	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0	0	0.0
アレルギー性皮膚炎	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
皮膚乾燥	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
湿疹	1	0.5	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
陥入爪	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6
汗疹	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
発疹	1	0.5	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
脂漏性皮膚炎	1	0.5	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0
皮下気腫	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
蕁麻疹	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
乾皮症	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0	0	0.0
瘢痕そう痒感	1	0.5	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
皮膚硬結	1	0.5	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0
筋骨格系および結合組織障害	43	23.0	6	3.2	13	7.0	8	4.3	8	4.4	6	3.4	7	4.0	2	1.1
関節痛	16	8.6	1	0.5	4	2.1	3	1.6	2	1.1	3	1.7	2	1.1	1	0.6
筋骨格硬直	9	4.8	2	1.1	2	1.1	1	0.5	2	1.1	1	0.6	2	1.1	0	0.0
背部痛	7	3.7	2	1.1	3	1.6	2	1.1	0	0.0	1	0.6	0	0.0	0	0.0
筋肉痛	3	1.6	1	0.5	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
関節周囲炎	3	1.6	0	0.0	1	0.5	1	0.5	0	0.0	1	0.6	0	0.0	0	0.0
足底筋膜炎	3	1.6	0	0.0	0	0.0	1	0.5	1	0.5	0	0.0	1	0.6	0	0.0
変形性関節症	2	1.1	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0
筋痙縮	1	0.5	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
骨吸収亢進	1	0.5	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0
腱鞘炎	1	0.5	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0
弾発指	1	0.5	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: Leuprorelin

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
骨減少症	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0
椎間板突出	1	0.5	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
足根洞症候群	1	0.5	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0
椎間板障害	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6
生殖系および乳房障害	140	74.9	128	68.4	24	12.8	12	6.5	11	6.0	7	3.9	4	2.3	3	1.7
月経中間期出血	106	56.7	98	52.4	16	8.6	7	3.8	7	3.8	5	2.8	4	2.3	2	1.1
異常子宮出血	12	6.4	10	5.3	3	1.6	2	1.1	0	0.0	0	0.0	0	0.0	0	0.0
重度月経出血	9	4.8	8	4.3	1	0.5	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0
子宮出血	6	3.2	6	3.2	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
閉経期症状	5	2.7	4	2.1	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
乳房不快感	3	1.6	2	1.1	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0	0	0.0
卵巣嚢胞	2	1.1	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6
腟分泌物	2	1.1	2	1.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
腟出血	2	1.1	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
性器出血	2	1.1	1	0.5	1	0.5	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0
萎縮性外陰腟炎	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0	0	0.0
乳汁漏出症	1	0.5	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
月経障害	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
不規則月経	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
外陰嚢胞	1	0.5	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0
外陰腟そう痒症	1	0.5	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0
外陰腟痛	1	0.5	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
一般・全身障害および投与部位の状態	36	19.3	10	5.3	12	6.4	4	2.2	4	2.2	5	2.8	4	2.3	2	1.1
倦怠感	11	5.9	4	2.1	3	1.6	2	1.1	0	0.0	1	0.6	0	0.0	1	0.6
発熱	6	3.2	0	0.0	0	0.0	1	0.5	1	0.5	1	0.6	2	1.1	1	0.6
浮腫	5	2.7	5	2.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: Leuprorelin

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
注射部位内出血	3	1.6	0	0.0	2	1.1	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0
注射部位硬結	3	1.6	1	0.5	2	1.1	0	0.0	1	0.5	1	0.6	0	0.0	0	0.0
冷感	2	1.1	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6
末梢性浮腫	2	1.1	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	1	0.6	0	0.0
投与部位硬結	2	1.1	0	0.0	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
胸部不快感	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
疲労	1	0.5	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
注射部位疼痛	1	0.5	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
注射部位反応	1	0.5	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
腋窩痛	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0
末梢腫脹	1	0.5	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
投与部位疼痛	1	0.5	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
穿刺部位疼痛	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0	0	0.0
ワクチン接種部位関節痛	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0	0	0.0
臨床検査	38	20.3	1	0.5	3	1.6	9	4.9	13	7.1	5	2.8	7	4.0	9	5.2
酒石酸抵抗性酸ホスファターゼ増加	9	4.8	0	0.0	0	0.0	1	0.5	3	1.6	0	0.0	3	1.7	2	1.1
血中トリグリセリド増加	6	3.2	0	0.0	0	0.0	3	1.6	1	0.5	1	0.6	0	0.0	1	0.6
生化学的骨代謝マーカー上昇	6	3.2	0	0.0	0	0.0	2	1.1	3	1.6	0	0.0	0	0.0	1	0.6
γーグルタミルトランスフェラーゼ増加	5	2.7	0	0.0	1	0.5	2	1.1	0	0.0	1	0.6	0	0.0	1	0.6
血中コレステロール増加	4	2.1	0	0.0	2	1.1	0	0.0	2	1.1	0	0.0	0	0.0	0	0.0
低比重リポ蛋白増加	4	2.1	0	0.0	1	0.5	0	0.0	1	0.5	1	0.6	1	0.6	0	0.0
骨密度減少	4	2.1	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	1	0.6	2	1.1
血中アルカリホスファターゼ増加	3	1.6	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	2	1.1
Ｎ－テロペプチド	3	1.6	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	1	0.6	1	0.6
アラニンアミノトランスフェラーゼ増加	2	1.1	0	0.0	0	0.0	1	0.5	0	0.0	1	0.6	0	0.0	0	0.0
活性化部分トロンボプラスチン時間延長	1	0.5	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-1
Occurrence of Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: Leuprorelin

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
心電図ＱＴ延長	1	0.5	1	0.5	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0
眼圧上昇	1	0.5	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
体重増加	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0	0	0.0
Ａ型インフルエンザウイルス検査陽性	1	0.5	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0
肝機能検査値上昇	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0	0	0.0
ＳＡＲＳ－ＣｏＶ－２検査陽性	1	0.5	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
傷害、中毒および処置合併症	8	4.3	1	0.5	0	0.0	2	1.1	1	0.5	1	0.6	2	1.1	1	0.6
節足動物刺傷	2	1.1	1	0.5	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
足骨折	1	0.5	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
靭帯捻挫	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0
尾骨骨折	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0
挫傷	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6
靭帯断裂	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0	0	0.0
剥離骨折	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
熱中症	1	0.5	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0

Table 8.3.6-2
Occurrence of Treatment-Related Adverse Events by Onset Time
Safety Set

Study: KLH2301
Group: KLH-2109 200 mg

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
N	143	---	143	---	143	---	139	---	139	---	136	---	136	---	132	---
Any Treatment-Related AEs	120	83.9	89	62.2	59	41.3	44	31.7	26	18.7	19	14.0	15	11.0	11	8.3
Leading to Death	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Other Serious Events	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Leading to Discontinuation	8	5.6	4	2.8	3	2.1	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
Leading to Interruption	2	1.4	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
感染症および寄生虫症	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
膣感染	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
代謝および栄養障害	5	3.5	0	0.0	3	2.1	2	1.4	0	0.0	0	0.0	0	0.0	0	0.0
脂質異常症	5	3.5	0	0.0	3	2.1	2	1.4	0	0.0	0	0.0	0	0.0	0	0.0
精神障害	7	4.9	2	1.4	2	1.4	0	0.0	2	1.4	1	0.7	0	0.0	0	0.0
不眠症	3	2.1	0	0.0	1	0.7	0	0.0	1	0.7	1	0.7	0	0.0	0	0.0
うつ病	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
易刺激性	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
中期不眠症	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
睡眠障害	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
神経系障害	17	11.9	7	4.9	7	4.9	1	0.7	1	0.7	1	0.7	1	0.7	0	0.0
頭痛	9	6.3	4	2.8	3	2.1	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0
浮動性めまい	4	2.8	2	1.4	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0
傾眠	3	2.1	1	0.7	2	1.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
記憶障害	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
くも膜下出血	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
耳および迷路障害	2	1.4	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
回転性めまい	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
耳不快感	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
心臓障害	7	4.9	4	2.8	2	1.4	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0

Table 8.3.6-2
Occurrence of Treatment-Related Adverse Events by Onset Time
Safety Set

Study: KLH2301
Group: KLH-2109 200 mg

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
動悸	7	4.9	4	2.8	2	1.4	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0
血管障害	77	53.8	31	21.7	26	18.2	14	10.1	4	2.9	3	2.2	0	0.0	0	0.0
ほてり	77	53.8	31	21.7	26	18.2	14	10.1	4	2.9	3	2.2	0	0.0	0	0.0
高血圧	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
呼吸器、胸郭および縦隔障害	3	2.1	1	0.7	2	1.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
咽喉絞扼感	2	1.4	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
呼吸困難	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胃腸障害	6	4.2	1	0.7	3	2.1	0	0.0	0	0.0	1	0.7	0	0.0	1	0.8
便秘	2	1.4	0	0.0	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
悪心	2	1.4	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
腹痛	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.8
下痢	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
肝胆道系障害	4	2.8	0	0.0	0	0.0	1	0.7	1	0.7	1	0.7	0	0.0	1	0.8
肝機能異常	4	2.8	0	0.0	0	0.0	1	0.7	1	0.7	1	0.7	0	0.0	1	0.8
脂肪肝	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
皮膚および皮下組織障害	24	16.8	10	7.0	8	5.6	3	2.2	2	1.4	1	0.7	0	0.0	0	0.0
多汗症	19	13.3	8	5.6	7	4.9	2	1.4	1	0.7	1	0.7	0	0.0	0	0.0
脱毛症	4	2.8	2	1.4	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
冷汗	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
湿疹	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
そう痒症	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
蕁麻疹	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
筋骨格系および結合組織障害	25	17.5	6	4.2	4	2.8	5	3.6	5	3.6	3	2.2	4	2.9	2	1.5
関節痛	13	9.1	3	2.1	2	1.4	2	1.4	2	1.4	2	1.5	1	0.7	1	0.8
筋骨格硬直	10	7.0	3	2.1	1	0.7	1	0.7	3	2.2	1	0.7	1	0.7	0	0.0
背部痛	2	1.4	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0

Table 8.3.6-2
Occurrence of Treatment-Related Adverse Events by Onset Time
Safety Set

Study: KLH2301
Group: KLH-2109 200 mg

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
骨吸収亢進	2	1.4	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	1	0.8
腱鞘炎	2	1.4	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0
筋痙縮	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
四肢痛	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
腎および尿路障害	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
夜間頻尿	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
生殖系および乳房障害	74	51.7	65	45.5	14	9.8	9	6.5	5	3.6	8	5.9	6	4.4	3	2.3
月経中間期出血	53	37.1	45	31.5	10	7.0	5	3.6	3	2.2	6	4.4	4	2.9	2	1.5
閉経期症状	8	5.6	4	2.8	2	1.4	2	1.4	0	0.0	0	0.0	0	0.0	0	0.0
子宮出血	6	4.2	6	4.2	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
重度月経出血	6	4.2	6	4.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
異常子宮出血	6	4.2	4	2.8	3	2.1	1	0.7	1	0.7	1	0.7	1	0.7	1	0.8
不規則月経	3	2.1	2	1.4	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
腟分泌物	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
腟出血	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	1	0.7	0	0.0
乳房不快感	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
性器出血	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
一般・全身障害および投与部位の状態	12	8.4	2	1.4	6	4.2	2	1.4	3	2.2	1	0.7	1	0.7	0	0.0
倦怠感	8	5.6	2	1.4	4	2.8	1	0.7	2	1.4	1	0.7	0	0.0	0	0.0
浮腫	3	2.1	0	0.0	1	0.7	0	0.0	2	1.4	0	0.0	1	0.7	0	0.0
疲労	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
異常感	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
臨床検査	35	24.5	2	1.4	7	4.9	14	10.1	9	6.5	2	1.5	5	3.7	4	3.0
生化学的骨代謝マーカー上昇	10	7.0	0	0.0	0	0.0	8	5.8	1	0.7	1	0.7	0	0.0	0	0.0
骨密度減少	8	5.6	0	0.0	0	0.0	0	0.0	3	2.2	0	0.0	3	2.2	2	1.5
アラニンアミノトランスフェラーゼ増加	7	4.9	0	0.0	2	1.4	1	0.7	2	1.4	1	0.7	1	0.7	0	0.0

Table 8.3.6-2
Occurrence of Treatment-Related Adverse Events by Onset Time
Safety Set

Study: KLH2301
Group: KLH-2109 200 mg

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
酒石酸抵抗性酸ホスファターゼ増加	7	4.9	0	0.0	0	0.0	2	1.4	2	1.4	0	0.0	2	1.5	1	0.8
γーグルタミルトランスフェラーゼ増加	5	3.5	0	0.0	1	0.7	2	1.4	1	0.7	0	0.0	0	0.0	1	0.8
アスパラギン酸アミノトランスフェラーゼ増加	4	2.8	0	0.0	1	0.7	1	0.7	1	0.7	1	0.7	0	0.0	0	0.0
血中コレステロール増加	4	2.8	0	0.0	2	1.4	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0
血中トリグリセリド増加	3	2.1	0	0.0	1	0.7	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0
低比重リポ蛋白増加	2	1.4	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
肝機能検査値上昇	2	1.4	0	0.0	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
活性化部分トロンボプラスチン時間延長	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
心電図ＱＴ延長	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血中アルカリホスファターゼ増加	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.8
肝酵素上昇	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-2
Occurrence of Treatment-Related Adverse Events by Onset Time
Safety Set

Study: KLH2301
Group: Leuprorelin

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
N	144	---	144	---	144	---	142	---	140	---	137	---	135	---	133	---
Any Treatment-Related AEs	131	91.0	106	73.6	68	47.2	43	30.3	38	27.1	20	14.6	16	11.9	10	7.5
Leading to Death	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Other Serious Events	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Leading to Discontinuation	6	4.2	2	1.4	1	0.7	2	1.4	0	0.0	1	0.7	0	0.0	0	0.0
Leading to Interruption	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
感染症および寄生虫症	2	1.4	0	0.0	0	0.0	2	1.4	0	0.0	0	0.0	0	0.0	0	0.0
膀胱炎	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
細菌性外陰腟炎	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
代謝および栄養障害	2	1.4	0	0.0	2	1.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
脂質異常症	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
２型糖尿病	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
精神障害	13	9.0	3	2.1	5	3.5	5	3.5	1	0.7	0	0.0	0	0.0	1	0.8
不眠症	5	3.5	1	0.7	1	0.7	2	1.4	1	0.7	0	0.0	0	0.0	0	0.0
抑うつ気分	2	1.4	1	0.7	2	1.4	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
易刺激性	2	1.4	0	0.0	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
うつ病	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
睡眠障害	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
抑うつ症状	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.8
気分の落ち込み	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
神経系障害	18	12.5	9	6.3	5	3.5	2	1.4	3	2.1	3	2.2	1	0.7	0	0.0
頭痛	10	6.9	5	3.5	5	3.5	0	0.0	1	0.7	1	0.7	0	0.0	0	0.0
浮動性めまい	3	2.1	2	1.4	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
感覚鈍麻	2	1.4	0	0.0	0	0.0	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0
傾眠	2	1.4	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
手根管症候群	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
頚腕症候群	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-2
Occurrence of Treatment-Related Adverse Events by Onset Time
Safety Set

Study: KLH2301
Group: Leuprorelin

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
片頭痛	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
神経痛	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0
起立不耐性	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
眼障害	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
緑内障	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
耳および迷路障害	2	1.4	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
耳鳴	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
回転性めまい	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
心臓障害	3	2.1	1	0.7	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
動悸	2	1.4	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
洞性徐脈	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血管障害	77	53.5	17	11.8	39	27.1	13	9.2	8	5.7	3	2.2	2	1.5	2	1.5
ほてり	77	53.5	17	11.8	38	26.4	13	9.2	8	5.7	2	1.5	2	1.5	2	1.5
高血圧	2	1.4	0	0.0	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
呼吸器、胸郭および縦隔障害	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
呼吸困難	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胃腸障害	4	2.8	2	1.4	2	1.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
便秘	2	1.4	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
下腹部痛	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
消化不良	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
肝胆道系障害	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0
肝機能異常	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0
皮膚および皮下組織障害	25	17.4	8	5.6	9	6.3	4	2.8	4	2.9	1	0.7	0	0.0	0	0.0
多汗症	17	11.8	5	3.5	5	3.5	4	2.8	2	1.4	1	0.7	0	0.0	0	0.0
ざ瘡	4	2.8	3	2.1	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
寝汗	2	1.4	0	0.0	2	1.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-2
Occurrence of Treatment-Related Adverse Events by Onset Time
Safety Set

