付録 2.7.4-47
部分集団別の有害事象の要約
第 IIb 相及び第 III 相試験：プラセボ対照安全性併合解析
1 回以上投与された被験者

	Placebo		MK-3222 100 mg		MK-3222 200 mg		MK-3222 100/200 mg		Etanercept 50 mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Body weight: ≤ 90 kg										
Subjects in population	211	(100.0)	416	(100.0)	415	(100.0)	831	(100.0)	180	(100.0)
with one or more adverse events	112	(53.1)	197	(47.4)	201	(48.4)	398	(47.9)	105	(58.3)
with no adverse events	99	(46.9)	219	(52.6)	214	(51.6)	433	(52.1)	75	(41.7)
with drug-related† adverse events	29	(13.7)	62	(14.9)	63	(15.2)	125	(15.0)	59	(32.8)
with serious adverse events	2	(0.9)	5	(1.2)	9	(2.2)	14	(1.7)	4	(2.2)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	2	(0.5)	2	(0.2)	2	(1.1)
who died	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
discontinued‡ due to an adverse event	2	(0.9)	3	(0.7)	3	(0.7)	6	(0.7)	3	(1.7)
discontinued due to a drug-related adverse event	1	(0.5)	1	(0.2)	1	(0.2)	2	(0.2)	3	(1.7)
discontinued due to a serious adverse event	0	(0.0)	1	(0.2)	3	(0.7)	4	(0.5)	1	(0.6)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	1	(0.6)
Body weight: > 90 kg										
Subjects in population	144	(100.0)	289	(100.0)	293	(100.0)	582	(100.0)	133	(100.0)
with one or more adverse events	79	(54.9)	143	(49.5)	138	(47.1)	281	(48.3)	64	(48.1)
with no adverse events	65	(45.1)	146	(50.5)	155	(52.9)	301	(51.7)	69	(51.9)
with drug-related† adverse events	18	(12.5)	42	(14.5)	36	(12.3)	78	(13.4)	33	(24.8)
with serious adverse events	4	(2.8)	5	(1.7)	7	(2.4)	12	(2.1)	3	(2.3)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.2)	0	(0.0)
who died	0	(0.0)	1	(0.3)	0	(0.0)	1	(0.2)	0	(0.0)
discontinued‡ due to an adverse event	2	(1.4)	1	(0.3)	6	(2.0)	7	(1.2)	3	(2.3)
discontinued due to a drug-related adverse event	1	(0.7)	0	(0.0)	2	(0.7)	2	(0.3)	1	(0.8)

Adverse Events Summary by Subgroup
Phase 2 and 3: Placebo-Controlled Safety Pool
All Subjects as Treated

	Placebo		MK-3222 100 mg		MK-3222 200 mg		MK-3222 100/200 mg		Etanercept 50 mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
discontinued due to a serious adverse event	0	(0.0)	1	(0.3)	2	(0.7)	3	(0.5)	1	(0.8)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Prior exposure to biologic therapy for psoriasis: Yes										
Subjects in population	67	(100.0)	125	(100.0)	128	(100.0)	253	(100.0)	37	(100.0)
with one or more adverse events	38	(56.7)	62	(49.6)	63	(49.2)	125	(49.4)	20	(54.1)
with no adverse events	29	(43.3)	63	(50.4)	65	(50.8)	128	(50.6)	17	(45.9)
with drug-related† adverse events	5	(7.5)	13	(10.4)	18	(14.1)	31	(12.3)	10	(27.0)
with serious adverse events	0	(0.0)	2	(1.6)	3	(2.3)	5	(2.0)	2	(5.4)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	1	(0.8)	1	(0.4)	1	(2.7)
who died	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued‡ due to an adverse event	0	(0.0)	0	(0.0)	3	(2.3)	3	(1.2)	3	(8.1)
discontinued due to a drug-related adverse event	0	(0.0)	0	(0.0)	1	(0.8)	1	(0.4)	3	(8.1)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	2	(1.6)	2	(0.8)	1	(2.7)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	1	(0.8)	1	(0.4)	1	(2.7)
Prior exposure to biologic therapy for psoriasis: No										
Subjects in population	288	(100.0)	580	(100.0)	580	(100.0)	1160	(100.0)	276	(100.0)
with one or more adverse events	153	(53.1)	278	(47.9)	276	(47.6)	554	(47.8)	149	(54.0)
with no adverse events	135	(46.9)	302	(52.1)	304	(52.4)	606	(52.2)	127	(46.0)
with drug-related† adverse events	42	(14.6)	91	(15.7)	81	(14.0)	172	(14.8)	82	(29.7)
with serious adverse events	6	(2.1)	8	(1.4)	13	(2.2)	21	(1.8)	5	(1.8)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	2	(0.3)	2	(0.2)	1	(0.4)
who died	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.2)	0	(0.0)

Adverse Events Summary by Subgroup
Phase 2 and 3: Placebo-Controlled Safety Pool
All Subjects as Treated

	Placebo		MK-3222 100 mg		MK-3222 200 mg		MK-3222 100/200 mg		Etanercept 50 mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
discontinued‡ due to an adverse event	4	(1.4)	4	(0.7)	6	(1.0)	10	(0.9)	3	(1.1)
discontinued due to a drug-related adverse event	2	(0.7)	1	(0.2)	2	(0.3)	3	(0.3)	1	(0.4)
discontinued due to a serious adverse event	0	(0.0)	2	(0.3)	3	(0.5)	5	(0.4)	1	(0.4)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Age: < 65										
Subjects in population	319	(100.0)	644	(100.0)	650	(100.0)	1294	(100.0)	282	(100.0)
with one or more adverse events	173	(54.2)	311	(48.3)	310	(47.7)	621	(48.0)	150	(53.2)
with no adverse events	146	(45.8)	333	(51.7)	340	(52.3)	673	(52.0)	132	(46.8)
with drug-related† adverse events	44	(13.8)	96	(14.9)	93	(14.3)	189	(14.6)	88	(31.2)
with serious adverse events	6	(1.9)	8	(1.2)	13	(2.0)	21	(1.6)	6	(2.1)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	3	(0.5)	3	(0.2)	2	(0.7)
who died	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.2)	0	(0.0)
discontinued‡ due to an adverse event	4	(1.3)	4	(0.6)	7	(1.1)	11	(0.9)	6	(2.1)
discontinued due to a drug-related adverse event	2	(0.6)	1	(0.2)	3	(0.5)	4	(0.3)	4	(1.4)
discontinued due to a serious adverse event	0	(0.0)	2	(0.3)	3	(0.5)	5	(0.4)	2	(0.7)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	1	(0.4)
Age: ≥ 65										
Subjects in population	36	(100.0)	61	(100.0)	58	(100.0)	119	(100.0)	31	(100.0)
with one or more adverse events	18	(50.0)	29	(47.5)	29	(50.0)	58	(48.7)	19	(61.3)
with no adverse events	18	(50.0)	32	(52.5)	29	(50.0)	61	(51.3)	12	(38.7)
with drug-related† adverse events	3	(8.3)	8	(13.1)	6	(10.3)	14	(11.8)	4	(12.9)
with serious adverse events	0	(0.0)	2	(3.3)	3	(5.2)	5	(4.2)	1	(3.2)

Adverse Events Summary by Subgroup
Phase 2 and 3: Placebo-Controlled Safety Pool
All Subjects as Treated

	Placebo		MK-3222 100 mg		MK-3222 200 mg		MK-3222 100/200 mg		Etanercept 50 mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
who died	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued‡ due to an adverse event	0	(0.0)	0	(0.0)	2	(3.4)	2	(1.7)	0	(0.0)
discontinued due to a drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	2	(3.4)	2	(1.7)	0	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Gender: Female										
Subjects in population	106	(100.0)	202	(100.0)	192	(100.0)	394	(100.0)	91	(100.0)
with one or more adverse events	62	(58.5)	104	(51.5)	106	(55.2)	210	(53.3)	54	(59.3)
with no adverse events	44	(41.5)	98	(48.5)	86	(44.8)	184	(46.7)	37	(40.7)
with drug-related† adverse events	14	(13.2)	31	(15.3)	37	(19.3)	68	(17.3)	32	(35.2)
with serious adverse events	0	(0.0)	2	(1.0)	7	(3.6)	9	(2.3)	2	(2.2)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
who died	0	(0.0)	1	(0.5)	0	(0.0)	1	(0.3)	0	(0.0)
discontinued‡ due to an adverse event	1	(0.9)	2	(1.0)	3	(1.6)	5	(1.3)	1	(1.1)
discontinued due to a drug-related adverse event	1	(0.9)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
discontinued due to a serious adverse event	0	(0.0)	1	(0.5)	2	(1.0)	3	(0.8)	0	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Gender: Male										
Subjects in population	249	(100.0)	503	(100.0)	516	(100.0)	1019	(100.0)	222	(100.0)
with one or more adverse events	129	(51.8)	236	(46.9)	233	(45.2)	469	(46.0)	115	(51.8)
with no adverse events	120	(48.2)	267	(53.1)	283	(54.8)	550	(54.0)	107	(48.2)