Study: KLH2301
Group: Leuprorelin

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
脱毛症	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
皮膚炎	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
発疹	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
脂漏性皮膚炎	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
筋骨格系および結合組織障害	24	16.7	1	0.7	7	4.9	5	3.5	5	3.6	5	3.6	1	0.7	1	0.8
関節痛	13	9.0	1	0.7	3	2.1	3	2.1	2	1.4	3	2.2	0	0.0	1	0.8
筋骨格硬直	3	2.1	0	0.0	1	0.7	1	0.7	1	0.7	1	0.7	0	0.0	0	0.0
関節周囲炎	2	1.4	0	0.0	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
背部痛	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
筋痙縮	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
変形性関節症	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
骨吸収亢進	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
弾発指	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
骨減少症	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0
生殖系および乳房障害	103	71.5	96	66.7	19	13.2	10	7.0	7	5.0	4	2.9	4	3.0	0	0.0
月経中間期出血	77	53.5	71	49.3	12	8.3	7	4.9	5	3.6	4	2.9	4	3.0	0	0.0
異常子宮出血	12	8.3	10	6.9	3	2.1	2	1.4	0	0.0	0	0.0	0	0.0	0	0.0
子宮出血	6	4.2	6	4.2	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
閉経期症状	4	2.8	4	2.8	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
重度月経出血	4	2.8	3	2.1	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
腟分泌物	2	1.4	2	1.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
腟出血	2	1.4	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
乳房不快感	2	1.4	2	1.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
性器出血	2	1.4	1	0.7	1	0.7	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0
月経障害	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
不規則月経	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-2
Occurrence of Treatment-Related Adverse Events by Onset Time
Safety Set

Study: KLH2301
Group: Leuprorelin

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
卵巣嚢胞	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
外陰腟そう痒症	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
一般・全身障害および投与部位の状態	19	13.2	8	5.6	9	6.3	2	1.4	2	1.4	1	0.7	1	0.7	0	0.0
倦怠感	8	5.6	4	2.8	3	2.1	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
注射部位硬結	3	2.1	1	0.7	2	1.4	0	0.0	1	0.7	1	0.7	0	0.0	0	0.0
浮腫	3	2.1	3	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
投与部位硬結	2	1.4	0	0.0	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0
胸部不快感	1	0.7	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
疲労	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
冷感	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
注射部位内出血	1	0.7	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0
注射部位反応	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
末梢性浮腫	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0
投与部位疼痛	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
臨床検査	30	20.8	0	0.0	3	2.1	7	4.9	10	7.1	5	3.6	6	4.4	7	5.3
酒石酸抵抗性酸ホスファターゼ増加	9	6.3	0	0.0	0	0.0	1	0.7	3	2.1	0	0.0	3	2.2	2	1.5
生化学的骨代謝マーカー上昇	6	4.2	0	0.0	0	0.0	2	1.4	3	2.1	0	0.0	0	0.0	1	0.8
血中トリグリセリド増加	5	3.5	0	0.0	0	0.0	3	2.1	1	0.7	1	0.7	0	0.0	0	0.0
γ－グルタミルトランスフェラーゼ増加	5	3.5	0	0.0	1	0.7	2	1.4	0	0.0	1	0.7	0	0.0	1	0.8
血中コレステロール増加	4	2.8	0	0.0	2	1.4	0	0.0	2	1.4	0	0.0	0	0.0	0	0.0
低比重リポ蛋白増加	4	2.8	0	0.0	1	0.7	0	0.0	1	0.7	1	0.7	1	0.7	0	0.0
骨密度減少	4	2.8	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	1	0.7	2	1.5
アラニンアミノトランスフェラーゼ増加	2	1.4	0	0.0	0	0.0	1	0.7	0	0.0	1	0.7	0	0.0	0	0.0
血中アルカリホスファターゼ増加	2	1.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	1	0.8
活性化部分トロンボプラスチン時間延長	1	0.7	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-2
Occurrence of Treatment-Related Adverse Events by Onset Time
Safety Set

Study: KLH2301
Group: Leuprorelin

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
体重増加	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0
肝機能検査値上昇	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	1	0.7	0	0.0	0	0.0

Table 8.3.6-2
Occurrence of Treatment-Related Adverse Events by Onset Time
Safety Set

Study: KLH2302
Group: KLH-2109 200 mg

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
N	48	---	48	---	48	---	48	---	47	---	27	---	0	---	0	---
Any Treatment-Related AEs	39	81.3	32	66.7	18	37.5	2	4.2	0	0.0	0	0.0	0	0.0	0	0.0
Leading to Death	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Other Serious Events	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Leading to Discontinuation	1	2.1	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Leading to Interruption	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
代謝および栄養障害	1	2.1	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
食欲減退	1	2.1	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
精神障害	1	2.1	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
中期不眠症	1	2.1	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
神経系障害	5	10.4	2	4.2	4	8.3	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
頭痛	3	6.3	2	4.2	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
浮動性めまい	2	4.2	0	0.0	2	4.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
傾眠	1	2.1	0	0.0	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血管障害	23	47.9	9	18.8	14	29.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
ほてり	23	47.9	9	18.8	14	29.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胃腸障害	3	6.3	3	6.3	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
上腹部痛	1	2.1	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
便秘	1	2.1	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
悪心	1	2.1	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
肝胆道系障害	1	2.1	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
肝機能異常	1	2.1	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
皮膚および皮下組織障害	6	12.5	4	8.3	2	4.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
多汗症	6	12.5	4	8.3	2	4.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
生殖系および乳房障害	25	52.1	25	52.1	1	2.1	2	4.2	0	0.0	0	0.0	0	0.0	0	0.0
月経中間期出血	20	41.7	20	41.7	1	2.1	2	4.2	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-2
Occurrence of Treatment-Related Adverse Events by Onset Time
Safety Set

Study: KLH2302
Group: KLH-2109 200 mg

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
異常子宮出血	4	8.3	4	8.3	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
性器出血	1	2.1	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
一般・全身障害および投与部位の状態	2	4.2	0	0.0	2	4.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
熱感	1	2.1	0	0.0	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
倦怠感	1	2.1	0	0.0	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
臨床検査	3	6.3	0	0.0	3	6.3	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血中コレステロール増加	2	4.2	0	0.0	2	4.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
低比重リポ蛋白増加	2	4.2	0	0.0	2	4.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
γ－グルタミルトランスフェラーゼ増加	1	2.1	0	0.0	1	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-2
Occurrence of Treatment-Related Adverse Events by Onset Time
Safety Set

Study: KLH2302
Group: Placebo

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
N	41	---	41	---	41	---	40	---	40	---	17	---	0	---	0	---
Any Treatment-Related AEs	17	41.5	9	22.0	10	24.4	11	27.5	2	5.0	0	0.0	0	0.0	0	0.0
Leading to Death	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Other Serious Events	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Leading to Discontinuation	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Leading to Interruption	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
耳および迷路障害	1	2.4	0	0.0	1	2.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
回転性めまい	1	2.4	0	0.0	1	2.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
皮膚および皮下組織障害	1	2.4	0	0.0	1	2.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
多汗症	1	2.4	0	0.0	1	2.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
生殖系および乳房障害	15	36.6	9	22.0	8	19.5	11	27.5	2	5.0	0	0.0	0	0.0	0	0.0
月経中間期出血	13	31.7	9	22.0	8	19.5	9	22.5	2	5.0	0	0.0	0	0.0	0	0.0
不規則月経	2	4.9	0	0.0	0	0.0	2	5.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-2
Occurrence of Treatment-Related Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 200 mg

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
N	498	---	498	---	483	---	471	---	460	---	411	---	357	---	297	---
Any Treatment-Related AEs	315	63.3	243	48.8	127	26.3	71	15.1	48	10.4	27	6.6	19	5.3	12	4.0
Leading to Death	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Other Serious Events	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Leading to Discontinuation	33	6.6	16	3.2	7	1.4	5	1.1	3	0.7	0	0.0	3	0.8	1	0.3
Leading to Interruption	6	1.2	3	0.6	1	0.2	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0
感染症および寄生虫症	3	0.6	1	0.2	2	0.4	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0
尿路感染	1	0.2	0	0.0	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
腟感染	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
外陰腟真菌感染	1	0.2	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
カンジダ感染	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
代謝および栄養障害	8	1.6	2	0.4	4	0.8	2	0.4	0	0.0	0	0.0	0	0.0	0	0.0
脂質異常症	5	1.0	0	0.0	3	0.6	2	0.4	0	0.0	0	0.0	0	0.0	0	0.0
食欲減退	3	0.6	2	0.4	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
精神障害	34	6.8	21	4.2	7	1.4	3	0.6	2	0.4	2	0.5	0	0.0	0	0.0
リビドー減退	7	1.4	3	0.6	2	0.4	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0
不眠症	6	1.2	2	0.4	2	0.4	1	0.2	1	0.2	1	0.2	0	0.0	0	0.0
不安	5	1.0	4	0.8	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
気分動揺	5	1.0	3	0.6	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
うつ病	2	0.4	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
易刺激性	2	0.4	1	0.2	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
中期不眠症	2	0.4	2	0.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
感情不安定	2	0.4	2	0.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
錯乱状態	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
神経過敏	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
睡眠障害	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
睡眠の質低下	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-2
Occurrence of Treatment-Related Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 200 mg

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
神経系障害	64	12.9	40	8.0	18	3.7	5	1.1	5	1.1	2	0.5	1	0.3	0	0.0
頭痛	40	8.0	25	5.0	7	1.4	4	0.8	4	0.9	2	0.5	0	0.0	0	0.0
浮動性めまい	14	2.8	8	1.6	5	1.0	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0
傾眠	7	1.4	4	0.8	3	0.6	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
片頭痛	3	0.6	2	0.4	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
嗜眠	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
記憶障害	1	0.2	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
鎮静	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
くも膜下出血	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
振戦	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
認知障害	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
眼障害	2	0.4	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
眼部腫脹	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
霧視	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
耳および迷路障害	2	0.4	1	0.2	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
回転性めまい	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
耳不快感	1	0.2	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
心臓障害	8	1.6	5	1.0	2	0.4	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0
動悸	7	1.4	4	0.8	2	0.4	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0
頻脈	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血管障害	215	43.2	117	23.5	72	14.9	23	4.9	9	2.0	4	1.0	0	0.0	0	0.0
ほてり	214	43.0	117	23.5	72	14.9	22	4.7	9	2.0	4	1.0	0	0.0	0	0.0
潮紅	1	0.2	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
高血圧	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
呼吸器、胸郭および縦隔障害	4	0.8	1	0.2	3	0.6	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
咽喉絞扼感	2	0.4	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-2
Occurrence of Treatment-Related Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 200 mg

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
呼吸困難	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
アレルギー性咳嗽	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胃腸障害	36	7.2	28	5.6	7	1.4	0	0.0	1	0.2	1	0.2	0	0.0	1	0.3
悪心	20	4.0	18	3.6	3	0.6	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
便秘	5	1.0	2	0.4	1	0.2	0	0.0	1	0.2	1	0.2	0	0.0	0	0.0
上腹部痛	3	0.6	2	0.4	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
下痢	3	0.6	2	0.4	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
腹部不快感	2	0.4	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
腹痛	2	0.4	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.3
嘔吐	2	0.4	2	0.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
腹部膨満	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
消化不良	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胃炎	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
肝胆道系障害	6	1.2	1	0.2	0	0.0	2	0.4	1	0.2	1	0.2	0	0.0	1	0.3
肝機能異常	5	1.0	1	0.2	0	0.0	1	0.2	1	0.2	1	0.2	0	0.0	1	0.3
脂肪肝	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0
高トランスアミナーゼ血症	1	0.2	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
皮膚および皮下組織障害	49	9.8	21	4.2	17	3.5	7	1.5	4	0.9	2	0.5	0	0.0	0	0.0
多汗症	36	7.2	15	3.0	13	2.7	4	0.8	2	0.4	2	0.5	0	0.0	0	0.0
脱毛症	6	1.2	3	0.6	1	0.2	0	0.0	2	0.4	0	0.0	0	0.0	0	0.0
寝汗	4	0.8	2	0.4	2	0.4	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
ざ瘡	2	0.4	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
冷汗	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
アレルギー性皮膚炎	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
湿疹	1	0.2	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
そう痒症	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-2
Occurrence of Treatment-Related Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 200 mg

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
蕁麻疹	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
筋骨格系および結合組織障害	33	6.6	7	1.4	4	0.8	6	1.3	7	1.5	6	1.5	5	1.4	2	0.7
関節痛	19	3.8	3	0.6	2	0.4	3	0.6	3	0.7	5	1.2	2	0.6	1	0.3
筋骨格硬直	11	2.2	4	0.8	1	0.2	1	0.2	3	0.7	1	0.2	1	0.3	0	0.0
背部痛	2	0.4	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	1	0.3	0	0.0
骨吸収亢進	2	0.4	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	1	0.3
腱鞘炎	2	0.4	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	1	0.3	0	0.0
筋痙縮	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
四肢痛	1	0.2	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
骨喪失	1	0.2	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
腎および尿路障害	3	0.6	2	0.4	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
頻尿	2	0.4	2	0.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
夜間頻尿	1	0.2	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
生殖系および乳房障害	141	28.3	122	24.5	21	4.3	14	3.0	9	2.0	9	2.2	6	1.7	3	1.0
月経中間期出血	95	19.1	85	17.1	13	2.7	8	1.7	4	0.9	6	1.5	4	1.1	2	0.7
重度月経出血	12	2.4	11	2.2	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
異常子宮出血	10	2.0	8	1.6	3	0.6	1	0.2	1	0.2	1	0.2	1	0.3	1	0.3
閉経期症状	8	1.6	4	0.8	2	0.4	2	0.4	0	0.0	0	0.0	0	0.0	0	0.0
子宮出血	6	1.2	6	1.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
外陰腟乾燥	6	1.2	3	0.6	2	0.4	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
腟出血	5	1.0	4	0.8	0	0.0	0	0.0	0	0.0	2	0.5	1	0.3	0	0.0
不規則月経	3	0.6	2	0.4	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
骨盤痛	3	0.6	2	0.4	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
腟分泌物	2	0.4	1	0.2	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
乳房不快感	2	0.4	2	0.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
性器出血	2	0.4	2	0.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-2
Occurrence of Treatment-Related Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 200 mg

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
無月経	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
月経困難症	1	0.2	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
子宮内膜増殖症	1	0.2	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0
乳汁漏出症	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
月経遅延	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
外陰腟不快感	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
外陰腟灼熱感	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
一般・全身障害および投与部位の状態	25	5.0	7	1.4	11	2.3	4	0.8	3	0.7	1	0.2	2	0.6	0	0.0
倦怠感	12	2.4	3	0.6	6	1.2	2	0.4	2	0.4	1	0.2	0	0.0	0	0.0
疲労	5	1.0	2	0.4	2	0.4	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
浮腫	4	0.8	1	0.2	1	0.2	0	0.0	2	0.4	0	0.0	1	0.3	0	0.0
疼痛	2	0.4	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
無力症	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
異常感	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
熱感	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
末梢腫脹	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.3	0	0.0
臨床検査	69	13.9	13	2.6	18	3.7	19	4.0	14	3.0	4	1.0	8	2.2	5	1.7
アラニンアミノトランスフェラーゼ増加	18	3.6	4	0.8	5	1.0	2	0.4	4	0.9	2	0.5	1	0.3	0	0.0
γーグルタミルトランスフェラーゼ増加	12	2.4	1	0.2	7	1.4	2	0.4	1	0.2	0	0.0	0	0.0	1	0.3
骨密度減少	12	2.4	0	0.0	0	0.0	0	0.0	3	0.7	0	0.0	6	1.7	3	1.0
アスパラギン酸アミノトランスフェラーゼ増加	11	2.2	2	0.4	3	0.6	2	0.4	3	0.7	1	0.2	0	0.0	0	0.0
血中コレステロール増加	11	2.2	3	0.6	4	0.8	2	0.4	2	0.4	0	0.0	0	0.0	0	0.0
生化学的骨代謝マーカー上昇	10	2.0	0	0.0	0	0.0	8	1.7	1	0.2	1	0.2	0	0.0	0	0.0
低比重リポ蛋白増加	9	1.8	4	0.8	3	0.6	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0
酒石酸抵抗性酸ホスファターゼ増加	7	1.4	0	0.0	0	0.0	2	0.4	2	0.4	0	0.0	2	0.6	1	0.3

Table 8.3.6-2
Occurrence of Treatment-Related Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 200 mg

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
グアナーゼ増加	6	1.2	3	0.6	1	0.2	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0
血中トリグリセリド増加	4	0.8	1	0.2	1	0.2	2	0.4	1	0.2	0	0.0	0	0.0	0	0.0
活性化部分トロンボプラスチン時間延長	3	0.6	2	0.4	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
肝機能検査値上昇	3	0.6	0	0.0	2	0.4	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
遊離脂肪酸増加	2	0.4	2	0.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血中アルカリホスファターゼ増加	2	0.4	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	1	0.3
肝酵素上昇	2	0.4	0	0.0	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
血圧上昇	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
心電図ＱＴ延長	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
尿中ブドウ糖陽性	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
高比重リポ蛋白増加	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
プロトロンビン時間短縮	1	0.2	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0
体重減少	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
体重増加	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0	0	0.0
トランスアミナーゼ上昇	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-2
Occurrence of Treatment-Related Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 ALL

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
N	1452	---	1452	---	1416	---	1385	---	1334	---	1182	---	1016	---	843	---
Any Treatment-Related AEs	729	50.2	496	34.2	275	19.4	190	13.7	123	9.2	71	6.0	56	5.5	32	3.8
Leading to Death	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Other Serious Events	4	0.3	0	0.0	1	0.1	1	0.1	0	0.0	2	0.2	0	0.0	0	0.0
Leading to Discontinuation	66	4.5	29	2.0	17	1.2	9	0.6	6	0.4	5	0.4	3	0.3	1	0.1
Leading to Interruption	12	0.8	4	0.3	2	0.1	2	0.1	1	0.1	3	0.3	0	0.0	0	0.0
感染症および寄生虫症	8	0.6	3	0.2	3	0.2	2	0.1	2	0.1	0	0.0	0	0.0	0	0.0
膿疱性ざ瘡	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
結膜炎	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胃腸炎	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
尿路感染	1	0.1	0	0.0	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
腟感染	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
外陰部腟カンジダ症	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
癜風	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
外陰腟真菌感染	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
カンジダ感染	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
血管腫	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
血液およびリンパ系障害	5	0.3	1	0.1	1	0.1	2	0.1	1	0.1	0	0.0	0	0.0	0	0.0
貧血	3	0.2	0	0.0	1	0.1	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0
好中球減少症	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血小板減少症	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
代謝および栄養障害	17	1.2	9	0.6	4	0.3	3	0.2	1	0.1	0	0.0	0	0.0	1	0.1
脂質異常症	10	0.7	3	0.2	3	0.2	3	0.2	1	0.1	0	0.0	0	0.0	1	0.1
食欲減退	5	0.3	4	0.3	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
過食	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-2
Occurrence of Treatment-Related Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 ALL

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
食欲亢進	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
精神障害	61	4.2	34	2.3	11	0.8	9	0.6	4	0.3	3	0.3	1	0.1	0	0.0
気分動揺	16	1.1	8	0.6	2	0.1	4	0.3	1	0.1	1	0.1	0	0.0	0	0.0
リビドー減退	10	0.7	5	0.3	3	0.2	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0
不眠症	7	0.5	2	0.1	3	0.2	1	0.1	1	0.1	1	0.1	0	0.0	0	0.0
感情不安定	7	0.5	5	0.3	0	0.0	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0
不安	6	0.4	5	0.3	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
易刺激性	5	0.3	1	0.1	1	0.1	1	0.1	2	0.1	0	0.0	0	0.0	0	0.0
うつ病	3	0.2	2	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
中期不眠症	2	0.1	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
気分変化	2	0.1	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
睡眠障害	2	0.1	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
錯乱状態	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
抑うつ気分	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
リビドー消失	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
神経過敏	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
睡眠の質低下	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
注意欠如・多動性障害	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
神経系障害	152	10.5	100	6.9	34	2.4	16	1.2	12	0.9	7	0.6	4	0.4	0	0.0
頭痛	104	7.2	67	4.6	17	1.2	14	1.0	10	0.7	7	0.6	2	0.2	0	0.0
浮動性めまい	31	2.1	18	1.2	9	0.6	2	0.1	2	0.1	0	0.0	1	0.1	0	0.0
傾眠	13	0.9	10	0.7	3	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
片頭痛	8	0.6	4	0.3	3	0.2	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
体位性めまい	3	0.2	2	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
くも膜下出血	2	0.1	0	0.0	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
認知障害	2	0.1	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-2
Occurrence of Treatment-Related Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 ALL

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
味覚不全	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
感覚鈍麻	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
嗜眠	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
記憶障害	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
眼振	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
鎮静	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
緊張性頭痛	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
振戦	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
眼障害	2	0.1	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
眼部腫脹	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
霧視	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
耳および迷路障害	6	0.4	3	0.2	2	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
回転性めまい	5	0.3	3	0.2	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
耳不快感	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
心臓障害	16	1.1	9	0.6	4	0.3	4	0.3	1	0.1	0	0.0	0	0.0	1	0.1
動悸	10	0.7	6	0.4	3	0.2	3	0.2	1	0.1	0	0.0	0	0.0	0	0.0
狭心症	2	0.1	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
頻脈	2	0.1	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
上室性期外収縮	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
心室性期外収縮	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1
血管障害	359	24.7	201	13.8	105	7.4	38	2.7	20	1.5	9	0.8	5	0.5	0	0.0
ほてり	356	24.5	200	13.8	105	7.4	37	2.7	20	1.5	8	0.7	5	0.5	0	0.0
高血圧	3	0.2	1	0.1	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
潮紅	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
呼吸器、胸郭および縦隔障害	6	0.4	1	0.1	3	0.2	0	0.0	1	0.1	1	0.1	0	0.0	0	0.0
咽喉絞扼感	3	0.2	1	0.1	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0

Table 8.3.6-2
Occurrence of Treatment-Related Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 ALL

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
喘息	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
呼吸困難	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
アレルギー性咳嗽	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胃腸障害	92	6.3	62	4.3	19	1.3	3	0.2	8	0.6	5	0.4	1	0.1	1	0.1
悪心	40	2.8	31	2.1	7	0.5	2	0.1	3	0.2	1	0.1	1	0.1	0	0.0
上腹部痛	11	0.8	6	0.4	3	0.2	0	0.0	0	0.0	2	0.2	0	0.0	0	0.0
便秘	10	0.7	3	0.2	3	0.2	1	0.1	2	0.1	1	0.1	0	0.0	0	0.0
下痢	9	0.6	7	0.5	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
腹部不快感	7	0.5	5	0.3	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
腹痛	7	0.5	4	0.3	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	1	0.1
嘔吐	6	0.4	6	0.4	1	0.1	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0
腹部膨満	5	0.3	4	0.3	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
鼓腸	2	0.1	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
下腹部痛	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
消化不良	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胃炎	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胃食道逆流性疾患	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胃酸過多	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
肝胆道系障害	7	0.5	1	0.1	1	0.1	2	0.1	1	0.1	1	0.1	0	0.0	1	0.1
肝機能異常	5	0.3	1	0.1	0	0.0	1	0.1	1	0.1	1	0.1	0	0.0	1	0.1
脂肪肝	2	0.1	0	0.0	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
高トランスアミナーゼ血症	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
皮膚および皮下組織障害	87	6.0	35	2.4	30	2.1	14	1.0	7	0.5	4	0.3	0	0.0	0	0.0
多汗症	48	3.3	20	1.4	15	1.1	8	0.6	3	0.2	2	0.2	0	0.0	0	0.0
脱毛症	12	0.8	6	0.4	4	0.3	0	0.0	2	0.1	0	0.0	0	0.0	0	0.0
ざ瘡	11	0.8	3	0.2	3	0.2	3	0.2	1	0.1	1	0.1	0	0.0	0	0.0

Table 8.3.6-2
Occurrence of Treatment-Related Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 ALL

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
寝汗	8	0.6	3	0.2	3	0.2	2	0.1	1	0.1	0	0.0	0	0.0	0	0.0
蕁麻疹	4	0.3	2	0.1	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
アレルギー性皮膚炎	2	0.1	0	0.0	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
発疹	2	0.1	0	0.0	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
円形脱毛症	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
冷汗	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
皮膚炎	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
湿疹	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
男性型多毛症	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
ばら色粃糠疹	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
そう痒症	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
筋骨格系および結合組織障害	54	3.7	14	1.0	7	0.5	9	0.6	11	0.8	11	0.9	5	0.5	2	0.2
関節痛	27	1.9	4	0.3	4	0.3	4	0.3	5	0.4	8	0.7	2	0.2	1	0.1
筋骨格硬直	18	1.2	7	0.5	2	0.1	2	0.1	5	0.4	1	0.1	1	0.1	0	0.0
背部痛	3	0.2	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0
筋肉痛	2	0.1	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
四肢痛	2	0.1	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
骨吸収亢進	2	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1
腱鞘炎	2	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
骨喪失	2	0.1	0	0.0	0	0.0	0	0.0	1	0.1	1	0.1	0	0.0	0	0.0
骨痛	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
筋痙縮	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
筋緊張	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
腎および尿路障害	6	0.4	3	0.2	2	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
頻尿	4	0.3	3	0.2	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
排尿困難	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-2
Occurrence of Treatment-Related Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 ALL

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
夜間頻尿	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
生殖系および乳房障害	336	23.1	242	16.7	78	5.5	71	5.1	38	2.8	32	2.7	25	2.5	17	2.0
月経中間期出血	240	16.5	171	11.8	63	4.4	57	4.1	26	1.9	23	1.9	19	1.9	9	1.1
重度月経出血	58	4.0	39	2.7	4	0.3	3	0.2	6	0.4	3	0.3	4	0.4	5	0.6
閉経期症状	12	0.8	5	0.3	3	0.2	3	0.2	1	0.1	0	0.0	0	0.0	0	0.0
外陰腟乾燥	11	0.8	6	0.4	2	0.1	3	0.2	0	0.0	0	0.0	0	0.0	0	0.0
異常子宮出血	10	0.7	8	0.6	3	0.2	1	0.1	1	0.1	1	0.1	1	0.1	1	0.1
腟出血	8	0.6	5	0.3	0	0.0	2	0.1	0	0.0	2	0.2	1	0.1	0	0.0
無月経	7	0.5	5	0.3	0	0.0	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0
子宮出血	7	0.5	7	0.5	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
骨盤痛	6	0.4	3	0.2	1	0.1	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0
腟分泌物	5	0.3	2	0.1	1	0.1	0	0.0	1	0.1	1	0.1	0	0.0	0	0.0
不規則月経	3	0.2	2	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
乳房不快感	3	0.2	3	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
月経障害	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0	2	0.2	0	0.0	0	0.0
性器出血	2	0.1	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
外陰腟灼熱感	2	0.1	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
乳房痛	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
乳房圧痛	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1
月経困難症	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
子宮内膜増殖症	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
乳汁漏出症	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
月経遅延	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
希発月経	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
卵巣嚢胞	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1
月経前症候群	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-2
Occurrence of Treatment-Related Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 ALL

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
外陰腟不快感	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
外陰腟そう痒症	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
一般・全身障害および投与部位の状態	52	3.6	16	1.1	19	1.3	9	0.6	8	0.6	2	0.2	2	0.2	0	0.0
倦怠感	19	1.3	6	0.4	8	0.6	3	0.2	3	0.2	2	0.2	0	0.0	0	0.0
疲労	8	0.6	3	0.2	2	0.1	1	0.1	2	0.1	0	0.0	0	0.0	0	0.0
浮腫	7	0.5	2	0.1	3	0.2	0	0.0	2	0.1	0	0.0	1	0.1	0	0.0
異常感	5	0.3	1	0.1	2	0.1	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0
無力症	4	0.3	1	0.1	1	0.1	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0
末梢性浮腫	3	0.2	0	0.0	1	0.1	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0
熱感	2	0.1	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
疼痛	2	0.1	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
末梢腫脹	2	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0
悪寒	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
口渇	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
臨床検査	145	10.0	26	1.8	37	2.6	43	3.1	31	2.3	8	0.7	18	1.8	10	1.2
アラニンアミノトランスフェラーゼ増加	46	3.2	4	0.3	14	1.0	10	0.7	11	0.8	3	0.3	4	0.4	2	0.2
アスパラギン酸アミノトランスフェラーゼ増加	35	2.4	3	0.2	8	0.6	11	0.8	9	0.7	2	0.2	1	0.1	2	0.2
γ－グルタミルトランスフェラーゼ増加	22	1.5	1	0.1	12	0.8	3	0.2	5	0.4	0	0.0	0	0.0	1	0.1
血中コレステロール増加	21	1.4	4	0.3	7	0.5	6	0.4	4	0.3	0	0.0	0	0.0	0	0.0
骨密度減少	19	1.3	0	0.0	0	0.0	1	0.1	4	0.3	0	0.0	10	1.0	4	0.5
低比重リポ蛋白増加	14	1.0	4	0.3	4	0.3	3	0.2	3	0.2	0	0.0	0	0.0	0	0.0
グアナーゼ増加	14	1.0	5	0.3	4	0.3	3	0.2	2	0.1	0	0.0	0	0.0	0	0.0
生化学的骨代謝マーカー上昇	10	0.7	0	0.0	0	0.0	8	0.6	1	0.1	1	0.1	0	0.0	0	0.0
血中トリグリセリド増加	8	0.6	1	0.1	3	0.2	4	0.3	1	0.1	0	0.0	1	0.1	0	0.0
活性化部分トロンボプラスチン時間延長	7	0.5	2	0.1	1	0.1	2	0.1	1	0.1	0	0.0	1	0.1	0	0.0

Table 8.3.6-2
Occurrence of Treatment-Related Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 ALL

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
酒石酸抵抗性酸ホスファターゼ増加	7	0.5	0	0.0	0	0.0	2	0.1	2	0.1	0	0.0	2	0.2	1	0.1
体重増加	6	0.4	2	0.1	0	0.0	1	0.1	1	0.1	1	0.1	1	0.1	0	0.0
血中クレアチンホスホキナーゼ増加	5	0.3	0	0.0	0	0.0	2	0.1	1	0.1	1	0.1	0	0.0	1	0.1
血中ビリルビン増加	4	0.3	1	0.1	2	0.1	0	0.0	1	0.1	1	0.1	0	0.0	0	0.0
血圧上昇	4	0.3	3	0.2	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
高比重リポ蛋白増加	4	0.3	2	0.1	0	0.0	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0
血中アルカリホスファターゼ増加	4	0.3	0	0.0	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	2	0.2
体重減少	3	0.2	2	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
肝酵素上昇	3	0.2	0	0.0	1	0.1	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0
肝機能検査値上昇	3	0.2	0	0.0	2	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
血中乳酸脱水素酵素増加	2	0.1	0	0.0	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
心電図ＱＴ延長	2	0.1	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
遊離脂肪酸増加	2	0.1	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血小板数減少	2	0.1	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
プロトロンビン時間短縮	2	0.1	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
Ｎ－テロペプチド	2	0.1	0	0.0	0	0.0	2	0.1	0	0.0	0	0.0	0	0.0	0	0.0
血中クレアチニン増加	1	0.1	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0
血中尿素減少	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
体温低下	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
尿中ブドウ糖陽性	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
脂質増加	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
総蛋白増加	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0
白血球数減少	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血小板数増加	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
尿中蛋白陽性	1	0.1	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0

Table 8.3.6-2
Occurrence of Treatment-Related Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: KLH-2109 ALL

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
トランスアミナーゼ上昇	1	0.1	0	0.0	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
便潜血陽性	1	0.1	1	0.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-2
Occurrence of Treatment-Related Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: Placebo

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
N	415	---	415	---	405	---	397	---	355	---	219	---	173	---	110	---
Any Treatment-Related AEs	90	21.7	49	11.8	27	6.7	35	8.8	9	2.5	2	0.9	1	0.6	0	0.0
Leading to Death	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Other Serious Events	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Leading to Discontinuation	13	3.1	4	1.0	2	0.5	3	0.8	3	0.8	1	0.5	1	0.6	0	0.0
Leading to Interruption	3	0.7	1	0.2	0	0.0	2	0.5	0	0.0	0	0.0	0	0.0	0	0.0
感染症および寄生虫症	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
毛包炎	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血液およびリンパ系障害	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
貧血	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
代謝および栄養障害	2	0.5	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
高コレステロール血症	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
過食	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
高トリグリセリド血症	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
精神障害	9	2.2	8	1.9	0	0.0	2	0.5	0	0.0	0	0.0	0	0.0	0	0.0
気分動揺	6	1.4	6	1.4	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
不眠症	2	0.5	1	0.2	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
易刺激性	2	0.5	1	0.2	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
不安	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
うつ病	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
睡眠障害	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
睡眠の質低下	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
神経系障害	20	4.8	14	3.4	4	1.0	2	0.5	1	0.3	0	0.0	0	0.0	0	0.0
頭痛	12	2.9	9	2.2	2	0.5	1	0.3	1	0.3	0	0.0	0	0.0	0	0.0
片頭痛	3	0.7	2	0.5	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
傾眠	3	0.7	2	0.5	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
浮動性めまい	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-2
Occurrence of Treatment-Related Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: Placebo

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
体位性めまい	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
耳および迷路障害	2	0.5	0	0.0	2	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
回転性めまい	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
頭位性回転性めまい	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
心臓障害	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
動悸	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血管障害	17	4.1	9	2.2	3	0.7	3	0.8	1	0.3	1	0.5	0	0.0	0	0.0
ほてり	17	4.1	9	2.2	3	0.7	3	0.8	1	0.3	1	0.5	0	0.0	0	0.0
胃腸障害	9	2.2	4	1.0	2	0.5	1	0.3	2	0.6	0	0.0	0	0.0	0	0.0
腹部膨満	3	0.7	1	0.2	1	0.2	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0
下痢	2	0.5	2	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
上腹部痛	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
鼓腸	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
悪心	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
肛門周囲痛	1	0.2	0	0.0	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0
皮膚および皮下組織障害	7	1.7	2	0.5	3	0.7	2	0.5	1	0.3	0	0.0	0	0.0	0	0.0
ざ瘡	2	0.5	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0
脱毛症	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
紅斑	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
多汗症	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
寝汗	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
丘疹性皮疹	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
皮膚局面	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
筋骨格系および結合組織障害	4	1.0	1	0.2	0	0.0	0	0.0	2	0.6	0	0.0	1	0.6	0	0.0
背部痛	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
側腹部痛	1	0.2	0	0.0	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0