Adverse Events Summary by Subgroup
Phase 2 and 3: Placebo-Controlled Safety Pool
All Subjects as Treated

	Placebo		MK-3222 100 mg		MK-3222 200 mg		MK-3222 100/200 mg		Etanercept 50 mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
with drug-related† adverse events	33	(13.3)	73	(14.5)	62	(12.0)	135	(13.2)	60	(27.0)
with serious adverse events	6	(2.4)	8	(1.6)	9	(1.7)	17	(1.7)	5	(2.3)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	3	(0.6)	3	(0.3)	1	(0.5)
who died	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
discontinued‡ due to an adverse event	3	(1.2)	2	(0.4)	6	(1.2)	8	(0.8)	5	(2.3)
discontinued due to a drug-related adverse event	1	(0.4)	1	(0.2)	3	(0.6)	4	(0.4)	3	(1.4)
discontinued due to a serious adverse event	0	(0.0)	1	(0.2)	3	(0.6)	4	(0.4)	2	(0.9)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	1	(0.5)
Race: White										
Subjects in population	278	(100.0)	569	(100.0)	566	(100.0)	1135	(100.0)	289	(100.0)
with one or more adverse events	152	(54.7)	282	(49.6)	277	(48.9)	559	(49.3)	155	(53.6)
with no adverse events	126	(45.3)	287	(50.4)	289	(51.1)	576	(50.7)	134	(46.4)
with drug-related† adverse events	36	(12.9)	95	(16.7)	83	(14.7)	178	(15.7)	86	(29.8)
with serious adverse events	5	(1.8)	8	(1.4)	13	(2.3)	21	(1.9)	7	(2.4)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	2	(0.4)	2	(0.2)	2	(0.7)
who died	0	(0.0)	2	(0.4)	0	(0.0)	2	(0.2)	0	(0.0)
discontinued‡ due to an adverse event	2	(0.7)	4	(0.7)	8	(1.4)	12	(1.1)	5	(1.7)
discontinued due to a drug-related adverse event	1	(0.4)	1	(0.2)	3	(0.5)	4	(0.4)	3	(1.0)
discontinued due to a serious adverse event	0	(0.0)	2	(0.4)	4	(0.7)	6	(0.5)	2	(0.7)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	1	(0.3)
Race: Asian										
Subjects in population	56	(100.0)	93	(100.0)	109	(100.0)	202	(100.0)	10	(100.0)

Adverse Events Summary by Subgroup
Phase 2 and 3: Placebo-Controlled Safety Pool
All Subjects as Treated

	Placebo		MK-3222 100 mg		MK-3222 200 mg		MK-3222 100/200 mg		Etanercept 50 mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
with one or more adverse events	29	(51.8)	39	(41.9)	42	(38.5)	81	(40.1)	6	(60.0)
with no adverse events	27	(48.2)	54	(58.1)	67	(61.5)	121	(59.9)	4	(40.0)
with drug-related† adverse events	8	(14.3)	8	(8.6)	10	(9.2)	18	(8.9)	3	(30.0)
with serious adverse events	1	(1.8)	1	(1.1)	3	(2.8)	4	(2.0)	0	(0.0)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	1	(0.9)	1	(0.5)	0	(0.0)
who died	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued‡ due to an adverse event	2	(3.6)	0	(0.0)	1	(0.9)	1	(0.5)	1	(10.0)
discontinued due to a drug-related adverse event	1	(1.8)	0	(0.0)	0	(0.0)	0	(0.0)	1	(10.0)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	1	(0.9)	1	(0.5)	0	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Race: Black Or African American										
Subjects in population	7	(100.0)	21	(100.0)	16	(100.0)	37	(100.0)	8	(100.0)
with one or more adverse events	3	(42.9)	6	(28.6)	6	(37.5)	12	(32.4)	4	(50.0)
with no adverse events	4	(57.1)	15	(71.4)	10	(62.5)	25	(67.6)	4	(50.0)
with drug-related† adverse events	2	(28.6)	0	(0.0)	2	(12.5)	2	(5.4)	2	(25.0)
with serious adverse events	0	(0.0)	1	(4.8)	0	(0.0)	1	(2.7)	0	(0.0)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
who died	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued‡ due to an adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

Adverse Events Summary by Subgroup
Phase 2 and 3: Placebo-Controlled Safety Pool
All Subjects as Treated

	Placebo		MK-3222 100 mg		MK-3222 200 mg		MK-3222 100/200 mg		Etanercept 50 mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Race: Other Races										
Subjects in population	9	(100.0)	18	(100.0)	11	(100.0)	29	(100.0)	4	(100.0)
with one or more adverse events	4	(44.4)	11	(61.1)	9	(81.8)	20	(69.0)	4	(100.0)
with no adverse events	5	(55.6)	7	(38.9)	2	(18.2)	9	(31.0)	0	(0.0)
with drug-related† adverse events	0	(0.0)	1	(5.6)	2	(18.2)	3	(10.3)	1	(25.0)
with serious adverse events	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
who died	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued‡ due to an adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Region: North America										
Subjects in population	74	(100.0)	144	(100.0)	148	(100.0)	292	(100.0)	113	(100.0)
with one or more adverse events	36	(48.6)	63	(43.8)	68	(45.9)	131	(44.9)	57	(50.4)
with no adverse events	38	(51.4)	81	(56.3)	80	(54.1)	161	(55.1)	56	(49.6)
with drug-related† adverse events	9	(12.2)	13	(9.0)	20	(13.5)	33	(11.3)	29	(25.7)
with serious adverse events	1	(1.4)	1	(0.7)	2	(1.4)	3	(1.0)	2	(1.8)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
who died	0	(0.0)	1	(0.7)	0	(0.0)	1	(0.3)	0	(0.0)
discontinued‡ due to an adverse event	2	(2.7)	2	(1.4)	2	(1.4)	4	(1.4)	2	(1.8)
discontinued due to a drug-related adverse event	1	(1.4)	1	(0.7)	0	(0.0)	1	(0.3)	1	(0.9)

Adverse Events Summary by Subgroup
Phase 2 and 3: Placebo-Controlled Safety Pool
All Subjects as Treated

	Placebo		MK-3222 100 mg		MK-3222 200 mg		MK-3222 100/200 mg		Etanercept 50 mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
discontinued due to a serious adverse event	0	(0.0)	1	(0.7)	1	(0.7)	2	(0.7)	1	(0.9)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Region: Europe										
Subjects in population	120	(100.0)	241	(100.0)	242	(100.0)	483	(100.0)	200	(100.0)
with one or more adverse events	76	(63.3)	127	(52.7)	136	(56.2)	263	(54.5)	112	(56.0)
with no adverse events	44	(36.7)	114	(47.3)	106	(43.8)	220	(45.5)	88	(44.0)
with drug-related† adverse events	27	(22.5)	64	(26.6)	53	(21.9)	117	(24.2)	63	(31.5)
with serious adverse events	4	(3.3)	4	(1.7)	6	(2.5)	10	(2.1)	5	(2.5)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	2	(0.8)	2	(0.4)	2	(1.0)
who died	0	(0.0)	1	(0.4)	0	(0.0)	1	(0.2)	0	(0.0)
discontinued‡ due to an adverse event	1	(0.8)	2	(0.8)	2	(0.8)	4	(0.8)	4	(2.0)
discontinued due to a drug-related adverse event	1	(0.8)	0	(0.0)	1	(0.4)	1	(0.2)	3	(1.5)
discontinued due to a serious adverse event	0	(0.0)	1	(0.4)	1	(0.4)	2	(0.4)	1	(0.5)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	1	(0.4)	1	(0.2)	1	(0.5)
Region: Rest of World										
Subjects in population	129	(100.0)	256	(100.0)	256	(100.0)	512	(100.0)	0	(0.0)
with one or more adverse events	62	(48.1)	119	(46.5)	112	(43.8)	231	(45.1)	0	(0.0)
with no adverse events	67	(51.9)	137	(53.5)	144	(56.3)	281	(54.9)	0	(0.0)
with drug-related† adverse events	6	(4.7)	20	(7.8)	20	(7.8)	40	(7.8)	0	(0.0)
with serious adverse events	1	(0.8)	4	(1.6)	6	(2.3)	10	(2.0)	0	(0.0)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
who died	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

Adverse Events Summary by Subgroup
Phase 2 and 3: Placebo-Controlled Safety Pool
All Subjects as Treated