Table 8.3.6-2
Occurrence of Treatment-Related Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: Placebo

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
関節腫脹	1	0.2	0	0.0	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0
骨減少症	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0
腎および尿路障害	1	0.2	0	0.0	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0
腎臓痛	1	0.2	0	0.0	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0
生殖系および乳房障害	37	8.9	18	4.3	11	2.7	23	5.8	5	1.4	0	0.0	0	0.0	0	0.0
月経中間期出血	25	6.0	13	3.1	11	2.7	18	4.5	3	0.8	0	0.0	0	0.0	0	0.0
重度月経出血	5	1.2	1	0.2	0	0.0	2	0.5	2	0.6	0	0.0	0	0.0	0	0.0
不規則月経	2	0.5	0	0.0	0	0.0	2	0.5	0	0.0	0	0.0	0	0.0	0	0.0
腟出血	2	0.5	1	0.2	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
乳房うっ滞	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
乳房圧痛	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
骨盤痛	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
一般・全身障害および投与部位の状態	8	1.9	6	1.4	1	0.2	1	0.3	1	0.3	0	0.0	0	0.0	0	0.0
疲労	2	0.5	1	0.2	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
顔面浮腫	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
熱感	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
空腹	1	0.2	0	0.0	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0
倦怠感	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
発熱	1	0.2	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
末梢腫脹	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
臨床検査	9	2.2	2	0.5	2	0.5	2	0.5	3	0.8	1	0.5	0	0.0	0	0.0
アラニンアミノトランスフェラーゼ増加	2	0.5	0	0.0	0	0.0	1	0.3	1	0.3	0	0.0	0	0.0	0	0.0
活性化部分トロンボプラスチン時間延長	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
アスパラギン酸アミノトランスフェラーゼ増加	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
血中ビリルビン増加	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-2
Occurrence of Treatment-Related Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: Placebo

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
血中コレステロール増加	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血中クレアチンホスホキナーゼ増加	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
γ－グルタミルトランスフェラーゼ増加	1	0.2	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0	0	0.0
低比重リポ蛋白増加	1	0.2	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
プロトロンビン時間延長	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0
体重増加	1	0.2	0	0.0	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0
骨密度減少	1	0.2	0	0.0	0	0.0	0	0.0	1	0.3	0	0.0	0	0.0	0	0.0
尿中ケトン体陽性	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
肝酵素上昇	1	0.2	0	0.0	1	0.2	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-2
Occurrence of Treatment-Related Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: Leuprorelin

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
N	187	---	187	---	187	---	185	---	182	---	179	---	176	---	174	---
Any Treatment-Related AEs	172	92.0	140	74.9	85	45.5	52	28.1	47	25.8	25	14.0	19	10.8	13	7.5
Leading to Death	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Other Serious Events	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
Leading to Discontinuation	8	4.3	4	2.1	1	0.5	2	1.1	0	0.0	1	0.6	0	0.0	0	0.0
Leading to Interruption	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
感染症および寄生虫症	2	1.1	0	0.0	0	0.0	2	1.1	0	0.0	0	0.0	0	0.0	0	0.0
膀胱炎	1	0.5	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
細菌性外陰腟炎	1	0.5	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
代謝および栄養障害	4	2.1	0	0.0	3	1.6	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
脂質異常症	3	1.6	0	0.0	2	1.1	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
２型糖尿病	1	0.5	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
精神障害	16	8.6	3	1.6	5	2.7	7	3.8	1	0.5	0	0.0	0	0.0	2	1.1
不眠症	6	3.2	1	0.5	1	0.5	3	1.6	1	0.5	0	0.0	0	0.0	0	0.0
抑うつ気分	2	1.1	1	0.5	2	1.1	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
易刺激性	2	1.1	0	0.0	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
うつ病	1	0.5	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
中期不眠症	1	0.5	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
睡眠障害	1	0.5	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
抑うつ症状	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6
感情不安定	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6
気分の落ち込み	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
神経系障害	25	13.4	9	4.8	9	4.8	2	1.1	4	2.2	4	2.2	2	1.1	0	0.0
頭痛	15	8.0	5	2.7	8	4.3	0	0.0	2	1.1	2	1.1	0	0.0	0	0.0
浮動性めまい	4	2.1	2	1.1	1	0.5	0	0.0	0	0.0	1	0.6	0	0.0	0	0.0
傾眠	3	1.6	1	0.5	0	0.0	0	0.0	1	0.5	1	0.6	0	0.0	0	0.0
手根管症候群	2	1.1	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	1	0.6	0	0.0

Table 8.3.6-2
Occurrence of Treatment-Related Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: Leuprorelin

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
感覚鈍麻	2	1.1	0	0.0	0	0.0	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0
頚腕症候群	1	0.5	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
片頭痛	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
神経痛	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0
起立不耐性	1	0.5	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
眼障害	1	0.5	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
緑内障	1	0.5	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
耳および迷路障害	3	1.6	1	0.5	0	0.0	1	0.5	0	0.0	1	0.6	0	0.0	0	0.0
耳鳴	2	1.1	0	0.0	0	0.0	1	0.5	0	0.0	1	0.6	0	0.0	0	0.0
回転性めまい	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
心臓障害	6	3.2	2	1.1	2	1.1	0	0.0	2	1.1	0	0.0	0	0.0	0	0.0
動悸	5	2.7	2	1.1	1	0.5	0	0.0	2	1.1	0	0.0	0	0.0	0	0.0
洞性徐脈	1	0.5	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
血管障害	102	54.5	25	13.4	50	26.7	17	9.2	10	5.5	3	1.7	2	1.1	3	1.7
ほてり	102	54.5	25	13.4	49	26.2	17	9.2	10	5.5	2	1.1	2	1.1	3	1.7
高血圧	2	1.1	0	0.0	1	0.5	0	0.0	0	0.0	1	0.6	0	0.0	0	0.0
呼吸器、胸郭および縦隔障害	1	0.5	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
呼吸困難	1	0.5	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
胃腸障害	6	3.2	2	1.1	2	1.1	0	0.0	2	1.1	0	0.0	0	0.0	0	0.0
便秘	4	2.1	1	0.5	1	0.5	0	0.0	2	1.1	0	0.0	0	0.0	0	0.0
下腹部痛	1	0.5	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
消化不良	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
肝胆道系障害	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0
肝機能異常	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0
皮膚および皮下組織障害	31	16.6	10	5.3	11	5.9	5	2.7	4	2.2	2	1.1	0	0.0	0	0.0
多汗症	22	11.8	7	3.7	7	3.7	5	2.7	2	1.1	1	0.6	0	0.0	0	0.0

Table 8.3.6-2
Occurrence of Treatment-Related Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: Leuprorelin

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
ざ瘡	4	2.1	3	1.6	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0
寝汗	2	1.1	0	0.0	2	1.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
脱毛症	1	0.5	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
皮膚炎	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
発疹	1	0.5	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
脂漏性皮膚炎	1	0.5	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0
乾皮症	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0	0	0.0
筋骨格系および結合組織障害	30	16.0	3	1.6	10	5.3	5	2.7	6	3.3	5	2.8	2	1.1	1	0.6
関節痛	15	8.0	1	0.5	4	2.1	3	1.6	2	1.1	3	1.7	1	0.6	1	0.6
筋骨格硬直	6	3.2	1	0.5	2	1.1	1	0.5	2	1.1	1	0.6	0	0.0	0	0.0
筋肉痛	2	1.1	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
関節周囲炎	2	1.1	0	0.0	1	0.5	0	0.0	0	0.0	1	0.6	0	0.0	0	0.0
背部痛	1	0.5	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
筋痙縮	1	0.5	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
変形性関節症	1	0.5	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
骨吸収亢進	1	0.5	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0
弾発指	1	0.5	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0
骨減少症	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0
生殖系および乳房障害	136	72.7	125	66.8	24	12.8	10	5.4	10	5.5	6	3.4	4	2.3	1	0.6
月経中間期出血	103	55.1	95	50.8	16	8.6	7	3.8	7	3.8	5	2.8	4	2.3	1	0.6
異常子宮出血	12	6.4	10	5.3	3	1.6	2	1.1	0	0.0	0	0.0	0	0.0	0	0.0
重度月経出血	9	4.8	8	4.3	1	0.5	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0
子宮出血	6	3.2	6	3.2	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
閉経期症状	5	2.7	4	2.1	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
腟分泌物	2	1.1	2	1.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
腟出血	2	1.1	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0

Table 8.3.6-2
Occurrence of Treatment-Related Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: Leuprorelin

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
乳房不快感	2	1.1	2	1.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
性器出血	2	1.1	1	0.5	1	0.5	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0
萎縮性外陰腟炎	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0	0	0.0
月経障害	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
不規則月経	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
卵巣嚢胞	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
外陰腟そう痒症	1	0.5	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0
一般・全身障害および投与部位の状態	23	12.3	9	4.8	9	4.8	2	1.1	3	1.6	3	1.7	1	0.6	0	0.0
倦怠感	9	4.8	4	2.1	3	1.6	1	0.5	0	0.0	1	0.6	0	0.0	0	0.0
浮腫	4	2.1	4	2.1	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
注射部位硬結	3	1.6	1	0.5	2	1.1	0	0.0	1	0.5	1	0.6	0	0.0	0	0.0
末梢性浮腫	2	1.1	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	1	0.6	0	0.0
投与部位硬結	2	1.1	0	0.0	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
胸部不快感	1	0.5	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
疲労	1	0.5	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
冷感	1	0.5	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
注射部位内出血	1	0.5	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0
注射部位反応	1	0.5	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
投与部位疼痛	1	0.5	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0
穿刺部位疼痛	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0	0	0.0
臨床検査	33	17.6	0	0.0	3	1.6	7	3.8	11	6.0	5	2.8	7	4.0	8	4.6
酒石酸抵抗性酸ホスファターゼ増加	9	4.8	0	0.0	0	0.0	1	0.5	3	1.6	0	0.0	3	1.7	2	1.1
生化学的骨代謝マーカー上昇	6	3.2	0	0.0	0	0.0	2	1.1	3	1.6	0	0.0	0	0.0	1	0.6
血中トリグリセリド増加	5	2.7	0	0.0	0	0.0	3	1.6	1	0.5	1	0.6	0	0.0	0	0.0
γ－グルタミルトランスフェラーゼ増加	5	2.7	0	0.0	1	0.5	2	1.1	0	0.0	1	0.6	0	0.0	1	0.6
血中コレステロール増加	4	2.1	0	0.0	2	1.1	0	0.0	2	1.1	0	0.0	0	0.0	0	0.0

Table 8.3.6-2
Occurrence of Treatment-Related Adverse Events by Onset Time
Safety Set

Study: Overall Population
Group: Leuprorelin

Time to Onset (days)	Overall		1<= <=28		29<= <=56		57<= <=84		85<= <=112		113<= <=140		141<= <=168		169<=	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
低比重リポ蛋白増加	4	2.1	0	0.0	1	0.5	0	0.0	1	0.5	1	0.6	1	0.6	0	0.0
骨密度減少	4	2.1	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	1	0.6	2	1.1
血中アルカリホスファターゼ増加	3	1.6	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	2	1.1
Ｎ－テロペプチド	3	1.6	0	0.0	0	0.0	0	0.0	1	0.5	0	0.0	1	0.6	1	0.6
アラニンアミノトランスフェラーゼ増加	2	1.1	0	0.0	0	0.0	1	0.5	0	0.0	1	0.6	0	0.0	0	0.0
活性化部分トロンボプラスチン時間延長	1	0.5	0	0.0	0	0.0	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0
体重増加	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0	0	0.0
肝機能検査値上昇	1	0.5	0	0.0	0	0.0	0	0.0	0	0.0	1	0.6	0	0.0	0	0.0

Table 8.3.7-3
Summary of Adverse Events with Special Interest
Safety Set

AESI: 骨密度の減少

Study		KLH2301						KLH2302					
Group		KLH-2109 200 mg			Leuprorelin			KLH-2109 200 mg			Placebo		
Item	Category	Events	n	%	Events	n	%	Events	n	%	Events	n	%
N	---	---	143	---	---	144	---	---	48	---	---	41	---
Any AEs	---	22	20	14.0	12	12	8.3	0	0	0.0	0	0	0.0
Leading to Death	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Other Serious Events	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Leading to Discontinuation	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Leading to Interruption	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Severity	Mild	22	20	14.0	12	12	8.3	0	0	0.0	0	0	0.0
	Moderate	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
	Severe	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0

For the number of subjects with event by severity, a subject was counted only once based on the most severe event.

Table 8.3.7-3
Summary of Adverse Events with Special Interest
Safety Set

AESI: 骨密度の減少

Study Group		Overall Population											
		KLH-2109 200 mg			KLH-2109 ALL			Placebo			Leuprorelin		
Item	Category	Events	n	%	Events	n	%	Events	n	%	Events	n	%
N	---	---	498	---	---	1452	---	---	415	---	---	187	---
Any AEs	---	27	25	5.0	40	37	2.5	2	2	0.5	12	12	6.4
Leading to Death	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Other Serious Events	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Leading to Discontinuation	---	3	3	0.6	8	8	0.6	2	2	0.5	0	0	0.0
Leading to Interruption	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Severity	Mild	25	23	4.6	35	32	2.2	1	1	0.2	12	12	6.4
	Moderate	2	2	0.4	5	5	0.3	0	0	0.0	0	0	0.0
	Severe	0	0	0.0	0	0	0.0	1	1	0.2	0	0	0.0

For the number of subjects with event by severity, a subject was counted only once based on the most severe event.

Table 8.3.7-3
Summary of Adverse Events with Special Interest
Safety Set

AESI: 更年期様症状

Study		KLH2301						KLH2302					
Group		KLH-2109 200 mg			Leuprorelin			KLH-2109 200 mg			Placebo		
Item	Category	Events	n	%	Events	n	%	Events	n	%	Events	n	%
N	---	---	143	---	---	144	---	---	48	---	---	41	---
Any AEs	---	207	105	73.4	202	103	71.5	42	26	54.2	7	5	12.2
Leading to Death	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Other Serious Events	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Leading to Discontinuation	---	7	6	4.2	6	6	4.2	0	0	0.0	0	0	0.0
Leading to Interruption	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Severity	Mild	201	101	70.6	189	95	66.0	42	26	54.2	6	4	9.8
	Moderate	6	4	2.8	13	8	5.6	0	0	0.0	1	1	2.4
	Severe	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0

For the number of subjects with event by severity, a subject was counted only once based on the most severe event.

Table 8.3.7-3
Summary of Adverse Events with Special Interest
Safety Set

AESI: 更年期様症状

Study Group		Overall Population											
		KLH-2109 200 mg			KLH-2109 ALL			Placebo			Leuprorelin		
Item	Category	Events	n	%	Events	n	%	Events	n	%	Events	n	%
N	---	---	498	---	---	1452	---	---	415	---	---	187	---
Any AEs	---	596	292	58.6	1161	594	40.9	145	84	20.2	266	135	72.2
Leading to Death	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Other Serious Events	---	0	0	0.0	0	0	0.0	1	1	0.2	0	0	0.0
Leading to Discontinuation	---	36	24	4.8	65	46	3.2	15	11	2.7	9	8	4.3
Leading to Interruption	---	4	4	0.8	6	6	0.4	3	2	0.5	0	0	0.0
Severity	Mild	474	227	45.6	886	445	30.6	89	49	11.8	242	120	64.2
	Moderate	98	48	9.6	227	117	8.1	49	29	7.0	24	15	8.0
	Severe	24	17	3.4	46	32	2.2	7	6	1.4	0	0	0.0

For the number of subjects with event by severity, a subject was counted only once based on the most severe event.

Table 8.3.7-3
Summary of Adverse Events with Special Interest
Safety Set

AESI: 子宮出血関連事象

Study		KLH2301						KLH2302					
Group		KLH-2109 200 mg			Leuprorelin			KLH-2109 200 mg			Placebo		
Item	Category	Events	n	%	Events	n	%	Events	n	%	Events	n	%
N	---	---	143	---	---	144	---	---	48	---	---	41	---
Any AEs	---	125	75	52.4	157	105	72.9	33	26	54.2	31	15	36.6
Leading to Death	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Other Serious Events	---	0	0	0.0	1	1	0.7	0	0	0.0	0	0	0.0
Leading to Discontinuation	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Leading to Interruption	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Severity	Mild	125	75	52.4	156	104	72.2	33	26	54.2	30	14	34.1
	Moderate	0	0	0.0	1	1	0.7	0	0	0.0	1	1	2.4
	Severe	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0

For the number of subjects with event by severity, a subject was counted only once based on the most severe event.

Table 8.3.7-3
Summary of Adverse Events with Special Interest
Safety Set

AESI: 子宮出血関連事象

Study Group		Overall Population											
		KLH-2109 200 mg			KLH-2109 ALL			Placebo			Leuprorelin		
Item	Category	Events	n	%	Events	n	%	Events	n	%	Events	n	%
N	---	---	498	---	---	1452	---	---	415	---	---	187	---
Any AEs	---	201	133	26.7	574	312	21.5	61	37	8.9	198	136	72.7
Leading to Death	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Other Serious Events	---	0	0	0.0	3	2	0.1	0	0	0.0	1	1	0.5
Leading to Discontinuation	---	3	3	0.6	5	5	0.3	0	0	0.0	0	0	0.0
Leading to Interruption	---	0	0	0.0	2	2	0.1	1	1	0.2	0	0	0.0
Severity	Mild	197	129	25.9	553	295	20.3	56	32	7.7	197	135	72.2
	Moderate	3	3	0.6	17	13	0.9	4	4	1.0	1	1	0.5
	Severe	1	1	0.2	4	4	0.3	1	1	0.2	0	0	0.0

For the number of subjects with event by severity, a subject was counted only once based on the most severe event.

Table 8.3.7-3
Summary of Adverse Events with Special Interest
Safety Set

AESI: 肝酵素上昇

Study		KLH2301						KLH2302					
Group		KLH-2109 200 mg			Leuprorelin			KLH-2109 200 mg			Placebo		
Item	Category	Events	n	%	Events	n	%	Events	n	%	Events	n	%
N	---	---	143	---	---	144	---	---	48	---	---	41	---
Any AEs	---	31	20	14.0	11	9	6.3	2	2	4.2	1	1	2.4
Leading to Death	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Other Serious Events	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Leading to Discontinuation	---	1	1	0.7	0	0	0.0	1	1	2.1	0	0	0.0
Leading to Interruption	---	1	1	0.7	0	0	0.0	0	0	0.0	0	0	0.0
Severity	Mild	31	20	14.0	11	9	6.3	2	2	4.2	1	1	2.4
	Moderate	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
	Severe	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0

For the number of subjects with event by severity, a subject was counted only once based on the most severe event.

Table 8.3.7-3
Summary of Adverse Events with Special Interest
Safety Set

AESI: 肝酵素上昇

Study Group		Overall Population											
		KLH-2109 200 mg			KLH-2109 ALL			Placebo			Leuprorelin		
Item	Category	Events	n	%	Events	n	%	Events	n	%	Events	n	%
N	---	---	498	---	---	1452	---	---	415	---	---	187	---
Any AEs	---	80	51	10.2	197	113	7.8	22	17	4.1	12	10	5.3
Leading to Death	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Other Serious Events	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Leading to Discontinuation	---	8	6	1.2	19	14	1.0	7	5	1.2	0	0	0.0
Leading to Interruption	---	2	2	0.4	2	2	0.1	3	1	0.2	0	0	0.0
Severity	Mild	71	46	9.2	175	98	6.7	15	13	3.1	12	10	5.3
	Moderate	9	5	1.0	22	15	1.0	6	3	0.7	0	0	0.0
	Severe	0	0	0.0	0	0	0.0	1	1	0.2	0	0	0.0

For the number of subjects with event by severity, a subject was counted only once based on the most severe event.

Table 8.3.7-3
Summary of Adverse Events with Special Interest
Safety Set

AESI: QTc間隔の延長

Study		KLH2301						KLH2302					
Group		KLH-2109 200 mg			Leuprorelin			KLH-2109 200 mg			Placebo		
Item	Category	Events	n	%	Events	n	%	Events	n	%	Events	n	%
N	---	---	143	---	---	144	---	---	48	---	---	41	---
Any AEs	---	1	1	0.7	2	1	0.7	0	0	0.0	0	0	0.0
Leading to Death	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Other Serious Events	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Leading to Discontinuation	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Leading to Interruption	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Severity	Mild	1	1	0.7	2	1	0.7	0	0	0.0	0	0	0.0
	Moderate	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
	Severe	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0

For the number of subjects with event by severity, a subject was counted only once based on the most severe event.

Table 8.3.7-3
Summary of Adverse Events with Special Interest
Safety Set

AESI: QTc間隔の延長

Study Group		Overall Population											
		KLH-2109 200 mg			KLH-2109 ALL			Placebo			Leuprorelin		
Item	Category	Events	n	%	Events	n	%	Events	n	%	Events	n	%
N	---	---	498	---	---	1452	---	---	415	---	---	187	---
Any AEs	---	1	1	0.2	3	3	0.2	0	0	0.0	2	1	0.5
Leading to Death	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Other Serious Events	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Leading to Discontinuation	---	0	0	0.0	1	1	0.1	0	0	0.0	0	0	0.0
Leading to Interruption	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Severity	Mild	1	1	0.2	3	3	0.2	0	0	0.0	2	1	0.5
	Moderate	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
	Severe	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0

For the number of subjects with event by severity, a subject was counted only once based on the most severe event.

Table 8.3.7-3
Summary of Adverse Events with Special Interest
Safety Set

AESI: 代謝及び心血管系の変化

Study		KLH2301						KLH2302					
Group		KLH-2109 200 mg			Leuprorelin			KLH-2109 200 mg			Placebo		
Item	Category	Events	n	%	Events	n	%	Events	n	%	Events	n	%
N	---	---	143	---	---	144	---	---	48	---	---	41	---
Any AEs	---	24	20	14.0	27	20	13.9	5	3	6.3	1	1	2.4
Leading to Death	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Other Serious Events	---	1	1	0.7	0	0	0.0	0	0	0.0	0	0	0.0
Leading to Discontinuation	---	1	1	0.7	2	1	0.7	0	0	0.0	0	0	0.0
Leading to Interruption	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Severity	Mild	23	19	13.3	27	20	13.9	5	3	6.3	1	1	2.4
	Moderate	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
	Severe	1	1	0.7	0	0	0.0	0	0	0.0	0	0	0.0

For the number of subjects with event by severity, a subject was counted only once based on the most severe event.

Table 8.3.7-3
Summary of Adverse Events with Special Interest
Safety Set

AESI: 代謝及び心血管系の変化

Study Group		Overall Population											
		KLH-2109 200 mg			KLH-2109 ALL			Placebo			Leuprorelin		
Item	Category	Events	n	%	Events	n	%	Events	n	%	Events	n	%
N	---	---	498	---	---	1452	---	---	415	---	---	187	---
Any AEs	---	78	60	12.0	192	144	9.9	31	25	6.0	32	25	13.4
Leading to Death	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Other Serious Events	---	2	2	0.4	5	5	0.3	1	1	0.2	0	0	0.0
Leading to Discontinuation	---	6	5	1.0	15	12	0.8	4	2	0.5	3	2	1.1
Leading to Interruption	---	0	0	0.0	2	2	0.1	0	0	0.0	0	0	0.0
Severity	Mild	66	50	10.0	155	112	7.7	19	15	3.6	32	25	13.4
	Moderate	10	8	1.6	31	26	1.8	10	8	1.9	0	0	0.0
	Severe	2	2	0.4	5	5	0.3	2	2	0.5	0	0	0.0

For the number of subjects with event by severity, a subject was counted only once based on the most severe event.

Table 8.3.7-3
Summary of Adverse Events with Special Interest
Safety Set

AESI: うつ

Study		KLH2301						KLH2302					
Group		KLH-2109 200 mg			Leuprorelin			KLH-2109 200 mg			Placebo		
Item	Category	Events	n	%	Events	n	%	Events	n	%	Events	n	%
N	---	---	143	---	---	144	---	---	48	---	---	41	---
Any AEs	---	4	4	2.8	8	6	4.2	1	1	2.1	0	0	0.0
Leading to Death	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Other Serious Events	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Leading to Discontinuation	---	1	1	0.7	2	2	1.4	0	0	0.0	0	0	0.0
Leading to Interruption	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Severity	Mild	4	4	2.8	6	4	2.8	1	1	2.1	0	0	0.0
	Moderate	0	0	0.0	2	2	1.4	0	0	0.0	0	0	0.0
	Severe	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0

For the number of subjects with event by severity, a subject was counted only once based on the most severe event.

Table 8.3.7-3
Summary of Adverse Events with Special Interest
Safety Set

AESI: うつ

Study Group		Overall Population											
		KLH-2109 200 mg			KLH-2109 ALL			Placebo			Leuprorelin		
Item	Category	Events	n	%	Events	n	%	Events	n	%	Events	n	%
N	---	---	498	---	---	1452	---	---	415	---	---	187	---
Any AEs	---	17	17	3.4	47	46	3.2	11	9	2.2	10	8	4.3
Leading to Death	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Other Serious Events	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Leading to Discontinuation	---	4	4	0.8	6	6	0.4	1	1	0.2	2	2	1.1
Leading to Interruption	---	0	0	0.0	1	1	0.1	0	0	0.0	0	0	0.0
Severity	Mild	15	15	3.0	36	35	2.4	7	6	1.4	8	6	3.2
	Moderate	1	1	0.2	8	8	0.6	4	3	0.7	2	2	1.1
	Severe	1	1	0.2	3	3	0.2	0	0	0.0	0	0	0.0

For the number of subjects with event by severity, a subject was counted only once based on the most severe event.

Table 8.3.7-4
Summary of Treatment-Related Adverse Events with Special Interest
Safety Set

AESI: 骨密度の減少

Study		KLH2301						KLH2302					
Group		KLH-2109 200 mg			Leuprorelin			KLH-2109 200 mg			Placebo		
Item	Category	Events	n	%	Events	n	%	Events	n	%	Events	n	%
N	---	---	143	---	---	144	---	---	48	---	---	41	---
Any Treatment-Related AEs	---	20	19	13.3	12	12	8.3	0	0	0.0	0	0	0.0
Leading to Death	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Other Serious Events	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Leading to Discontinuation	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Leading to Interruption	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Severity	Mild	20	19	13.3	12	12	8.3	0	0	0.0	0	0	0.0
	Moderate	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
	Severe	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0

For the number of subjects with event by severity, a subject was counted only once based on the most severe event.

Table 8.3.7-4
Summary of Treatment-Related Adverse Events with Special Interest
Safety Set

AESI: 骨密度の減少

Study		Overall Population											
Group		KLH-2109 200 mg			KLH-2109 ALL			Placebo			Leuprorelin		
Item	Category	Events	n	%	Events	n	%	Events	n	%	Events	n	%
N	---	---	498	---	---	1452	---	---	415	---	---	187	---
Any Treatment-Related AEs	---	25	24	4.8	33	32	2.2	2	2	0.5	12	12	6.4
Leading to Death	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Other Serious Events	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Leading to Discontinuation	---	3	3	0.6	6	6	0.4	2	2	0.5	0	0	0.0
Leading to Interruption	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Severity	Mild	23	22	4.4	30	29	2.0	1	1	0.2	12	12	6.4
	Moderate	2	2	0.4	3	3	0.2	0	0	0.0	0	0	0.0
	Severe	0	0	0.0	0	0	0.0	1	1	0.2	0	0	0.0

For the number of subjects with event by severity, a subject was counted only once based on the most severe event.

Table 8.3.7-4
Summary of Treatment-Related Adverse Events with Special Interest
Safety Set

AESI: 更年期様症状

Study		KLH2301						KLH2302					
Group		KLH-2109 200 mg			Leuprorelin			KLH-2109 200 mg			Placebo		
Item	Category	Events	n	%	Events	n	%	Events	n	%	Events	n	%
N	---	---	143	---	---	144	---	---	48	---	---	41	---
Any Treatment-Related AEs	---	180	96	67.1	178	95	66.0	39	25	52.1	2	2	4.9
Leading to Death	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Other Serious Events	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Leading to Discontinuation	---	7	6	4.2	6	6	4.2	0	0	0.0	0	0	0.0
Leading to Interruption	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Severity	Mild	175	93	65.0	165	87	60.4	39	25	52.1	2	2	4.9
	Moderate	5	3	2.1	13	8	5.6	0	0	0.0	0	0	0.0
	Severe	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0

For the number of subjects with event by severity, a subject was counted only once based on the most severe event.

Table 8.3.7-4
Summary of Treatment-Related Adverse Events with Special Interest
Safety Set

AESI: 更年期様症状

Study		Overall Population											
Group		KLH-2109 200 mg			KLH-2109 ALL			Placebo			Leuprorelin		
Item	Category	Events	n	%	Events	n	%	Events	n	%	Events	n	%
N	---	---	498	---	---	1452	---	---	415	---	---	187	---
Any Treatment-Related AEs	---	464	255	51.2	849	488	33.6	66	44	10.6	234	126	67.4
Leading to Death	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Other Serious Events	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Leading to Discontinuation	---	32	21	4.2	56	39	2.7	11	8	1.9	9	8	4.3
Leading to Interruption	---	4	4	0.8	6	6	0.4	1	1	0.2	0	0	0.0
Severity	Mild	379	204	41.0	676	378	26.0	43	28	6.7	212	112	59.9
	Moderate	64	37	7.4	140	86	5.9	19	12	2.9	22	14	7.5
	Severe	21	14	2.8	31	23	1.6	4	4	1.0	0	0	0.0

For the number of subjects with event by severity, a subject was counted only once based on the most severe event.

Table 8.3.7-4
Summary of Treatment-Related Adverse Events with Special Interest
Safety Set

AESI: 子宮出血関連事象

Study		KLH2301						KLH2302					
Group		KLH-2109 200 mg			Leuprorelin			KLH-2109 200 mg			Placebo		
Item	Category	Events	n	%	Events	n	%	Events	n	%	Events	n	%
N	---	---	143	---	---	144	---	---	48	---	---	41	---
Any Treatment-Related AEs	---	118	71	49.7	153	102	70.8	31	25	52.1	31	15	36.6
Leading to Death	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Other Serious Events	---	0	0	0.0	1	1	0.7	0	0	0.0	0	0	0.0
Leading to Discontinuation	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Leading to Interruption	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Severity	Mild	118	71	49.7	152	101	70.1	31	25	52.1	30	14	34.1
	Moderate	0	0	0.0	1	1	0.7	0	0	0.0	1	1	2.4
	Severe	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0

For the number of subjects with event by severity, a subject was counted only once based on the most severe event.

Table 8.3.7-4
Summary of Treatment-Related Adverse Events with Special Interest
Safety Set

AESI: 子宮出血関連事象

Study		Overall Population											
Group		KLH-2109 200 mg			KLH-2109 ALL			Placebo			Leuprorelin		
Item	Category	Events	n	%	Events	n	%	Events	n	%	Events	n	%
N	---	---	498	---	---	1452	---	---	415	---	---	187	---
Any Treatment-Related AEs	---	191	127	25.5	556	303	20.9	58	34	8.2	194	133	71.1
Leading to Death	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Other Serious Events	---	0	0	0.0	1	1	0.1	0	0	0.0	1	1	0.5
Leading to Discontinuation	---	2	2	0.4	4	4	0.3	0	0	0.0	0	0	0.0
Leading to Interruption	---	0	0	0.0	2	2	0.1	1	1	0.2	0	0	0.0
Severity	Mild	188	124	24.9	540	289	19.9	55	31	7.5	193	132	70.6
	Moderate	2	2	0.4	12	10	0.7	2	2	0.5	1	1	0.5
	Severe	1	1	0.2	4	4	0.3	1	1	0.2	0	0	0.0

For the number of subjects with event by severity, a subject was counted only once based on the most severe event.

Table 8.3.7-4
Summary of Treatment-Related Adverse Events with Special Interest
Safety Set

AESI: 肝酵素上昇

Study		KLH2301						KLH2302					
Group		KLH-2109 200 mg			Leuprorelin			KLH-2109 200 mg			Placebo		
Item	Category	Events	n	%	Events	n	%	Events	n	%	Events	n	%
N	---	---	143	---	---	144	---	---	48	---	---	41	---
Any Treatment-Related AEs	---	25	17	11.9	11	9	6.3	2	2	4.2	0	0	0.0
Leading to Death	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Other Serious Events	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Leading to Discontinuation	---	1	1	0.7	0	0	0.0	1	1	2.1	0	0	0.0
Leading to Interruption	---	1	1	0.7	0	0	0.0	0	0	0.0	0	0	0.0
Severity	Mild	25	17	11.9	11	9	6.3	2	2	4.2	0	0	0.0
	Moderate	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
	Severe	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0

For the number of subjects with event by severity, a subject was counted only once based on the most severe event.

Table 8.3.7-4
Summary of Treatment-Related Adverse Events with Special Interest
Safety Set

AESI: 肝酵素上昇

Study		Overall Population											
Group		KLH-2109 200 mg			KLH-2109 ALL			Placebo			Leuprorelin		
Item	Category	Events	n	%	Events	n	%	Events	n	%	Events	n	%
N	---	---	498	---	---	1452	---	---	415	---	---	187	---
Any Treatment-Related AEs	---	62	39	7.8	144	78	5.4	7	5	1.2	12	10	5.3
Leading to Death	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Other Serious Events	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Leading to Discontinuation	---	5	5	1.0	12	9	0.6	4	2	0.5	0	0	0.0
Leading to Interruption	---	1	1	0.2	1	1	0.1	3	1	0.2	0	0	0.0
Severity	Mild	57	36	7.2	132	70	4.8	3	3	0.7	12	10	5.3
	Moderate	5	3	0.6	12	8	0.6	3	1	0.2	0	0	0.0
	Severe	0	0	0.0	0	0	0.0	1	1	0.2	0	0	0.0

For the number of subjects with event by severity, a subject was counted only once based on the most severe event.