	Placebo		MK-3222 100 mg		MK-3222 200 mg		MK-3222 100/200 mg		Etanercept 50 mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
discontinued‡ due to an adverse event	1	(0.8)	0	(0.0)	4	(1.6)	4	(0.8)	0	(0.0)
discontinued due to a drug-related adverse event	0	(0.0)	0	(0.0)	2	(0.8)	2	(0.4)	0	(0.0)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	2	(0.8)	2	(0.4)	0	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Failure of at least one traditional systemic therapy (methotrexate, cyclosporine, phototherapy): Yes										
Subjects in population	139	(100.0)	268	(100.0)	286	(100.0)	554	(100.0)	195	(100.0)
with one or more adverse events	80	(57.6)	126	(47.0)	133	(46.5)	259	(46.8)	102	(52.3)
with no adverse events	59	(42.4)	142	(53.0)	153	(53.5)	295	(53.2)	93	(47.7)
with drug-related† adverse events	22	(15.8)	46	(17.2)	47	(16.4)	93	(16.8)	56	(28.7)
with serious adverse events	4	(2.9)	4	(1.5)	5	(1.7)	9	(1.6)	3	(1.5)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.2)	1	(0.5)
who died	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued‡ due to an adverse event	1	(0.7)	2	(0.7)	1	(0.3)	3	(0.5)	5	(2.6)
discontinued due to a drug-related adverse event	1	(0.7)	1	(0.4)	0	(0.0)	1	(0.2)	3	(1.5)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	2	(1.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.5)
Failure of at least one traditional systemic therapy (methotrexate, cyclosporine, phototherapy): No										
Subjects in population	129	(100.0)	257	(100.0)	254	(100.0)	511	(100.0)	118	(100.0)
with one or more adverse events	71	(55.0)	132	(51.4)	126	(49.6)	258	(50.5)	67	(56.8)
with no adverse events	58	(45.0)	125	(48.6)	128	(50.4)	253	(49.5)	51	(43.2)
with drug-related† adverse events	19	(14.7)	40	(15.6)	38	(15.0)	78	(15.3)	36	(30.5)
with serious adverse events	1	(0.8)	4	(1.6)	6	(2.4)	10	(2.0)	4	(3.4)

Adverse Events Summary by Subgroup
Phase 2 and 3: Placebo-Controlled Safety Pool
All Subjects as Treated

	Placebo		MK-3222 100 mg		MK-3222 200 mg		MK-3222 100/200 mg		Etanercept 50 mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	2	(0.8)	2	(0.4)	1	(0.8)
who died	0	(0.0)	2	(0.8)	0	(0.0)	2	(0.4)	0	(0.0)
discontinued‡ due to an adverse event	2	(1.6)	2	(0.8)	4	(1.6)	6	(1.2)	1	(0.8)
discontinued due to a drug-related adverse event	1	(0.8)	0	(0.0)	1	(0.4)	1	(0.2)	1	(0.8)
discontinued due to a serious adverse event	0	(0.0)	2	(0.8)	3	(1.2)	5	(1.0)	0	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	1	(0.4)	1	(0.2)	0	(0.0)
TNF antagonist response among subjects previously treated for psoriasis: Yes										
Subjects in population	35	(100.0)	60	(100.0)	61	(100.0)	121	(100.0)	13	(100.0)
with one or more adverse events	20	(57.1)	30	(50.0)	28	(45.9)	58	(47.9)	6	(46.2)
with no adverse events	15	(42.9)	30	(50.0)	33	(54.1)	63	(52.1)	7	(53.8)
with drug-related† adverse events	4	(11.4)	4	(6.7)	6	(9.8)	10	(8.3)	3	(23.1)
with serious adverse events	0	(0.0)	1	(1.7)	3	(4.9)	4	(3.3)	0	(0.0)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
who died	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued‡ due to an adverse event	0	(0.0)	0	(0.0)	1	(1.6)	1	(0.8)	1	(7.7)
discontinued due to a drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(7.7)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	1	(1.6)	1	(0.8)	0	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
TNF antagonist response among subjects previously treated for psoriasis: No										
Subjects in population	13	(100.0)	18	(100.0)	25	(100.0)	43	(100.0)	6	(100.0)
with one or more adverse events	8	(61.5)	13	(72.2)	11	(44.0)	24	(55.8)	5	(83.3)
with no adverse events	5	(38.5)	5	(27.8)	14	(56.0)	19	(44.2)	1	(16.7)

Adverse Events Summary by Subgroup
Phase 2 and 3: Placebo-Controlled Safety Pool
All Subjects as Treated

	Placebo		MK-3222 100 mg		MK-3222 200 mg		MK-3222 100/200 mg		Etanercept 50 mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
with drug-related† adverse events	0	(0.0)	3	(16.7)	2	(8.0)	5	(11.6)	2	(33.3)
with serious adverse events	0	(0.0)	1	(5.6)	0	(0.0)	1	(2.3)	0	(0.0)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
who died	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued‡ due to an adverse event	0	(0.0)	0	(0.0)	1	(4.0)	1	(2.3)	0	(0.0)
discontinued due to a drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Psoriatic Arthritis: Yes										
Subjects in population	53	(100.0)	118	(100.0)	117	(100.0)	235	(100.0)	41	(100.0)
with one or more adverse events	34	(64.2)	52	(44.1)	63	(53.8)	115	(48.9)	24	(58.5)
with no adverse events	19	(35.8)	66	(55.9)	54	(46.2)	120	(51.1)	17	(41.5)
with drug-related† adverse events	13	(24.5)	25	(21.2)	17	(14.5)	42	(17.9)	10	(24.4)
with serious adverse events	3	(5.7)	2	(1.7)	5	(4.3)	7	(3.0)	2	(4.9)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	1	(0.9)	1	(0.4)	0	(0.0)
who died	0	(0.0)	1	(0.8)	0	(0.0)	1	(0.4)	0	(0.0)
discontinued‡ due to an adverse event	1	(1.9)	2	(1.7)	2	(1.7)	4	(1.7)	2	(4.9)
discontinued due to a drug-related adverse event	1	(1.9)	0	(0.0)	0	(0.0)	0	(0.0)	1	(2.4)
discontinued due to a serious adverse event	0	(0.0)	1	(0.8)	1	(0.9)	2	(0.9)	1	(2.4)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Psoriatic Arthritis: No										
Subjects in population	302	(100.0)	587	(100.0)	591	(100.0)	1178	(100.0)	272	(100.0)

Adverse Events Summary by Subgroup
Phase 2 and 3: Placebo-Controlled Safety Pool
All Subjects as Treated

	Placebo		MK-3222 100 mg		MK-3222 200 mg		MK-3222 100/200 mg		Etanercept 50 mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
with one or more adverse events	157	(52.0)	288	(49.1)	276	(46.7)	564	(47.9)	145	(53.3)
with no adverse events	145	(48.0)	299	(50.9)	315	(53.3)	614	(52.1)	127	(46.7)
with drug-related† adverse events	34	(11.3)	79	(13.5)	82	(13.9)	161	(13.7)	82	(30.1)
with serious adverse events	3	(1.0)	8	(1.4)	11	(1.9)	19	(1.6)	5	(1.8)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	2	(0.3)	2	(0.2)	2	(0.7)
who died	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
discontinued‡ due to an adverse event	3	(1.0)	2	(0.3)	7	(1.2)	9	(0.8)	4	(1.5)
discontinued due to a drug-related adverse event	1	(0.3)	1	(0.2)	3	(0.5)	4	(0.3)	3	(1.1)
discontinued due to a serious adverse event	0	(0.0)	1	(0.2)	4	(0.7)	5	(0.4)	1	(0.4)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	1	(0.4)
Anti-drug antibody status: Positive ‡‡										
Subjects in population	0	(0.0)	30	(100.0)	29	(100.0)	59	(100.0)	0	(0.0)
with one or more adverse events	0	(0.0)	15	(50.0)	18	(62.1)	33	(55.9)	0	(0.0)
with no adverse events	0	(0.0)	15	(50.0)	11	(37.9)	26	(44.1)	0	(0.0)
with drug-related† adverse events	0	(0.0)	3	(10.0)	4	(13.8)	7	(11.9)	0	(0.0)
with serious adverse events	0	(0.0)	1	(3.3)	0	(0.0)	1	(1.7)	0	(0.0)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
who died	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued‡ due to an adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

Adverse Events Summary by Subgroup
Phase 2 and 3: Placebo-Controlled Safety Pool
All Subjects as Treated

	Placebo		MK-3222 100 mg		MK-3222 200 mg		MK-3222 100/200 mg		Etanercept 50 mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Anti-drug antibody status: Negative ††										
Subjects in population	0	(0.0)	632	(100.0)	629	(100.0)	1261	(100.0)	0	(0.0)
with one or more adverse events	0	(0.0)	308	(48.7)	304	(48.3)	612	(48.5)	0	(0.0)
with no adverse events	0	(0.0)	324	(51.3)	325	(51.7)	649	(51.5)	0	(0.0)
with drug-related† adverse events	0	(0.0)	96	(15.2)	89	(14.1)	185	(14.7)	0	(0.0)
with serious adverse events	0	(0.0)	9	(1.4)	14	(2.2)	23	(1.8)	0	(0.0)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	3	(0.5)	3	(0.2)	0	(0.0)
who died	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.2)	0	(0.0)
discontinued‡ due to an adverse event	0	(0.0)	3	(0.5)	7	(1.1)	10	(0.8)	0	(0.0)
discontinued due to a drug-related adverse event	0	(0.0)	1	(0.2)	3	(0.5)	4	(0.3)	0	(0.0)
discontinued due to a serious adverse event	0	(0.0)	2	(0.3)	3	(0.5)	5	(0.4)	0	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Disease duration category(< 15 years)										
Subjects in population	171	(100.0)	338	(100.0)	338	(100.0)	676	(100.0)	144	(100.0)
with one or more adverse events	90	(52.6)	162	(47.9)	155	(45.9)	317	(46.9)	72	(50.0)
with no adverse events	81	(47.4)	176	(52.1)	183	(54.1)	359	(53.1)	72	(50.0)
with drug-related† adverse events	24	(14.0)	45	(13.3)	44	(13.0)	89	(13.2)	47	(32.6)
with serious adverse events	4	(2.3)	5	(1.5)	6	(1.8)	11	(1.6)	3	(2.1)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	2	(0.6)	2	(0.3)	2	(1.4)
who died	0	(0.0)	2	(0.6)	0	(0.0)	2	(0.3)	0	(0.0)
discontinued‡ due to an adverse event	2	(1.2)	3	(0.9)	4	(1.2)	7	(1.0)	4	(2.8)
discontinued due to a drug-related adverse event	1	(0.6)	0	(0.0)	3	(0.9)	3	(0.4)	3	(2.1)

Adverse Events Summary by Subgroup
Phase 2 and 3: Placebo-Controlled Safety Pool
All Subjects as Treated

	Placebo		MK-3222 100 mg		MK-3222 200 mg		MK-3222 100/200 mg		Etanercept 50 mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
discontinued due to a serious adverse event	0	(0.0)	2	(0.6)	1	(0.3)	3	(0.4)	1	(0.7)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.1)	1	(0.7)
Disease duration category(≥ 15 years)										
Subjects in population	182	(100.0)	362	(100.0)	367	(100.0)	729	(100.0)	169	(100.0)
with one or more adverse events	100	(54.9)	174	(48.1)	182	(49.6)	356	(48.8)	97	(57.4)
with no adverse events	82	(45.1)	188	(51.9)	185	(50.4)	373	(51.2)	72	(42.6)
with drug-related† adverse events	23	(12.6)	57	(15.7)	55	(15.0)	112	(15.4)	45	(26.6)
with serious adverse events	2	(1.1)	5	(1.4)	10	(2.7)	15	(2.1)	4	(2.4)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.1)	0	(0.0)
who died	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued‡ due to an adverse event	2	(1.1)	1	(0.3)	5	(1.4)	6	(0.8)	2	(1.2)
discontinued due to a drug-related adverse event	1	(0.5)	1	(0.3)	0	(0.0)	1	(0.1)	1	(0.6)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	4	(1.1)	4	(0.5)	1	(0.6)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Baseline BSA involvement category(< 30%)										
Subjects in population	200	(100.0)	409	(100.0)	406	(100.0)	815	(100.0)	162	(100.0)
with one or more adverse events	105	(52.5)	202	(49.4)	214	(52.7)	416	(51.0)	93	(57.4)
with no adverse events	95	(47.5)	207	(50.6)	192	(47.3)	399	(49.0)	69	(42.6)
with drug-related† adverse events	27	(13.5)	63	(15.4)	66	(16.3)	129	(15.8)	57	(35.2)
with serious adverse events	3	(1.5)	4	(1.0)	10	(2.5)	14	(1.7)	2	(1.2)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
who died	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

Adverse Events Summary by Subgroup
Phase 2 and 3: Placebo-Controlled Safety Pool
All Subjects as Treated

	Placebo		MK-3222 100 mg		MK-3222 200 mg		MK-3222 100/200 mg		Etanercept 50 mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
discontinued‡ due to an adverse event	1	(0.5)	1	(0.2)	6	(1.5)	7	(0.9)	2	(1.2)
discontinued due to a drug-related adverse event	1	(0.5)	0	(0.0)	2	(0.5)	2	(0.2)	2	(1.2)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	3	(0.7)	3	(0.4)	0	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Baseline BSA involvement category(>= 30%)										
Subjects in population	154	(100.0)	296	(100.0)	297	(100.0)	593	(100.0)	148	(100.0)
with one or more adverse events	85	(55.2)	138	(46.6)	123	(41.4)	261	(44.0)	74	(50.0)
with no adverse events	69	(44.8)	158	(53.4)	174	(58.6)	332	(56.0)	74	(50.0)
with drug-related† adverse events	20	(13.0)	41	(13.9)	32	(10.8)	73	(12.3)	35	(23.6)
with serious adverse events	3	(1.9)	6	(2.0)	6	(2.0)	12	(2.0)	5	(3.4)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	2	(0.7)	2	(0.3)	2	(1.4)
who died	0	(0.0)	2	(0.7)	0	(0.0)	2	(0.3)	0	(0.0)
discontinued‡ due to an adverse event	3	(1.9)	3	(1.0)	3	(1.0)	6	(1.0)	4	(2.7)
discontinued due to a drug-related adverse event	1	(0.6)	1	(0.3)	1	(0.3)	2	(0.3)	2	(1.4)
discontinued due to a serious adverse event	0	(0.0)	2	(0.7)	2	(0.7)	4	(0.7)	2	(1.4)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.2)	1	(0.7)
Baseline PASI category(< 20)										
Subjects in population	232	(100.0)	439	(100.0)	444	(100.0)	883	(100.0)	186	(100.0)
with one or more adverse events	124	(53.4)	215	(49.0)	228	(51.4)	443	(50.2)	107	(57.5)
with no adverse events	108	(46.6)	224	(51.0)	216	(48.6)	440	(49.8)	79	(42.5)
with drug-related† adverse events	28	(12.1)	72	(16.4)	71	(16.0)	143	(16.2)	61	(32.8)
with serious adverse events	4	(1.7)	4	(0.9)	10	(2.3)	14	(1.6)	3	(1.6)

Adverse Events Summary by Subgroup
Phase 2 and 3: Placebo-Controlled Safety Pool
All Subjects as Treated

	Placebo		MK-3222 100 mg		MK-3222 200 mg		MK-3222 100/200 mg		Etanercept 50 mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.5)
who died	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued‡ due to an adverse event	2	(0.9)	0	(0.0)	5	(1.1)	5	(0.6)	3	(1.6)
discontinued due to a drug-related adverse event	1	(0.4)	0	(0.0)	2	(0.5)	2	(0.2)	2	(1.1)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	2	(0.5)	2	(0.2)	0	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Baseline PASI category(≥ 20)										
Subjects in population	122	(100.0)	266	(100.0)	264	(100.0)	530	(100.0)	126	(100.0)
with one or more adverse events	66	(54.1)	125	(47.0)	111	(42.0)	236	(44.5)	61	(48.4)
with no adverse events	56	(45.9)	141	(53.0)	153	(58.0)	294	(55.5)	65	(51.6)
with drug-related† adverse events	19	(15.6)	32	(12.0)	28	(10.6)	60	(11.3)	31	(24.6)
with serious adverse events	2	(1.6)	6	(2.3)	6	(2.3)	12	(2.3)	4	(3.2)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	3	(1.1)	3	(0.6)	1	(0.8)
who died	0	(0.0)	2	(0.8)	0	(0.0)	2	(0.4)	0	(0.0)
discontinued‡ due to an adverse event	2	(1.6)	4	(1.5)	4	(1.5)	8	(1.5)	3	(2.4)
discontinued due to a drug-related adverse event	1	(0.8)	1	(0.4)	1	(0.4)	2	(0.4)	2	(1.6)
discontinued due to a serious adverse event	0	(0.0)	2	(0.8)	3	(1.1)	5	(0.9)	2	(1.6)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	1	(0.4)	1	(0.2)	1	(0.8)
Baseline PGA category(≤ 3)										
Subjects in population	236	(100.0)	476	(100.0)	472	(100.0)	948	(100.0)	200	(100.0)
with one or more adverse events	130	(55.1)	220	(46.2)	230	(48.7)	450	(47.5)	110	(55.0)
with no adverse events	106	(44.9)	256	(53.8)	242	(51.3)	498	(52.5)	90	(45.0)

Adverse Events Summary by Subgroup
Phase 2 and 3: Placebo-Controlled Safety Pool
All Subjects as Treated