Table 8.3.7-4
Summary of Treatment-Related Adverse Events with Special Interest
Safety Set

AESI: QTc間隔の延長

Study		KLH2301						KLH2302					
Group		KLH-2109 200 mg			Leuprorelin			KLH-2109 200 mg			Placebo		
Item	Category	Events	n	%	Events	n	%	Events	n	%	Events	n	%
N	---	---	143	---	---	144	---	---	48	---	---	41	---
Any Treatment-Related AEs	---	1	1	0.7	0	0	0.0	0	0	0.0	0	0	0.0
Leading to Death	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Other Serious Events	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Leading to Discontinuation	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Leading to Interruption	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Severity	Mild	1	1	0.7	0	0	0.0	0	0	0.0	0	0	0.0
	Moderate	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
	Severe	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0

For the number of subjects with event by severity, a subject was counted only once based on the most severe event.

Table 8.3.7-4
Summary of Treatment-Related Adverse Events with Special Interest
Safety Set

AESI: QTc間隔の延長

Study Group		Overall Population											
		KLH-2109 200 mg			KLH-2109 ALL			Placebo			Leuprorelin		
Item	Category	Events	n	%	Events	n	%	Events	n	%	Events	n	%
N	---	---	498	---	---	1452	---	---	415	---	---	187	---
Any Treatment-Related AEs	---	1	1	0.2	2	2	0.1	0	0	0.0	0	0	0.0
Leading to Death	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Other Serious Events	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Leading to Discontinuation	---	0	0	0.0	1	1	0.1	0	0	0.0	0	0	0.0
Leading to Interruption	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Severity	Mild	1	1	0.2	2	2	0.1	0	0	0.0	0	0	0.0
	Moderate	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
	Severe	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0

For the number of subjects with event by severity, a subject was counted only once based on the most severe event.

Table 8.3.7-4
Summary of Treatment-Related Adverse Events with Special Interest
Safety Set

AESI: 代謝及び心血管系の変化

Study		KLH2301						KLH2302					
Group		KLH-2109 200 mg			Leuprorelin			KLH-2109 200 mg			Placebo		
Item	Category	Events	n	%	Events	n	%	Events	n	%	Events	n	%
N	---	---	143	---	---	144	---	---	48	---	---	41	---
Any Treatment-Related AEs	---	20	17	11.9	22	17	11.8	4	2	4.2	0	0	0.0
Leading to Death	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Other Serious Events	---	1	1	0.7	0	0	0.0	0	0	0.0	0	0	0.0
Leading to Discontinuation	---	1	1	0.7	0	0	0.0	0	0	0.0	0	0	0.0
Leading to Interruption	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Severity	Mild	19	16	11.2	22	17	11.8	4	2	4.2	0	0	0.0
	Moderate	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
	Severe	1	1	0.7	0	0	0.0	0	0	0.0	0	0	0.0

For the number of subjects with event by severity, a subject was counted only once based on the most severe event.

Table 8.3.7-4
Summary of Treatment-Related Adverse Events with Special Interest
Safety Set

AESI: 代謝及び心血管系の変化

Study		Overall Population											
Group		KLH-2109 200 mg			KLH-2109 ALL			Placebo			Leuprorelin		
Item	Category	Events	n	%	Events	n	%	Events	n	%	Events	n	%
N	---	---	498	---	---	1452	---	---	415	---	---	187	---
Any Treatment-Related AEs	---	43	31	6.2	103	74	5.1	10	7	1.7	26	21	11.2
Leading to Death	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Other Serious Events	---	1	1	0.2	3	3	0.2	0	0	0.0	0	0	0.0
Leading to Discontinuation	---	2	2	0.4	9	7	0.5	1	1	0.2	1	1	0.5
Leading to Interruption	---	0	0	0.0	1	1	0.1	0	0	0.0	0	0	0.0
Severity	Mild	42	30	6.0	89	63	4.3	8	5	1.2	26	21	11.2
	Moderate	0	0	0.0	11	8	0.6	2	2	0.5	0	0	0.0
	Severe	1	1	0.2	3	3	0.2	0	0	0.0	0	0	0.0

For the number of subjects with event by severity, a subject was counted only once based on the most severe event.

Table 8.3.7-4
Summary of Treatment-Related Adverse Events with Special Interest
Safety Set

AESI: うつ

Study		KLH2301						KLH2302					
Group		KLH-2109 200 mg			Leuprorelin			KLH-2109 200 mg			Placebo		
Item	Category	Events	n	%	Events	n	%	Events	n	%	Events	n	%
N	---	---	143	---	---	144	---	---	48	---	---	41	---
Any Treatment-Related AEs	---	3	3	2.1	7	5	3.5	1	1	2.1	0	0	0.0
Leading to Death	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Other Serious Events	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Leading to Discontinuation	---	1	1	0.7	2	2	1.4	0	0	0.0	0	0	0.0
Leading to Interruption	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Severity	Mild	3	3	2.1	5	3	2.1	1	1	2.1	0	0	0.0
	Moderate	0	0	0.0	2	2	1.4	0	0	0.0	0	0	0.0
	Severe	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0

For the number of subjects with event by severity, a subject was counted only once based on the most severe event.

Table 8.3.7-4
Summary of Treatment-Related Adverse Events with Special Interest
Safety Set

AESI: うつ

Study Group		Overall Population											
		KLH-2109 200 mg			KLH-2109 ALL			Placebo			Leuprorelin		
Item	Category	Events	n	%	Events	n	%	Events	n	%	Events	n	%
N	---	---	498	---	---	1452	---	---	415	---	---	187	---
Any Treatment-Related AEs	---	13	13	2.6	33	33	2.3	9	7	1.7	9	7	3.7
Leading to Death	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Other Serious Events	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Leading to Discontinuation	---	3	3	0.6	4	4	0.3	1	1	0.2	2	2	1.1
Leading to Interruption	---	0	0	0.0	0	0	0.0	0	0	0.0	0	0	0.0
Severity	Mild	11	11	2.2	26	26	1.8	5	4	1.0	7	5	2.7
	Moderate	1	1	0.2	5	5	0.3	4	3	0.7	2	2	1.1
	Severe	1	1	0.2	2	2	0.1	0	0	0.0	0	0	0.0

For the number of subjects with event by severity, a subject was counted only once based on the most severe event.

Table 8.3.7-5
Occurrence of Adverse Events with Special Interest - Primary SOC and PT
Safety Set

AESI: 骨密度の減少

Study	KLH2301				KLH2302				Overall Population							
Group	KLH-2109 200 mg		Leuprorelin		KLH-2109 200 mg		Placebo		KLH-2109 200 mg		KLH-2109 ALL		Placebo		Leuprorelin	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
N	143	---	144	---	48	---	41	---	498	---	1452	---	415	---	187	---
Any AEs	20	14.0	12	8.3	0	0.0	0	0.0	25	5.0	37	2.5	2	0.5	12	6.4
筋骨格系および結合組織障害	2	1.4	2	1.4	0	0.0	0	0.0	3	0.6	5	0.3	1	0.2	2	1.1
骨吸収亢進	2	1.4	1	0.7	0	0.0	0	0.0	2	0.4	2	0.1	0	0.0	1	0.5
骨喪失	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	2	0.1	0	0.0	0	0.0
骨減少症	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	1	0.1	1	0.2	1	0.5
骨粗鬆症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
臨床検査	18	12.6	10	6.9	0	0.0	0	0.0	22	4.4	31	2.1	1	0.2	10	5.3
骨密度減少	9	6.3	4	2.8	0	0.0	0	0.0	13	2.6	22	1.5	1	0.2	4	2.1
生化学的骨代謝マーカー上昇	10	7.0	6	4.2	0	0.0	0	0.0	10	2.0	10	0.7	0	0.0	6	3.2
傷害、中毒および処置合併症	1	0.7	0	0.0	0	0.0	0	0.0	1	0.2	2	0.1	0	0.0	0	0.0
肋骨骨折	1	0.7	0	0.0	0	0.0	0	0.0	1	0.2	1	0.1	0	0.0	0	0.0
橈骨骨折	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0

Table 8.3.7-5
Occurrence of Adverse Events with Special Interest - Primary SOC and PT
Safety Set

AESI: 更年期様症状

Study	KLH2301				KLH2302				Overall Population							
Group	KLH-2109 200 mg		Leuprorelin		KLH-2109 200 mg		Placebo		KLH-2109 200 mg		KLH-2109 ALL		Placebo		Leuprorelin	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
N	143	---	144	---	48	---	41	---	498	---	1452	---	415	---	187	---
Any AEs	105	73.4	103	71.5	26	54.2	5	12.2	292	58.6	594	40.9	84	20.2	135	72.2
代謝および栄養障害	1	0.7	2	1.4	1	2.1	0	0.0	4	0.8	6	0.4	1	0.2	2	1.1
食欲減退	1	0.7	2	1.4	1	2.1	0	0.0	4	0.8	6	0.4	1	0.2	2	1.1
精神障害	10	7.0	14	9.7	1	2.1	0	0.0	40	8.0	80	5.5	12	2.9	18	9.6
気分動揺	0	0.0	0	0.0	0	0.0	0	0.0	5	1.0	19	1.3	8	1.9	0	0.0
不眠症	5	3.5	6	4.2	0	0.0	0	0.0	9	1.8	14	1.0	3	0.7	8	4.3
リビドー減退	0	0.0	0	0.0	0	0.0	0	0.0	7	1.4	10	0.7	0	0.0	0	0.0
不安	0	0.0	0	0.0	0	0.0	0	0.0	6	1.2	10	0.7	2	0.5	0	0.0
感情不安定	0	0.0	1	0.7	0	0.0	0	0.0	3	0.6	9	0.6	0	0.0	2	1.1
うつ病	1	0.7	1	0.7	0	0.0	0	0.0	3	0.6	7	0.5	1	0.2	1	0.5
易刺激性	1	0.7	2	1.4	0	0.0	0	0.0	2	0.4	6	0.4	2	0.5	2	1.1
睡眠障害	2	1.4	1	0.7	0	0.0	0	0.0	3	0.6	4	0.3	1	0.2	1	0.5
中期不眠症	1	0.7	0	0.0	1	2.1	0	0.0	2	0.4	2	0.1	0	0.0	1	0.5
気分変化	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	2	0.1	0	0.0	0	0.0
睡眠の質低下	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	1	0.1	1	0.2	0	0.0
神経過敏	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	1	0.1	0	0.0	0	0.0
抑うつ気分	0	0.0	2	1.4	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	2	1.1
抑うつ気分を伴う適応障害	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
リビドー消失	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
注意欠如・多動性障害	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
抑うつ症状	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.5
気分の落ち込み	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.5
神経系障害	19	13.3	24	16.7	5	10.4	2	4.9	87	17.5	227	15.6	44	10.6	33	17.6
頭痛	15	10.5	15	10.4	3	6.3	1	2.4	67	13.5	172	11.8	30	7.2	22	11.8
浮動性めまい	4	2.8	4	2.8	2	4.2	0	0.0	15	3.0	43	3.0	5	1.2	6	3.2

Table 8.3.7-5
Occurrence of Adverse Events with Special Interest - Primary SOC and PT
Safety Set

AESI: 更年期様症状

Study	KLH2301				KLH2302				Overall Population							
Group	KLH-2109 200 mg		Leuprorelin		KLH-2109 200 mg		Placebo		KLH-2109 200 mg		KLH-2109 ALL		Placebo		Leuprorelin	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
片頭痛	0	0.0	1	0.7	0	0.0	1	2.4	5	1.0	17	1.2	5	1.2	1	0.5
傾眠	3	2.1	4	2.8	1	2.1	0	0.0	7	1.4	16	1.1	3	0.7	5	2.7
体位性めまい	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	3	0.2	1	0.2	1	0.5
錯感覚	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	1	0.1	1	0.2	0	0.0
手根管症候群	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	2	1.1
眼障害	0	0.0	0	0.0	0	0.0	0	0.0	2	0.4	2	0.1	0	0.0	0	0.0
霧視	0	0.0	0	0.0	0	0.0	0	0.0	2	0.4	2	0.1	0	0.0	0	0.0
耳および迷路障害	2	1.4	4	2.8	1	2.1	1	2.4	3	0.6	13	0.9	2	0.5	5	2.7
回転性めまい	2	1.4	2	1.4	0	0.0	1	2.4	2	0.4	10	0.7	2	0.5	2	1.1
耳鳴	0	0.0	2	1.4	1	2.1	0	0.0	1	0.2	3	0.2	0	0.0	3	1.6
心臓障害	7	4.9	2	1.4	0	0.0	0	0.0	8	1.6	14	1.0	1	0.2	5	2.7
動悸	7	4.9	2	1.4	0	0.0	0	0.0	8	1.6	14	1.0	1	0.2	5	2.7
血管障害	77	53.8	77	53.5	23	47.9	0	0.0	221	44.4	366	25.2	21	5.1	103	55.1
ほてり	77	53.8	77	53.5	23	47.9	0	0.0	220	44.2	365	25.1	21	5.1	103	55.1
潮紅	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	1	0.1	0	0.0	0	0.0
皮膚および皮下組織障害	23	16.1	20	13.9	6	12.5	1	2.4	46	9.2	70	4.8	5	1.2	25	13.4
多汗症	19	13.3	17	11.8	6	12.5	1	2.4	36	7.2	48	3.3	2	0.5	22	11.8
脱毛症	4	2.8	1	0.7	0	0.0	0	0.0	7	1.4	14	1.0	2	0.5	1	0.5
寝汗	0	0.0	2	1.4	0	0.0	0	0.0	4	0.8	8	0.6	1	0.2	2	1.1
円形脱毛症	1	0.7	0	0.0	0	0.0	0	0.0	1	0.2	2	0.1	0	0.0	0	0.0
筋骨格系および結合組織障害	31	21.7	22	15.3	1	2.1	1	2.4	56	11.2	94	6.5	16	3.9	29	15.5
関節痛	18	12.6	14	9.7	0	0.0	1	2.4	33	6.6	52	3.6	9	2.2	16	8.6
筋骨格硬直	11	7.7	5	3.5	0	0.0	0	0.0	15	3.0	22	1.5	0	0.0	9	4.8
四肢痛	3	2.1	0	0.0	0	0.0	0	0.0	6	1.2	10	0.7	2	0.5	0	0.0
筋肉痛	0	0.0	1	0.7	1	2.1	0	0.0	2	0.4	6	0.4	1	0.2	3	1.6
筋痙縮	1	0.7	1	0.7	0	0.0	0	0.0	2	0.4	5	0.3	3	0.7	1	0.5

Table 8.3.7-5
Occurrence of Adverse Events with Special Interest - Primary SOC and PT
Safety Set

AESI: 更年期様症状

Study	KLH2301				KLH2302				Overall Population							
Group	KLH-2109 200 mg		Leuprorelin		KLH-2109 200 mg		Placebo		KLH-2109 200 mg		KLH-2109 ALL		Placebo		Leuprorelin	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
腱鞘炎	2	1.4	1	0.7	0	0.0	0	0.0	2	0.4	3	0.2	0	0.0	1	0.5
頚部痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	2	0.1	1	0.2	0	0.0
筋骨格痛	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	1	0.1	0	0.0	0	0.0
腱炎	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
筋緊張	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
弾発指	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.5
関節腫脹	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0
関節不安定	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0
生殖系および乳房障害	9	6.3	9	6.3	0	0.0	1	2.4	25	5.0	46	3.2	5	1.2	11	5.9
外陰腟乾燥	0	0.0	0	0.0	0	0.0	0	0.0	8	1.6	13	0.9	0	0.0	0	0.0
閉経期症状	8	5.6	4	2.8	0	0.0	0	0.0	8	1.6	12	0.8	0	0.0	5	2.7
乳房圧痛	0	0.0	0	0.0	0	0.0	0	0.0	4	0.8	6	0.4	2	0.5	0	0.0
外陰腟そう痒症	0	0.0	1	0.7	0	0.0	1	2.4	1	0.2	6	0.4	2	0.5	1	0.5
乳房不快感	1	0.7	3	2.1	0	0.0	0	0.0	2	0.4	3	0.2	0	0.0	3	1.6
外陰部湿疹	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	2	0.1	0	0.0	0	0.0
外陰腟灼熱感	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	2	0.1	0	0.0	0	0.0
萎縮性外陰腟炎	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	1	0.1	0	0.0	1	0.5
外陰腟不快感	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	1	0.1	0	0.0	0	0.0
外陰腟痛	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	1	0.5
乳房痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	1	0.2	0	0.0
一般・全身障害および投与部位の状態	12	8.4	12	8.3	3	6.3	1	2.4	28	5.6	45	3.1	8	1.9	14	7.5
倦怠感	11	7.7	9	6.3	2	4.2	1	2.4	18	3.6	25	1.7	3	0.7	11	5.9
疲労	1	0.7	1	0.7	0	0.0	0	0.0	8	1.6	14	1.0	4	1.0	1	0.5
無力症	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	4	0.3	0	0.0	0	0.0
熱感	0	0.0	0	0.0	1	2.1	0	0.0	1	0.2	2	0.1	1	0.2	0	0.0
冷感	0	0.0	2	1.4	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	2	1.1