	Placebo		MK-3222 100 mg		MK-3222 200 mg		MK-3222 100/200 mg		Etanercept 50 mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
with drug-related† adverse events	31	(13.1)	64	(13.4)	66	(14.0)	130	(13.7)	64	(32.0)
with serious adverse events	3	(1.3)	6	(1.3)	12	(2.5)	18	(1.9)	3	(1.5)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	1	(0.5)
who died	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
discontinued‡ due to an adverse event	4	(1.7)	1	(0.2)	7	(1.5)	8	(0.8)	4	(2.0)
discontinued due to a drug-related adverse event	2	(0.8)	0	(0.0)	3	(0.6)	3	(0.3)	3	(1.5)
discontinued due to a serious adverse event	0	(0.0)	1	(0.2)	4	(0.8)	5	(0.5)	1	(0.5)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Baseline PGA category(≥ 4)										
Subjects in population	118	(100.0)	229	(100.0)	233	(100.0)	462	(100.0)	110	(100.0)
with one or more adverse events	60	(50.8)	120	(52.4)	107	(45.9)	227	(49.1)	58	(52.7)
with no adverse events	58	(49.2)	109	(47.6)	126	(54.1)	235	(50.9)	52	(47.3)
with drug-related† adverse events	16	(13.6)	40	(17.5)	32	(13.7)	72	(15.6)	28	(25.5)
with serious adverse events	3	(2.5)	4	(1.7)	4	(1.7)	8	(1.7)	4	(3.6)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	2	(0.9)	2	(0.4)	1	(0.9)
who died	0	(0.0)	1	(0.4)	0	(0.0)	1	(0.2)	0	(0.0)
discontinued‡ due to an adverse event	0	(0.0)	3	(1.3)	2	(0.9)	5	(1.1)	2	(1.8)
discontinued due to a drug-related adverse event	0	(0.0)	1	(0.4)	0	(0.0)	1	(0.2)	1	(0.9)
discontinued due to a serious adverse event	0	(0.0)	1	(0.4)	1	(0.4)	2	(0.4)	1	(0.9)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.9)

† Determined by the investigator to be related to the drug.
‡ Study medication withdrawn.
‡‡ Positive anti-drug antibody status means treatment emergent positive.
†† Negative anti-drug antibody status means negative and inconclusive.
[Source: 5.3.5.3-10]

付録 2.7.4-48
第 IIb 相及び第 III 相試験の
プラセボ対照安全性併合解析における治験薬投与後の ADA 陽性例と，
陰性例＋未確定例（併合）の，有害事象に対する ADA の影響についての比較

	MK-3222 100 mg		MK-3222 200 mg		MK-3222 100/200 mg	
Treatment Emergent Positive	n	(%)	n	(%)	n	(%)
Subjects in population	30	100.0	29	100.0	59	100.0
with one or more adverse events	15	50.0	18	62.1	33	55.9
with serious adverse events	1	3.3	0	0.0	1	1.7
with drug related† adverse events	3	10.0	4	13.8	7	11.9
Negative and Inconclusive	n	(%)	n	(%)	n	(%)
Subjects in population	632	100.0	629	100.0	1261	100.0
with one or more adverse events	308	48.7	304	48.3	612	48.5
with serious adverse events	9	1.4	14	2.2	23	1.8
with drug related† adverse events	96	15.2	89	14.1	185	14.7

† Determined by the investigator to be related to the drug.

[Source: 5.3.5.3-10]

付録 2.7.4-49
プラセボ対照安全性併合解析における ADA 発現有無別被験者カテゴリー別の免疫原性に関連する
可能性のある有害事象に対する ADA の影響，
第 IIb 相及び第 III 相試験における 1 回以上投与された被験者

	MK-3222 100 mg		MK-3222 200 mg		Total	
ADA Subject Category	n	(%)	n	(%)	n	(%)
Inconclusive						
Subjects in the population	29		255		284	
With one or more immunogenicity related AEs	3	(10.3)	10	(3.9)	13	(4.6)
Hypersensitivity	0	(0.0)	0	(0.0)	0	(0.0)
Anaphylaxis	0	(0.0)	0	(0.0)	0	(0.0)
Injection site reactions	3	(10.3)	10	(3.9)	13	(4.6)
Negative						
Subjects in the population	603		374		977	
With one or more immunogenicity related AEs	18	(3.0)	13	(3.5)	31	(3.2)
Hypersensitivity	1	(0.2)	0	(0.0)	1	(0.1)
Anaphylaxis	0	(0.0)	0	(0.0)	0	(0.0)
Injection site reactions	18	(3.0)	13	(3.5)	31	(3.2)
Non-TE-POS NAb-NEG						
Subjects in the population	33		35		68	
With one or more immunogenicity related AEs	2	(6.1)	3	(8.6)	5	(7.4)
Hypersensitivity	0	(0.0)	0	(0.0)	0	(0.0)
Anaphylaxis	0	(0.0)	0	(0.0)	0	(0.0)
Injection site reactions	2	(6.1)	3	(8.6)	5	(7.4)
Non-TE-POS NAb-POS						
Subjects in the population	5		6		11	
With one or more immunogenicity related AEs	0	(0.0)	0	(0.0)	0	(0.0)
TE-POS NAb-NEG						
Subjects in the population	24		25		49	
With one or more immunogenicity related AEs	1	(4.2)	3	(12.0)	4	(8.2)
Hypersensitivity	0	(0.0)	1	(4.0)	1	(2.0)
Anaphylaxis	0	(0.0)	0	(0.0)	0	(0.0)
Injection site reactions	1	(4.2)	2	(8.0)	3	(6.1)
TE-POS NAb-POS						
Subjects in the population	4		4		8	
With one or more immunogenicity related AEs	0	(0.0)	0	(0.0)	0	(0.0)

Source: [5.3.5.3-17] [Table 5.3.5.3.3-psoriasis: 111], [Table 5.3.5.3.3-psoriasis: 112] [Table 5.3.5.3.3-psoriasis: 113] [Table 5.3.5.3.3-psoriasis: 114] [Table 5.3.5.3.3-psoriasis: 115] [Table 5.3.5.3.3-psoriasis: 116]

付録 2.7.4-50
ベース試験の安全性併合解析における ADA 発現有無別被験者カテゴリー別の免疫原性に関連する可能性のある有害事象に対する ADA の影響，第 IIb 相及び第 III 相試験における 1 回以上投与された被験者

	Continuous dosing MK-3222 100 mg		Continuous dosing MK-3222 200 mg		Continuous dosing MK-3222 100 mg/200 mg		Total	
ADA Subject Category	n	(%)	n	(%)	n	(%)	n	(%)
Inconclusive								
Subjects in the population	8		25		8		41	
with one or more immunogenicity related AEs	1	(12.5)	1	(4.0)	0	(0.0)	2	(4.9)
Hypersensitivity	1	(12.5)	0	(0.0)	0	(0.0)	1	(2.4)
Anaphylaxis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Injection site reactions	1	(12.5)	1	(4.0)	0	(0.0)	2	(4.9)
Negative								
Subjects in the population	342		299		171		812	
with one or more immunogenicity related AEs	19	(5.6)	18	(6.0)	13	(7.6)	50	(6.2)
Hypersensitivity	1	(0.3)	1	(0.3)	0	(0.0)	2	(0.2)
Anaphylaxis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Injection site reactions	19	(5.6)	17	(5.7)	13	(7.6)	49	(6.0)
Non-TE-POS NAb-NEG								
Subjects in the population	21		21		5		47	
with one or more immunogenicity related AEs	1	(4.8)	2	(9.5)	0	(0.0)	3	(6.4)
Hypersensitivity	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Anaphylaxis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Injection site reactions	1	(4.8)	2	(9.5)	0	(0.0)	3	(6.4)
Non-TE-POS NAb-POS								
Subjects in the population	3		4		1		8	
with one or more immunogenicity related AEs	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
TE-POS NAb-NEG								
Subjects in the population	16		19		15		50	
with one or more immunogenicity related AEs	1	(6.3)	4	(21.1)	1	(6.7)	6	(12.0)
Hypersensitivity	0	(0.0)	1	(5.3)	0	(0.0)	1	(2.0)
Anaphylaxis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Injection site reactions	1	(6.3)	3	(15.8)	1	(6.7)	5	(10.0)
TE-POS NAb-POS								
Subjects in the population	10		12		9		31	
with one or more immunogenicity related AEs	1	(10.0)	0	(0)	1	(11.1)	2	(6.5)
Hypersensitivity	0	(0)	0	(0)	0	(0)	0	(0)
Anaphylaxis	0	(0)	0	(0)	0	(0)	0	(0)
Injection site reactions	1	(10.0)	0	(0)	1	(11.1)	2	(6.5)

Source: [5.3.5.3-17], [Table 5.3.5.3.3-psoriasis: 117], [Table 5.3.5.3.3-psoriasis: 118] [Table 5.3.5.3.3-psoriasis: 119] [Table 5.3.5.3.3-psoriasis: 120] [Table 5.3.5.3.3-psoriasis: 121] [Table 5.3.5.3.3-psoriasis: 122]