Table 8.3.7-5
Occurrence of Adverse Events with Special Interest - Primary SOC and PT
Safety Set

AESI: 子宮出血関連事象

Study	KLH2301				KLH2302				Overall Population							
Group	KLH-2109 200 mg		Leuprorelin		KLH-2109 200 mg		Placebo		KLH-2109 200 mg		KLH-2109 ALL		Placebo		Leuprorelin	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
N	143	---	144	---	48	---	41	---	498	---	1452	---	415	---	187	---
Any AEs	75	52.4	105	72.9	26	54.2	15	36.6	133	26.7	312	21.5	37	8.9	136	72.7
生殖系および乳房障害	75	52.4	105	72.9	26	54.2	15	36.6	133	26.7	312	21.5	37	8.9	136	72.7
月経中間期出血	57	39.9	80	55.6	20	41.7	13	31.7	99	19.9	247	17.0	25	6.0	106	56.7
重度月経出血	7	4.9	4	2.8	1	2.1	0	0.0	14	2.8	61	4.2	6	1.4	9	4.8
異常子宮出血	6	4.2	12	8.3	4	8.3	0	0.0	10	2.0	10	0.7	0	0.0	12	6.4
腟出血	1	0.7	2	1.4	0	0.0	0	0.0	6	1.2	9	0.6	4	1.0	2	1.1
子宮出血	6	4.2	6	4.2	0	0.0	0	0.0	6	1.2	7	0.5	0	0.0	6	3.2
性器出血	1	0.7	2	1.4	2	4.2	0	0.0	3	0.6	3	0.2	0	0.0	2	1.1
不規則月経	3	2.1	1	0.7	0	0.0	2	4.9	3	0.6	3	0.2	2	0.5	1	0.5
月経障害	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	2	0.1	0	0.0	1	0.5
月経遅延	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	1	0.1	0	0.0	0	0.0
過長過多不規則月経	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
希発月経	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0

Table 8.3.7-5
Occurrence of Adverse Events with Special Interest - Primary SOC and PT
Safety Set

AESI: 肝酵素上昇

Study	KLH2301				KLH2302				Overall Population							
Group	KLH-2109 200 mg		Leuprorelin		KLH-2109 200 mg		Placebo		KLH-2109 200 mg		KLH-2109 ALL		Placebo		Leuprorelin	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
N	143	---	144	---	48	---	41	---	498	---	1452	---	415	---	187	---
Any AEs	20	14.0	9	6.3	2	4.2	1	2.4	51	10.2	113	7.8	17	4.1	10	5.3
良性、悪性および詳細不明の新生物（嚢胞およびポリープを含む）	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
肝臓血管腫	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
肝胆道系障害	5	3.5	1	0.7	1	2.1	1	2.4	8	1.6	11	0.8	1	0.2	1	0.5
肝機能異常	5	3.5	1	0.7	1	2.1	0	0.0	6	1.2	6	0.4	0	0.0	1	0.5
脂肪肝	1	0.7	0	0.0	0	0.0	0	0.0	1	0.2	3	0.2	0	0.0	0	0.0
非アルコール性脂肪肝	0	0.0	0	0.0	0	0.0	1	2.4	1	0.2	1	0.1	1	0.2	0	0.0
高トランスアミナーゼ血症	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	1	0.1	0	0.0	0	0.0
肝腫大	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
臨床検査	15	10.5	8	5.6	1	2.1	0	0.0	43	8.6	102	7.0	16	3.9	9	4.8
アラニンアミノトランスフェラーゼ増加	9	6.3	2	1.4	0	0.0	0	0.0	24	4.8	59	4.1	4	1.0	2	1.1
アスパラギン酸アミノトランスフェラーゼ増加	6	4.2	0	0.0	0	0.0	0	0.0	15	3.0	46	3.2	4	1.0	0	0.0
γーグルタミルトランスフェラーゼ増加	6	4.2	5	3.5	1	2.1	0	0.0	17	3.4	39	2.7	6	1.4	5	2.7
グアナーゼ増加	0	0.0	0	0.0	0	0.0	0	0.0	6	1.2	14	1.0	0	0.0	0	0.0
血中ビリルビン増加	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	8	0.6	2	0.5	0	0.0
血中アルカリホスファターゼ増加	1	0.7	2	1.4	0	0.0	0	0.0	2	0.4	4	0.3	1	0.2	3	1.6
肝酵素上昇	1	0.7	0	0.0	0	0.0	0	0.0	2	0.4	4	0.3	1	0.2	0	0.0
肝機能検査値上昇	2	1.4	1	0.7	0	0.0	0	0.0	3	0.6	3	0.2	1	0.2	1	0.5
トランスアミナーゼ上昇	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	1	0.1	0	0.0	0	0.0
国際標準比増加	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0
プロトロンビン時間延長	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0

Table 8.3.7-5
Occurrence of Adverse Events with Special Interest - Primary SOC and PT
Safety Set

AESI: QTc間隔の延長

Study	KLH2301				KLH2302				Overall Population							
Group	KLH-2109 200 mg		Leuprorelin		KLH-2109 200 mg		Placebo		KLH-2109 200 mg		KLH-2109 ALL		Placebo		Leuprorelin	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
N	143	---	144	---	48	---	41	---	498	---	1452	---	415	---	187	---
Any AEs	1	0.7	1	0.7	0	0.0	0	0.0	1	0.2	3	0.2	0	0.0	1	0.5
神経系障害	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
失神	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
臨床検査	1	0.7	1	0.7	0	0.0	0	0.0	1	0.2	2	0.1	0	0.0	1	0.5
心電図ＱＴ延長	1	0.7	1	0.7	0	0.0	0	0.0	1	0.2	2	0.1	0	0.0	1	0.5

Table 8.3.7-5
Occurrence of Adverse Events with Special Interest - Primary SOC and PT
Safety Set

AESI: 代謝及び心血管系の変化

Study	KLH2301				KLH2302				Overall Population							
Group	KLH-2109 200 mg		Leuprorelin		KLH-2109 200 mg		Placebo		KLH-2109 200 mg		KLH-2109 ALL		Placebo		Leuprorelin	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
N	143	---	144	---	48	---	41	---	498	---	1452	---	415	---	187	---
Any AEs	20	14.0	20	13.9	3	6.3	1	2.4	60	12.0	144	9.9	25	6.0	25	13.4
代謝および栄養障害	5	3.5	4	2.8	0	0.0	0	0.0	8	1.6	19	1.3	2	0.5	6	3.2
脂質異常症	5	3.5	1	0.7	0	0.0	0	0.0	5	1.0	10	0.7	0	0.0	3	1.6
食欲亢進	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	2	0.1	0	0.0	0	0.0
高脂血症	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	2	0.1	0	0.0	0	0.0
高コレステロール血症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	2	0.1	1	0.2	0	0.0
２型糖尿病	0	0.0	1	0.7	0	0.0	0	0.0	1	0.2	1	0.1	0	0.0	1	0.5
過食	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	1	0.2	0	0.0
高トリグリセリド血症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	1	0.2	0	0.0
肥満	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
脱水	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.5
糖尿病	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.5
神経系障害	1	0.7	0	0.0	0	0.0	0	0.0	2	0.4	3	0.2	0	0.0	0	0.0
くも膜下出血	1	0.7	0	0.0	0	0.0	0	0.0	1	0.2	2	0.1	0	0.0	0	0.0
構語障害	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	1	0.1	0	0.0	0	0.0
心臓障害	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	3	0.2	1	0.2	0	0.0
狭心症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	3	0.2	0	0.0	0	0.0
急性心筋梗塞	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0
冠動脈疾患	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0
虚血性心筋症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0
血管障害	3	2.1	3	2.1	0	0.0	0	0.0	9	1.8	16	1.1	4	1.0	3	1.6
高血圧	3	2.1	3	2.1	0	0.0	0	0.0	9	1.8	15	1.0	4	1.0	3	1.6
高血圧切迫症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
呼吸器、胸郭および縦隔障害	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	3	0.2	0	0.0	0	0.0
肺塞栓症	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	2	0.1	0	0.0	0	0.0

Table 8.3.7-5
Occurrence of Adverse Events with Special Interest - Primary SOC and PT
Safety Set

AESI: 代謝及び心血管系の変化

Study	KLH2301				KLH2302				Overall Population							
Group	KLH-2109 200 mg		Leuprorelin		KLH-2109 200 mg		Placebo		KLH-2109 200 mg		KLH-2109 ALL		Placebo		Leuprorelin	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
肺うっ血	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
腎および尿路障害	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0
糖尿	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0
一般・全身障害および投与部位の状態	3	2.1	6	4.2	0	0.0	0	0.0	5	1.0	15	1.0	7	1.7	8	4.3
浮腫	3	2.1	4	2.8	0	0.0	0	0.0	4	0.8	7	0.5	0	0.0	5	2.7
末梢性浮腫	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	4	0.3	4	1.0	2	1.1
末梢腫脹	0	0.0	1	0.7	0	0.0	0	0.0	1	0.2	3	0.2	2	0.5	1	0.5
口渇	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
空腹	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0
臨床検査	9	6.3	9	6.3	3	6.3	1	2.4	37	7.4	94	6.5	11	2.7	10	5.3
血中クレアチンホスホキナーゼ増加	0	0.0	0	0.0	1	2.1	0	0.0	9	1.8	31	2.1	5	1.2	0	0.0
血中コレステロール増加	4	2.8	4	2.8	2	4.2	0	0.0	12	2.4	23	1.6	1	0.2	4	2.1
低比重リポ蛋白増加	2	1.4	4	2.8	2	4.2	0	0.0	10	2.0	17	1.2	1	0.2	4	2.1
体重増加	0	0.0	1	0.7	0	0.0	0	0.0	3	0.6	14	1.0	1	0.2	1	0.5
血圧上昇	0	0.0	0	0.0	0	0.0	0	0.0	4	0.8	12	0.8	0	0.0	0	0.0
血中トリグリセリド増加	4	2.8	5	3.5	0	0.0	1	2.4	5	1.0	10	0.7	2	0.5	6	3.2
体重減少	0	0.0	0	0.0	0	0.0	0	0.0	2	0.4	5	0.3	0	0.0	0	0.0
高比重リポ蛋白増加	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	4	0.3	0	0.0	0	0.0
尿中ケトン体陽性	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	3	0.2	2	0.5	0	0.0
脂質増加	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	2	0.1	0	0.0	0	0.0
血中ブドウ糖異常	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	1	0.1	0	0.0	0	0.0
心電図Ｔ波逆転	1	0.7	0	0.0	0	0.0	0	0.0	1	0.2	1	0.1	0	0.0	0	0.0
尿中ブドウ糖陽性	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	1	0.1	0	0.0	0	0.0
心電図異常Ｔ波	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0

Table 8.3.7-5
Occurrence of Adverse Events with Special Interest - Primary SOC and PT
Safety Set

AESI: うつ

Study	KLH2301				KLH2302				Overall Population							
Group	KLH-2109 200 mg		Leuprorelin		KLH-2109 200 mg		Placebo		KLH-2109 200 mg		KLH-2109 ALL		Placebo		Leuprorelin	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
N	143	---	144	---	48	---	41	---	498	---	1452	---	415	---	187	---
Any AEs	4	2.8	6	4.2	1	2.1	0	0.0	17	3.4	46	3.2	9	2.2	8	4.3
精神障害	2	1.4	6	4.2	1	2.1	0	0.0	14	2.8	43	3.0	9	2.2	8	4.3
気分動揺	0	0.0	0	0.0	0	0.0	0	0.0	5	1.0	19	1.3	8	1.9	0	0.0
感情不安定	0	0.0	1	0.7	0	0.0	0	0.0	3	0.6	9	0.6	0	0.0	2	1.1
うつ病	1	0.7	1	0.7	0	0.0	0	0.0	3	0.6	7	0.5	1	0.2	1	0.5
中期不眠症	1	0.7	0	0.0	1	2.1	0	0.0	2	0.4	2	0.1	0	0.0	1	0.5
気分変化	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	2	0.1	0	0.0	0	0.0
睡眠の質低下	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	1	0.1	1	0.2	0	0.0
抑うつ気分	0	0.0	2	1.4	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	2	1.1
抑うつ気分を伴う適応障害	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
薬物乱用	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
抑うつ症状	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.5
気分の落ち込み	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.5
神経系障害	2	1.4	0	0.0	0	0.0	0	0.0	3	0.6	3	0.2	0	0.0	0	0.0
記憶障害	2	1.4	0	0.0	0	0.0	0	0.0	3	0.6	3	0.2	0	0.0	0	0.0
一般・全身障害および投与部位の状態	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
泣き	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0

Table 8.3.7-6
Occurrence of Treatment-Related Adverse Events with Special Interest - Primary SOC and PT
Safety Set

AESI: 骨密度の減少

Study	KLH2301				KLH2302				Overall Population							
Group	KLH-2109 200 mg		Leuprorelin		KLH-2109 200 mg		Placebo		KLH-2109 200 mg		KLH-2109 ALL		Placebo		Leuprorelin	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
N	143	---	144	---	48	---	41	---	498	---	1452	---	415	---	187	---
Any Treatment-Related AEs	19	13.3	12	8.3	0	0.0	0	0.0	24	4.8	32	2.2	2	0.5	12	6.4
筋骨格系および結合組織障害	2	1.4	2	1.4	0	0.0	0	0.0	3	0.6	4	0.3	1	0.2	2	1.1
骨吸収亢進	2	1.4	1	0.7	0	0.0	0	0.0	2	0.4	2	0.1	0	0.0	1	0.5
骨喪失	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	2	0.1	0	0.0	0	0.0
骨減少症	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	1	0.5
臨床検査	17	11.9	10	6.9	0	0.0	0	0.0	21	4.2	28	1.9	1	0.2	10	5.3
骨密度減少	8	5.6	4	2.8	0	0.0	0	0.0	12	2.4	19	1.3	1	0.2	4	2.1
生化学的骨代謝マーカー上昇	10	7.0	6	4.2	0	0.0	0	0.0	10	2.0	10	0.7	0	0.0	6	3.2

Table 8.3.7-6
Occurrence of Treatment-Related Adverse Events with Special Interest - Primary SOC and PT
Safety Set

AESI: 更年期様症状

Study	KLH2301				KLH2302				Overall Population							
Group	KLH-2109 200 mg		Leuprorelin		KLH-2109 200 mg		Placebo		KLH-2109 200 mg		KLH-2109 ALL		Placebo		Leuprorelin	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
N	143	---	144	---	48	---	41	---	498	---	1452	---	415	---	187	---
Any Treatment-Related AEs	96	67.1	95	66.0	25	52.1	2	4.9	255	51.2	488	33.6	44	10.6	126	67.4
代謝および栄養障害	0	0.0	0	0.0	1	2.1	0	0.0	3	0.6	5	0.3	0	0.0	0	0.0
食欲減退	0	0.0	0	0.0	1	2.1	0	0.0	3	0.6	5	0.3	0	0.0	0	0.0
精神障害	7	4.9	13	9.0	1	2.1	0	0.0	33	6.6	60	4.1	9	2.2	16	8.6
気分動揺	0	0.0	0	0.0	0	0.0	0	0.0	5	1.0	16	1.1	6	1.4	0	0.0
リビドー減退	0	0.0	0	0.0	0	0.0	0	0.0	7	1.4	10	0.7	0	0.0	0	0.0
不眠症	3	2.1	5	3.5	0	0.0	0	0.0	6	1.2	7	0.5	2	0.5	6	3.2
感情不安定	0	0.0	0	0.0	0	0.0	0	0.0	2	0.4	7	0.5	0	0.0	1	0.5
不安	0	0.0	0	0.0	0	0.0	0	0.0	5	1.0	6	0.4	1	0.2	0	0.0
易刺激性	1	0.7	2	1.4	0	0.0	0	0.0	2	0.4	5	0.3	2	0.5	2	1.1
うつ病	1	0.7	1	0.7	0	0.0	0	0.0	2	0.4	3	0.2	1	0.2	1	0.5
中期不眠症	1	0.7	0	0.0	1	2.1	0	0.0	2	0.4	2	0.1	0	0.0	1	0.5
睡眠障害	1	0.7	1	0.7	0	0.0	0	0.0	1	0.2	2	0.1	1	0.2	1	0.5
気分変化	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	2	0.1	0	0.0	0	0.0
睡眠の質低下	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	1	0.1	1	0.2	0	0.0
神経過敏	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	1	0.1	0	0.0	0	0.0
抑うつ気分	0	0.0	2	1.4	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	2	1.1
リビドー消失	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
注意欠如・多動性障害	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
抑うつ症状	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.5
気分の落ち込み	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.5
神経系障害	15	10.5	15	10.4	5	10.4	0	0.0	61	12.2	144	9.9	20	4.8	22	11.8
頭痛	9	6.3	10	6.9	3	6.3	0	0.0	40	8.0	104	7.2	12	2.9	15	8.0
浮動性めまい	4	2.8	3	2.1	2	4.2	0	0.0	14	2.8	31	2.1	1	0.2	4	2.1
傾眠	3	2.1	2	1.4	1	2.1	0	0.0	7	1.4	13	0.9	3	0.7	3	1.6