付録 2.7.4-51
第 III 相試験の延長試験データにおける有害事象コーディングの不一致及び矛盾

Study Number	Subject Allocation Number	Reported Terms for Adverse Event	Current Dictionary Derived Term	Correct Dictionary Derived Term	Current Body System or Organ Class	Correct Body System or Organ Class
3222-010	[redacted]	Axial spondyloarthropathy	Axial spondyloarthritis	Spondyloarthropathy	Musculoskeletal and connective tissue disorders	Musculoskeletal and connective tissue disorders
3222-011	[redacted]	Common cold virus	Viral upper respiratory tract infection	Nasopharyngitis	Infections and infestations	Infections and infestations
3222-011	[redacted]	Dental root inflammation	Tooth infection	Pulpitis dental	Infections and infestations	Infections and infestations
3222-011	[redacted]	Flu Symptoms	Influenza like illness	Influenza	General disorders and administration site conditions	Infections and infestations
3222-011	[redacted]	Flu Symptoms	Influenza like illness	Influenza	General disorders and administration site conditions	Infections and infestations
3222-011	[redacted]	Flu Symptoms	Influenza like illness	Influenza	General disorders and administration site conditions	Infections and infestations
3222-011	[redacted]	Flu Symptoms	Influenza like illness	Influenza	General disorders and administration site conditions	Infections and infestations
3222-011	[redacted]	Gastric hyperacidity	Gastric pH decreased	Hyperchlorhydria	Investigations	Gastrointestinal disorders
3222-010	[redacted]	Left knee strain	Joint injury	Muscle strain	Injury, poisoning and procedural complications	Injury, poisoning and procedural complications
3222-010	[redacted]	Left knee strain	Joint injury	Muscle strain	Injury, poisoning and procedural complications	Injury, poisoning and procedural complications
3222-010	[redacted]	Traumatic cervical syndrome	Cervicobrachial syndrome	Post-traumatic neck syndrome	Nervous system disorders	Injury, poisoning and procedural complications
3222-011	[redacted]	Viral common cold	Viral upper respiratory tract infection	Nasopharyngitis	Infections and infestations	Infections and infestations
3222-010	[redacted]	Viral nasopharyngitis	Viral upper respiratory tract infection	Nasopharyngitis	Infections and infestations	Infections and infestations

[Source: 5.3.5.3-10]

付録 2.7.4-52
第 III 相試験の延長試験データカットオフ日以降に入力され，コーディングされなかった有害事象

Study Number	Subject Allocation Number	Treatment Group Assignment	AE Reported Term	AE Severity	AE Serious (Y / N)
3222-011	[redacted]	MK-3222 100 mg	MTPI – gout	Mild	N
3222-011	[redacted]	MK-3222 100 mg	Adenopathy	Severe	Y
3222-011	[redacted]	MK-3222 100 mg	Photo dermatitis bilateral ankles	Moderate	N
3222-011	[redacted]	MK-3222 100 mg	Taste weakness	Mild	N
3222-011	[redacted]	MK-3222 100 mg	Minimal vascular sclerosis	Mild	N
3222-011	[redacted]	MK-3222 100 mg	Burn forearm left	Moderate	N
3222-011	[redacted]	MK-3222 200 mg	Blocking of vertebral bodies	Moderate	N

The date of data cutoff was 15-Apr-016.
[Source: 5.3.5.3-10]

付録 2.7.4-53
第 III 相試験の延長試験データカットオフ日以降に入力され，コーディングされなかった併用薬

Study Number	Subject Allocation Number	Treatment Group Assignment	Concomitant Medication Name
3222-010	[redacted]	MK-3222 200 mg	Hirudoid soft ointment
3222-011	[redacted]	MK-3222 200 mg	Fexofenadyne (Telfexo)
3222-011	[redacted]	MK-3222 200 mg	Novalgin 500 mg
3222-011	[redacted]	MK-3222 100 mg	Thromboprophylaxis

The date of data cutoff was 15-Apr-016.
[Source: 5.3.5.3-10]

付録 2.7.4-54
チルドラキズマブの予期される有害事象/副作用と判定される可能性が最も高い事象

	Tildrakizum		Placebo	Etanercept
	100 mg (N=705) N(%)	200 mg (N=708) N(%)	(N=355) N(%)	50 mg (N=313) N(%)
Diarrhea	13 (1.8)	9 (1.3)	5 (1.4)	4 (1.3)
Injection site pain	10 (1.4)	9 (1.3)	3 (0.8)	10 (3.2)
Back pain	9 (1.3)	11 (1.6)	4 (1.1)	4 (1.3)
Gastroenteritis	8 (1.1)	13 (1.8)	4 (1.1)	6 (1.9)
Nausea	7 (1.0)	11 (1.6)	3 (0.8)	1 (0.3)
Dizziness	5 (0.7)	10 (1.4)	0	6 (1.9)

付録 2.7.4-55
有害事象の要約 - 曝露期間で調整済み（20 週間の追跡調査に基づく）
第 IIb 相及び第 III 相試験：ベース試験の安全性併合解析
1 回以上投与された被験者 - ベース試験の最新データに基づく

	Placebo		MK-3222 100 mg		MK-3222 200 mg		MK-3222 100/200 mg		Etanercept 50 mg		Continuous exposure MK-3222 100 mg		Continuous exposure MK-3222 200 mg		Continuous exposure MK-3222 100 / 200 mg[a]	
	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)
Subject in Population	588		1083		1041		1911		313		381		363		933	
with one or more adverse events	337	(153.98)	779	(78.03)	755	(81.28)	1429	(74.15)	228	(148.61)	298	(60.54)	298	(62.60)	743	(61.63)
with no adverse events	251	(114.69)	304	(30.45)	286	(30.79)	482	(25.01)	85	(55.40)	83	(16.86)	65	(13.65)	190	(15.76)
with drug-related adverse events	84	(38.38)	243	(24.34)	241	(25.95)	468	(24.28)	112	(73.00)	104	(21.13)	98	(20.59)	244	(20.24)
with serious adverse events	14	(6.40)	64	(6.41)	68	(7.32)	131	(6.80)	20	(13.04)	24	(4.88)	24	(5.04)	54	(4.48)
with serious drug-related adverse events	2	(0.91)	4	(0.40)	10	(1.08)	14	(0.73)	5	(3.26)	1	(0.20)	1	(0.21)	3	(0.25)
who died	0	(0.00)	5	(0.50)	2	(0.22)	7	(0.36)	0	(0.00)	1	(0.20)	0	(0.00)	1	(0.08)
discontinued‡ due to an adverse event	5	(2.28)	22	(2.20)	20	(2.15)	42	(2.18)	9	(5.87)	2	(0.41)	1	(0.21)	3	(0.25)
discontinued due to a drug-related adverse event	2	(0.91)	8	(0.80)	8	(0.86)	16	(0.83)	4	(2.61)	1	(0.20)	0	(0.00)	1	(0.08)
discontinued due to a serious adverse event	1	(0.46)	11	(1.10)	11	(1.18)	22	(1.14)	5	(3.26)	1	(0.20)	0	(0.00)	1	(0.08)
discontinued due to a serious drug -related adverse event	0	(0.00)	1	(0.10)	5	(0.54)	6	(0.31)	1	(0.65)	0	(0.00)	0	(0.00)	0	(0.00)

† m is the number of subjects with event per 100-subject-year.

‡ Study medication withdrawn.

[a] Includes subjects who stayed on one of the 100 mg or 200 mg through out the whole Base period.

Results are shown using updated data extracted in June, 2016 after the database lock.

[Source: 5.3.5.3-10]

付録 2.7.4-56
重篤な有害事象を発現した被験者の一覧表
第 IIb 相及び第 III 相試験：ベース試験の安全性併合解析
1 回以上投与された被験者 - ベース試験の最新データに基づく

Site Number	Subject ID	Onset Treatment	Rel Day of Onset	Rel Day of Last Recorded Dose of Study Medication	Adverse Event	Intensity	Related	Action Taken	Outcome
Trial Number = 3222-003									
0115	[redacted]	MK-3222 25 mg	489	368	Hernia	Severe	Not Related		Recovered/Resolved
0235	[redacted]	MK-3222 100 mg	170	115	Rectal cancer	Severe	Not Related	Drug Withdrawn	Not Recovered/Not Resolved
0235	[redacted]	MK-3222 100 mg	355	370	Appendicitis	Severe	Not Related		Recovered/Resolved
0240	[redacted]	MK-3222 100 mg	185	379	Epiglottitis	Severe	Related	Drug Interrupted	Recovered/Resolved
0240	[redacted]	MK-3222 100 mg	353	379	Sinusitis	Mild	Not Related		Recovered/Resolved
0301	[redacted]	MK-3222 200 mg	245	364	Lower limb fracture	Severe	Not Related		Recovered/Resolved
0301	[redacted]	MK-3222 100 mg	288	366	Contusion	Moderate	Not Related		Not Recovered/Not Resolved
0301	[redacted]	MK-3222 100 mg	405	366	Arthropathy	Moderate	Not Related		Recovered/Resolved
0303	[redacted]	MK-3222 25 mg	286	195	Psoriatic arthropathy	Moderate	Not Related	Drug Withdrawn	Recovered/Resolved
0503	[redacted]	MK-3222 25 mg	135	113	Malignant melanoma	Severe	Related	Drug Withdrawn	Not Recovered/Not Resolved
0800	[redacted]	MK-3222 100 mg	197	116	Malignant melanoma in situ		Not Related	Drug Withdrawn	Recovered/Resolved
0800	[redacted]	MK-3222 100 mg	208	116	Malignant melanoma in situ		Not Related	Drug Withdrawn	Recovered/Resolved

Listing of Subjects with Serious Adverse Events
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated - Based on Updated Base Data