Table 8.3.7-6
Occurrence of Treatment-Related Adverse Events with Special Interest - Primary SOC and PT
Safety Set

AESI: 更年期様症状

Study	KLH2301				KLH2302				Overall Population							
Group	KLH-2109 200 mg		Leuprorelin		KLH-2109 200 mg		Placebo		KLH-2109 200 mg		KLH-2109 ALL		Placebo		Leuprorelin	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
片頭痛	0	0.0	1	0.7	0	0.0	0	0.0	3	0.6	8	0.6	3	0.7	1	0.5
体位性めまい	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	3	0.2	1	0.2	0	0.0
手根管症候群	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	2	1.1
眼障害	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	1	0.1	0	0.0	0	0.0
霧視	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	1	0.1	0	0.0	0	0.0
耳および迷路障害	1	0.7	2	1.4	0	0.0	1	2.4	1	0.2	5	0.3	1	0.2	3	1.6
回転性めまい	1	0.7	1	0.7	0	0.0	1	2.4	1	0.2	5	0.3	1	0.2	1	0.5
耳鳴	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	2	1.1
心臓障害	7	4.9	2	1.4	0	0.0	0	0.0	7	1.4	10	0.7	1	0.2	5	2.7
動悸	7	4.9	2	1.4	0	0.0	0	0.0	7	1.4	10	0.7	1	0.2	5	2.7
血管障害	77	53.8	77	53.5	23	47.9	0	0.0	215	43.2	357	24.6	17	4.1	102	54.5
ほてり	77	53.8	77	53.5	23	47.9	0	0.0	214	43.0	356	24.5	17	4.1	102	54.5
潮紅	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	1	0.1	0	0.0	0	0.0
皮膚および皮下組織障害	22	15.4	20	13.9	6	12.5	1	2.4	44	8.8	67	4.6	3	0.7	25	13.4
多汗症	19	13.3	17	11.8	6	12.5	1	2.4	36	7.2	48	3.3	1	0.2	22	11.8
脱毛症	4	2.8	1	0.7	0	0.0	0	0.0	6	1.2	12	0.8	1	0.2	1	0.5
寝汗	0	0.0	2	1.4	0	0.0	0	0.0	4	0.8	8	0.6	1	0.2	2	1.1
円形脱毛症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
筋骨格系および結合組織障害	24	16.8	18	12.5	0	0.0	0	0.0	31	6.2	50	3.4	1	0.2	24	12.8
関節痛	13	9.1	13	9.0	0	0.0	0	0.0	19	3.8	27	1.9	0	0.0	15	8.0
筋骨格硬直	10	7.0	3	2.1	0	0.0	0	0.0	11	2.2	18	1.2	0	0.0	6	3.2
腱鞘炎	2	1.4	0	0.0	0	0.0	0	0.0	2	0.4	2	0.1	0	0.0	0	0.0
四肢痛	1	0.7	0	0.0	0	0.0	0	0.0	1	0.2	2	0.1	0	0.0	0	0.0
筋肉痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	2	0.1	0	0.0	2	1.1
筋痙縮	1	0.7	1	0.7	0	0.0	0	0.0	1	0.2	1	0.1	0	0.0	1	0.5
筋緊張	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0

Table 8.3.7-6
Occurrence of Treatment-Related Adverse Events with Special Interest - Primary SOC and PT
Safety Set

AESI: 更年期様症状

Study	KLH2301				KLH2302				Overall Population							
Group	KLH-2109 200 mg		Leuprorelin		KLH-2109 200 mg		Placebo		KLH-2109 200 mg		KLH-2109 ALL		Placebo		Leuprorelin	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
弾発指	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.5
関節腫脹	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0
生殖系および乳房障害	9	6.3	7	4.9	0	0.0	0	0.0	18	3.6	32	2.2	1	0.2	9	4.8
閉経期症状	8	5.6	4	2.8	0	0.0	0	0.0	8	1.6	12	0.8	0	0.0	5	2.7
外陰腟乾燥	0	0.0	0	0.0	0	0.0	0	0.0	6	1.2	11	0.8	0	0.0	0	0.0
乳房不快感	1	0.7	2	1.4	0	0.0	0	0.0	2	0.4	3	0.2	0	0.0	2	1.1
外陰腟灼熱感	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	2	0.1	0	0.0	0	0.0
外陰腟不快感	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	1	0.1	0	0.0	0	0.0
外陰腟そう痒症	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	1	0.5
乳房圧痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	1	0.2	0	0.0
乳房痛	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
萎縮性外陰腟炎	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.5
一般・全身障害および投与部位の状態	9	6.3	10	6.9	2	4.2	0	0.0	19	3.8	33	2.3	4	1.0	11	5.9
倦怠感	8	5.6	8	5.6	1	2.1	0	0.0	12	2.4	19	1.3	1	0.2	9	4.8
疲労	1	0.7	1	0.7	0	0.0	0	0.0	5	1.0	8	0.6	2	0.5	1	0.5
無力症	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	4	0.3	0	0.0	0	0.0
熱感	0	0.0	0	0.0	1	2.1	0	0.0	1	0.2	2	0.1	1	0.2	0	0.0
冷感	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.5

Table 8.3.7-6
Occurrence of Treatment-Related Adverse Events with Special Interest - Primary SOC and PT
Safety Set

AESI: 子宮出血関連事象

Study	KLH2301				KLH2302				Overall Population							
Group	KLH-2109 200 mg		Leuprorelin		KLH-2109 200 mg		Placebo		KLH-2109 200 mg		KLH-2109 ALL		Placebo		Leuprorelin	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
N	143	---	144	---	48	---	41	---	498	---	1452	---	415	---	187	---
Any Treatment-Related AEs	71	49.7	102	70.8	25	52.1	15	36.6	127	25.5	303	20.9	34	8.2	133	71.1
生殖系および乳房障害	71	49.7	102	70.8	25	52.1	15	36.6	127	25.5	303	20.9	34	8.2	133	71.1
月経中間期出血	53	37.1	77	53.5	20	41.7	13	31.7	95	19.1	240	16.5	25	6.0	103	55.1
重度月経出血	6	4.2	4	2.8	0	0.0	0	0.0	12	2.4	58	4.0	5	1.2	9	4.8
異常子宮出血	6	4.2	12	8.3	4	8.3	0	0.0	10	2.0	10	0.7	0	0.0	12	6.4
腟出血	1	0.7	2	1.4	0	0.0	0	0.0	5	1.0	8	0.6	2	0.5	2	1.1
子宮出血	6	4.2	6	4.2	0	0.0	0	0.0	6	1.2	7	0.5	0	0.0	6	3.2
不規則月経	3	2.1	1	0.7	0	0.0	2	4.9	3	0.6	3	0.2	2	0.5	1	0.5
性器出血	1	0.7	2	1.4	1	2.1	0	0.0	2	0.4	2	0.1	0	0.0	2	1.1
月経障害	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	2	0.1	0	0.0	1	0.5
月経遅延	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	1	0.1	0	0.0	0	0.0
希発月経	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0

Table 8.3.7-6
Occurrence of Treatment-Related Adverse Events with Special Interest - Primary SOC and PT
Safety Set

AESI: 肝酵素上昇

Study	KLH2301				KLH2302				Overall Population							
Group	KLH-2109 200 mg		Leuprorelin		KLH-2109 200 mg		Placebo		KLH-2109 200 mg		KLH-2109 ALL		Placebo		Leuprorelin	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
N	143	---	144	---	48	---	41	---	498	---	1452	---	415	---	187	---
Any Treatment-Related AEs	17	11.9	9	6.3	2	4.2	0	0.0	39	7.8	78	5.4	5	1.2	10	5.3
肝胆道系障害	4	2.8	1	0.7	1	2.1	0	0.0	6	1.2	7	0.5	0	0.0	1	0.5
肝機能異常	4	2.8	1	0.7	1	2.1	0	0.0	5	1.0	5	0.3	0	0.0	1	0.5
脂肪肝	1	0.7	0	0.0	0	0.0	0	0.0	1	0.2	2	0.1	0	0.0	0	0.0
高トランスアミナーゼ血症	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	1	0.1	0	0.0	0	0.0
臨床検査	13	9.1	8	5.6	1	2.1	0	0.0	33	6.6	71	4.9	5	1.2	9	4.8
アラニンアミノトランスフェラーゼ増加	7	4.9	2	1.4	0	0.0	0	0.0	18	3.6	46	3.2	2	0.5	2	1.1
アスパラギン酸アミノトランスフェラーゼ増加	4	2.8	0	0.0	0	0.0	0	0.0	11	2.2	35	2.4	1	0.2	0	0.0
γーグルタミルトランスフェラーゼ増加	5	3.5	5	3.5	1	2.1	0	0.0	12	2.4	22	1.5	1	0.2	5	2.7
グアナーゼ増加	0	0.0	0	0.0	0	0.0	0	0.0	6	1.2	14	1.0	0	0.0	0	0.0
血中アルカリホスファターゼ増加	1	0.7	2	1.4	0	0.0	0	0.0	2	0.4	4	0.3	0	0.0	3	1.6
血中ビリルビン増加	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	4	0.3	1	0.2	0	0.0
肝機能検査値上昇	2	1.4	1	0.7	0	0.0	0	0.0	3	0.6	3	0.2	0	0.0	1	0.5
肝酵素上昇	1	0.7	0	0.0	0	0.0	0	0.0	2	0.4	3	0.2	1	0.2	0	0.0
トランスアミナーゼ上昇	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	1	0.1	0	0.0	0	0.0
プロトロンビン時間延長	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0

Table 8.3.7-6
Occurrence of Treatment-Related Adverse Events with Special Interest - Primary SOC and PT
Safety Set

AESI: QTc間隔の延長

Study	KLH2301				KLH2302				Overall Population							
Group	KLH-2109 200 mg		Leuprorelin		KLH-2109 200 mg		Placebo		KLH-2109 200 mg		KLH-2109 ALL		Placebo		Leuprorelin	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
N	143	---	144	---	48	---	41	---	498	---	1452	---	415	---	187	---
Any Treatment-Related AEs	1	0.7	0	0.0	0	0.0	0	0.0	1	0.2	2	0.1	0	0.0	0	0.0
臨床検査	1	0.7	0	0.0	0	0.0	0	0.0	1	0.2	2	0.1	0	0.0	0	0.0
心電図ＱＴ延長	1	0.7	0	0.0	0	0.0	0	0.0	1	0.2	2	0.1	0	0.0	0	0.0

Table 8.3.7-6
Occurrence of Treatment-Related Adverse Events with Special Interest - Primary SOC and PT
Safety Set

AESI: 代謝及び心血管系の変化

Study	KLH2301				KLH2302				Overall Population							
Group	KLH-2109 200 mg		Leuprorelin		KLH-2109 200 mg		Placebo		KLH-2109 200 mg		KLH-2109 ALL		Placebo		Leuprorelin	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
N	143	---	144	---	48	---	41	---	498	---	1452	---	415	---	187	---
Any Treatment-Related AEs	17	11.9	17	11.8	2	4.2	0	0.0	31	6.2	74	5.1	7	1.7	21	11.2
代謝および栄養障害	5	3.5	2	1.4	0	0.0	0	0.0	5	1.0	12	0.8	2	0.5	4	2.1
脂質異常症	5	3.5	1	0.7	0	0.0	0	0.0	5	1.0	10	0.7	0	0.0	3	1.6
過食	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	1	0.2	0	0.0
食欲亢進	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
２型糖尿病	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.5
高コレステロール血症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0
高トリグリセリド血症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0
神経系障害	1	0.7	0	0.0	0	0.0	0	0.0	1	0.2	2	0.1	0	0.0	0	0.0
くも膜下出血	1	0.7	0	0.0	0	0.0	0	0.0	1	0.2	2	0.1	0	0.0	0	0.0
心臓障害	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	2	0.1	0	0.0	0	0.0
狭心症	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	2	0.1	0	0.0	0	0.0
血管障害	1	0.7	2	1.4	0	0.0	0	0.0	1	0.2	3	0.2	0	0.0	2	1.1
高血圧	1	0.7	2	1.4	0	0.0	0	0.0	1	0.2	3	0.2	0	0.0	2	1.1
一般・全身障害および投与部位の状態	3	2.1	4	2.8	0	0.0	0	0.0	5	1.0	13	0.9	2	0.5	6	3.2
浮腫	3	2.1	3	2.1	0	0.0	0	0.0	4	0.8	7	0.5	0	0.0	4	2.1
末梢性浮腫	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	3	0.2	0	0.0	2	1.1
末梢腫脹	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	2	0.1	1	0.2	0	0.0
口渇	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
空腹	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0
臨床検査	7	4.9	9	6.3	2	4.2	0	0.0	19	3.8	45	3.1	3	0.7	9	4.8
血中コレステロール増加	4	2.8	4	2.8	2	4.2	0	0.0	11	2.2	21	1.4	1	0.2	4	2.1
低比重リポ蛋白増加	2	1.4	4	2.8	2	4.2	0	0.0	9	1.8	14	1.0	1	0.2	4	2.1
血中トリグリセリド増加	3	2.1	5	3.5	0	0.0	0	0.0	4	0.8	8	0.6	0	0.0	5	2.7
体重増加	0	0.0	1	0.7	0	0.0	0	0.0	1	0.2	6	0.4	1	0.2	1	0.5

Table 8.3.7-6
Occurrence of Treatment-Related Adverse Events with Special Interest - Primary SOC and PT
Safety Set

AESI: 代謝及び心血管系の変化

Study	KLH2301				KLH2302				Overall Population							
Group	KLH-2109 200 mg		Leuprorelin		KLH-2109 200 mg		Placebo		KLH-2109 200 mg		KLH-2109 ALL		Placebo		Leuprorelin	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
血中クレアチンホスホキナーゼ増加	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	5	0.3	1	0.2	0	0.0
血圧上昇	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	4	0.3	0	0.0	0	0.0
高比重リポ蛋白増加	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	4	0.3	0	0.0	0	0.0
体重減少	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	3	0.2	0	0.0	0	0.0
尿中ブドウ糖陽性	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	1	0.1	0	0.0	0	0.0
脂質増加	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	0	0.0
尿中ケトン体陽性	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	0	0.0

Table 8.3.7-6
Occurrence of Treatment-Related Adverse Events with Special Interest - Primary SOC and PT
Safety Set

AESI: うつ

Study	KLH2301				KLH2302				Overall Population							
Group	KLH-2109 200 mg		Leuprorelin		KLH-2109 200 mg		Placebo		KLH-2109 200 mg		KLH-2109 ALL		Placebo		Leuprorelin	
Primary SOC, PT	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
N	143	---	144	---	48	---	41	---	498	---	1452	---	415	---	187	---
Any Treatment-Related AEs	3	2.1	5	3.5	1	2.1	0	0.0	13	2.6	33	2.3	7	1.7	7	3.7
精神障害	2	1.4	5	3.5	1	2.1	0	0.0	12	2.4	32	2.2	7	1.7	7	3.7
気分動揺	0	0.0	0	0.0	0	0.0	0	0.0	5	1.0	16	1.1	6	1.4	0	0.0
感情不安定	0	0.0	0	0.0	0	0.0	0	0.0	2	0.4	7	0.5	0	0.0	1	0.5
うつ病	1	0.7	1	0.7	0	0.0	0	0.0	2	0.4	3	0.2	1	0.2	1	0.5
中期不眠症	1	0.7	0	0.0	1	2.1	0	0.0	2	0.4	2	0.1	0	0.0	1	0.5
気分変化	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	2	0.1	0	0.0	0	0.0
睡眠の質低下	0	0.0	0	0.0	0	0.0	0	0.0	1	0.2	1	0.1	1	0.2	0	0.0
抑うつ気分	0	0.0	2	1.4	0	0.0	0	0.0	0	0.0	1	0.1	0	0.0	2	1.1
抑うつ症状	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.5
気分の落ち込み	0	0.0	1	0.7	0	0.0	0	0.0	0	0.0	0	0.0	0	0.0	1	0.5
神経系障害	1	0.7	0	0.0	0	0.0	0	0.0	1	0.2	1	0.1	0	0.0	0	0.0
記憶障害	1	0.7	0	0.0	0	0.0	0	0.0	1	0.2	1	0.1	0	0.0	0	0.0