Site Number	Subject ID	Onset Treatment	Rel Day of Onset	Rel Day of Last Recorded Dose of Study Medication	Adverse Event	Intensity	Related	Action Taken	Outcome
0801	[redacted]	MK-3222 200 mg	29	1	Lymphoedema	Moderate	Related	Drug Withdrawn	Recovered/Resolved
0801	[redacted]	MK-3222 200 mg	8	1	Lymphoedema	Moderate	Related		Recovered/Resolved
0801	[redacted]	MK-3222 200 mg	.	379	Soft tissue infection	Moderate	Not Related		Recovered/Resolved
0801	[redacted]	MK-3222 200 mg	250	379	Bursitis	Severe	Not Related		Recovered/Resolved
0801	[redacted]	MK-3222 200 mg	303	379	Cellulitis	Moderate	Related		Recovered/Resolved
0803	[redacted]	MK-3222 200 mg	55	365	Ovarian cyst	Moderate	Not Related		Recovered/Resolved
0803	[redacted]	MK-3222 25 mg	59	365	Arthritis bacterial	Severe	Related		Recovered/Resolved
0803	[redacted]	MK-3222 25 mg	137	113	Ischaemic stroke	Severe	Related	Drug Withdrawn	Not Recovered/Not Resolved
0804	[redacted]	MK-3222 25 mg	365	372	Sinusitis	Moderate	Not Related		Recovered/Resolved
0804	[redacted]	MK-3222 200 mg	235	366	Back pain	Moderate	Not Related		Recovered/Resolved
0804	[redacted]	MK-3222 25 mg	266	373	Arthralgia	Severe	Not Related		Recovered/Resolved
0805	[redacted]	MK-3222 100 mg	231	366	Tendon rupture	Moderate	Not Related		Recovered/Resolved
0806	[redacted]	MK-3222 200 mg	498	367	Psoriatic arthropathy	Severe	Not Related		Recovered/Resolved

Listing of Subjects with Serious Adverse Events
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated - Based on Updated Base Data

Site Number	Subject ID	Onset Treatment	Rel Day of Onset	Rel Day of Last Recorded Dose of Study Medication	Adverse Event	Intensity	Related	Action Taken	Outcome
0808	[redacted]	Placebo	134	31	Psoriasis	Severe	Not Related		Not Recovered/Not Resolved
0808	[redacted]	MK-3222 100 mg	46	30	Death	Severe	Not Related	Drug Withdrawn	Fatal
1302	[redacted]	MK-3222 100 mg	478	365	Thrombotic cerebral infarction	Severe	Not Related	Drug Withdrawn	Not Recovered/Not Resolved
Trial Number = 3222-010									
0104	[redacted]	MK-3222 200 mg	449	456	Transient ischaemic attack	Mild	Not Related	Dose Not Changed	Recovered/Resolved
0106	[redacted]	MK-3222 200 mg	333	452	Non-cardiac chest pain	Moderate	Not Related	Dose Not Changed	Recovered/Resolved
0107	[redacted]	MK-3222 200 mg	415	451	Angina pectoris	Severe	Not Related	Dose Not Changed	Recovered/Resolved
0111	[redacted]	MK-3222 200 mg	28	113	Pancreatitis acute	Moderate	Not Related	Dose Not Changed	Recovered/Resolved
0113	[redacted]	MK-3222 200 mg	121	223	Coronary artery disease	Severe	Not Related	Drug Interrupted	Recovered/Resolved With Sequelae
0113	[redacted]	Placebo	501	449	Anaemia	Severe	Not Related	Not Applicable	Recovering/Resolving
0114	[redacted]	MK-3222 100 mg	185	114	Gastroenteritis	Severe	Not Related	Not Applicable	Recovered/Resolved
0114	[redacted]	MK-3222 200 mg	404	392	Aneurysm	Severe	Not Related	Dose Not Changed	Fatal
0114	[redacted]	MK-3222 200 mg	404	392	Coronary artery disease	Severe	Not Related	Dose Not Changed	Not Recovered/Not Resolved

Listing of Subjects with Serious Adverse Events
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated - Based on Updated Base Data

Site Number	Subject ID	Onset Treatment	Rel Day of Onset	Rel Day of Last Recorded Dose of Study Medication	Adverse Event	Intensity	Related	Action Taken	Outcome
0114	[redacted]	MK-3222 200 mg	316	446	Squamous cell carcinoma of skin	Moderate	Not Related	Dose Not Changed	Recovered/Resolved
0115	[redacted]	MK-3222 200 mg	443	448	Cholecystitis	Moderate	Not Related	Dose Not Changed	Recovered/Resolved
0115	[redacted]	MK-3222 100 mg	359	449	Non-cardiac chest pain	Moderate	Not Related	Dose Not Changed	Recovered/Resolved
0119	[redacted]	MK-3222 200 mg	-3	1	Chronic obstructive pulmonary disease	Moderate	Not Related	Drug Withdrawn	Recovered/Resolved With Sequelae
0122	[redacted]	MK-3222 100 mg	129	449	Diverticulitis	Moderate	Not Related	Dose Not Changed	Recovered/Resolved
0123	[redacted]	MK-3222 200 mg	9	197	Tachycardia	Severe	Not Related	Dose Not Changed	Recovered/Resolved
0124	[redacted]	MK-3222 100 mg	450	450	Squamous cell carcinoma of skin	Mild	Not Related	Dose Not Changed	Recovered/Resolved
0132	[redacted]	MK-3222 100 mg	308	398	Basal cell carcinoma	Moderate	Not Related	Dose Not Changed	Recovered/Resolved
0132	[redacted]	MK-3222 100 mg	308	398	Bowen's disease	Moderate	Not Related	Dose Not Changed	Recovered/Resolved
0132	[redacted]	Placebo	450	449	Cellulitis	Severe	Related	Not Applicable	Recovered/Resolved
0132	[redacted]	MK-3222 200 mg	53	31	Coronary artery disease	Severe	Not Related	Drug Withdrawn	Recovered/Resolved
0134	[redacted]	MK-3222 200 mg	319	447	Pulmonary embolism	Severe	Not Related	Drug Interrupted	Recovered/Resolved
0135	[redacted]	MK-3222 200 mg	211	452	Diverticulitis	Moderate	Not Related	Dose Not Changed	Recovered/Resolved

Listing of Subjects with Serious Adverse Events
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated - Based on Updated Base Data

Site Number	Subject ID	Onset Treatment	Rel Day of Onset	Rel Day of Last Recorded Dose of Study Medication	Adverse Event	Intensity	Related	Action Taken	Outcome
0136	[redacted]	MK-3222 200 mg	248	449	Squamous cell carcinoma of skin	Moderate	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
0136	[redacted]	MK-3222 200 mg	301	406	Anaphylactic reaction	Severe	Not Related	Dose Not Changed	Recovered/Resolved
0136	[redacted]	Placebo	306	365	Uterine haemorrhage	Severe	Not Related	Dose Not Changed	Recovered/Resolved
0137	[redacted]	MK-3222 100 mg	115	449	Diverticulum	Severe	Not Related	Dose Not Changed	Recovered/Resolved
0137	[redacted]	MK-3222 200 mg	118	29	Abortion spontaneous	Moderate	Not Related	Dose Not Changed	Recovered/Resolved
0138	[redacted]	MK-3222 200 mg	124	120	Deep vein thrombosis	Severe	Not Related	Dose Not Changed	Recovering/Resolving
0138	[redacted]	MK-3222 200 mg	124	120	Pulmonary embolism	Severe	Not Related	Dose Not Changed	Recovering/Resolving
0138	[redacted]	MK-3222 100 mg	67	30	Acute myocardial infarction	Severe	Not Related	Dose Not Changed	Recovered/Resolved
0139	[redacted]	Placebo	121	33	Presyncope	Moderate	Not Related	Not Applicable	Recovered/Resolved
0144	[redacted]	MK-3222 200 mg	155	113	Pancreatic carcinoma		Not Related	Drug Withdrawn	Not Recovered/Not Resolved
0145	[redacted]	MK-3222 200 mg	325	449	Non-cardiac chest pain	Moderate	Not Related	Dose Not Changed	Recovered/Resolved
1101	[redacted]	MK-3222 100 mg	19	449	Nephrolithiasis	Severe	Not Related	Dose Not Changed	Recovered/Resolved
1101	[redacted]	MK-3222 100 mg	196	449	Pancreatitis	Moderate	Not Related	Dose Not Changed	Recovered/Resolved

Listing of Subjects with Serious Adverse Events
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated - Based on Updated Base Data

Site Number	Subject ID	Onset Treatment	Rel Day of Onset	Rel Day of Last Recorded Dose of Study Medication	Adverse Event	Intensity	Related	Action Taken	Outcome
1102	[redacted]	MK-3222 200 mg	87	81	Psoriasis	Moderate	Related	Drug Withdrawn	Recovered/Resolved
1108	[redacted]	MK-3222 200 mg	286	462	Gastroenteritis salmonella	Moderate	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
1112	[redacted]	Placebo	334	451	Benign biliary neoplasm	Moderate	Related	Drug Interrupted	Recovered/Resolved
1114	[redacted]	Placebo	397	393	Cerebellar infarction	Severe	Not Related	Drug Withdrawn	Recovered/Resolved With Sequelae
1114	[redacted]	MK-3222 100 mg	40	118	Cellulitis	Severe	Not Related	Dose Not Changed	Recovered/Resolved
1117	[redacted]	MK-3222 200 mg	178	118	Bone tuberculosis	Moderate	Related	Drug Withdrawn	Recovered/Resolved
4402	[redacted]	MK-3222 100 mg	190	345	Squamous cell carcinoma of skin	Mild	Not Related	Drug Withdrawn	Recovered/Resolved
4402	[redacted]	MK-3222 200 mg	359	345	Gastroenteritis	Moderate	Not Related	Dose Not Changed	Recovered/Resolved
6101	[redacted]	Placebo	277	447	Food poisoning	Severe	Not Related	Dose Not Changed	Recovered/Resolved
6101	[redacted]	MK-3222 100 mg	368	447	Lower limb fracture	Severe	Not Related	Dose Not Changed	Recovered/Resolved
6101	[redacted]	MK-3222 100 mg	444	450	Sinusitis	Mild	Not Related	Dose Not Changed	Recovered/Resolved
6101	[redacted]	MK-3222 200 mg	246	441	Sciatica	Severe	Not Related	Dose Not Changed	Recovered/Resolved
6101	[redacted]	MK-3222 200 mg	246	441	Sciatica	Severe	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae

Listing of Subjects with Serious Adverse Events
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated - Based on Updated Base Data

Site Number	Subject ID	Onset Treatment	Rel Day of Onset	Rel Day of Last Recorded Dose of Study Medication	Adverse Event	Intensity	Related	Action Taken	Outcome
6102	[redacted]	MK-3222 100 mg	407	447	Cholelithiasis	Moderate	Not Related	Dose Not Changed	Recovered/Resolved
6102	[redacted]	MK-3222 100 mg	149	449	Basal cell carcinoma	Mild	Not Related	Dose Not Changed	Recovered/Resolved
6103	[redacted]	MK-3222 200 mg	338	451	Squamous cell carcinoma of skin	Severe	Not Related	Dose Not Changed	Recovered/Resolved
6103	[redacted]	MK-3222 200 mg	167	446	Basal cell carcinoma	Severe	Not Related	Dose Not Changed	Recovered/Resolved
6103	[redacted]	Placebo	382	421	Basal cell carcinoma	Mild	Not Related	Dose Not Changed	Recovered/Resolved
6104	[redacted]	MK-3222 100 mg	403	446	Squamous cell carcinoma of skin	Moderate	Not Related	Dose Not Changed	Recovered/Resolved
6104	[redacted]	MK-3222 200 mg	334	306	Pancreatic carcinoma	Severe	Not Related	Drug Withdrawn	Not Recovered/Not Resolved
6106	[redacted]	MK-3222 200 mg	157	112	Abortion spontaneous	Moderate	Not Related	Dose Not Changed	Recovered/Resolved
6106	[redacted]	MK-3222 200 mg	63	449	Salivary gland enlargement	Mild	Not Related	Dose Not Changed	Recovered/Resolved
6106	[redacted]	MK-3222 200 mg	451	480	Cellulitis	Severe	Related	Drug Interrupted	Recovered/Resolved
6106	[redacted]	MK-3222 200 mg	201	452	Tendon rupture	Moderate	Not Related	Dose Not Changed	Recovered/Resolved
6106	[redacted]	MK-3222 100 mg	70	448	Pneumothorax	Severe	Not Related	Dose Not Changed	Recovered/Resolved
6107	[redacted]	MK-3222 100 mg	117	456	Constipation	Severe	Not Related	Dose Not Changed	Recovered/Resolved

Listing of Subjects with Serious Adverse Events
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated - Based on Updated Base Data

Site Number	Subject ID	Onset Treatment	Rel Day of Onset	Rel Day of Last Recorded Dose of Study Medication	Adverse Event	Intensity	Related	Action Taken	Outcome
6107	[redacted]	Placebo	450	456	Squamous cell carcinoma of skin	Moderate	Not Related	Dose Not Changed	Recovered/Resolved
8104	[redacted]	MK-3222 200 mg	409	452	Cataract	Mild	Not Related	Dose Not Changed	Recovered/Resolved
8104	[redacted]	MK-3222 200 mg	409	452	Macular fibrosis	Mild	Not Related	Dose Not Changed	Recovered/Resolved
8108	[redacted]	MK-3222 100 mg	432	446	Sleep apnoea syndrome	Moderate	Not Related	Dose Not Changed	Not Recovered/Not Resolved
8112	[redacted]	MK-3222 200 mg	12	1	Suicide attempt	Severe	Not Related	Drug Withdrawn	Recovered/Resolved
8122	[redacted]	MK-3222 100 mg	64	29	Psoriasis	Moderate	Not Related	Dose Not Changed	Recovered/Resolved
8133	[redacted]	MK-3222 200 mg	78	29	Epiglottitis	Severe	Related	Not Applicable	Recovered/Resolved
8139	[redacted]	MK-3222 200 mg	111	448	Lacunar infarction	Mild	Not Related	Dose Not Changed	Not Recovered/Not Resolved
Trial Number = 3222-011									
0168	[redacted]	MK-3222 100 mg	96	82	Cardiomyopathy alcoholic	Severe	Not Related	Drug Withdrawn	Fatal
0168	[redacted]	MK-3222 100 mg	96	82	Steatohepatitis	Severe	Not Related	Drug Withdrawn	Fatal
0169	[redacted]	Placebo	28	363	Pericarditis	Moderate	Not Related	Dose Not Changed	Recovered/Resolved
0172	[redacted]	Etanercept 50 mg	99	365	Renal oncocytoma	Severe	Not Related	Drug Interrupted	Recovered/Resolved

Listing of Subjects with Serious Adverse Events
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated - Based on Updated Base Data

Site Number	Subject ID	Onset Treatment	Rel Day of Onset	Rel Day of Last Recorded Dose of Study Medication	Adverse Event	Intensity	Related	Action Taken	Outcome
0172	[redacted]	MK-3222 200 mg	112	364	Basal cell carcinoma	Moderate	Not Related	Dose Not Changed	Recovered/Resolved
0172	[redacted]	MK-3222 100 mg	240	191	Nephrolithiasis	Severe	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
0172	[redacted]	MK-3222 100 mg	343	342	Malignant melanoma in situ	Moderate	Not Related	Drug Interrupted	Recovered/Resolved
0172	[redacted]	MK-3222 200 mg	361	337	Diverticulitis	Severe	Not Related	Dose Not Changed	Not Recovered/Not Resolved
0176	[redacted]	MK-3222 100 mg	278	369	Bipolar disorder	Severe	Not Related	Dose Not Changed	Recovered/Resolved
0176	[redacted]	MK-3222 100 mg	278	369	Depression	Severe	Not Related	Dose Not Changed	Recovered/Resolved
0176	[redacted]	Etanercept 50 mg	139	197	Alcoholism	Severe	Not Related	Drug Withdrawn	Recovered/Resolved
0177	[redacted]	MK-3222 100 mg	320	257	Acute myeloid leukaemia	Moderate	Not Related	Drug Withdrawn	Fatal
0178	[redacted]	Etanercept 50 mg	71	105	Basal cell carcinoma	Mild	Not Related	Drug Withdrawn	Recovered/Resolved
0178	[redacted]	Etanercept 50 mg	14	193	Cardiac failure congestive	Severe	Not Related	Dose Not Changed	Recovered/Resolved
0182	[redacted]	MK-3222 100 mg	252	360	Bowen's disease	Mild	Not Related	Dose Not Changed	Recovered/Resolved
0184	[redacted]	MK-3222 200 mg	99	365	Obstructive uropathy	Severe	Not Related	Dose Not Changed	Recovered/Resolved
0184	[redacted]	MK-3222 200 mg	99	365	Pyelonephritis	Severe	Not Related	Dose Not Changed	Recovered/Resolved

Listing of Subjects with Serious Adverse Events
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated - Based on Updated Base Data

Site Number	Subject ID	Onset Treatment	Rel Day of Onset	Rel Day of Last Recorded Dose of Study Medication	Adverse Event	Intensity	Related	Action Taken	Outcome
0187	[redacted]	MK-3222 200 mg	30	22	Atrial fibrillation	Severe	Not Related	Drug Withdrawn	Recovered/Resolved
0188	[redacted]	MK-3222 100 mg	168	369	Hand fracture	Moderate	Not Related	Dose Not Changed	Recovered/Resolved
0188	[redacted]	MK-3222 200 mg	78	250	Carotid artery stenosis	Severe	Not Related	Dose Not Changed	Recovered/Resolved
0195	[redacted]	MK-3222 100 mg	117	337	Appendicitis	Severe	Not Related	Dose Not Changed	Recovered/Resolved
1163	[redacted]	MK-3222 100 mg	268	367	Cervical spinal stenosis	Moderate	Not Related	Drug Interrupted	Recovered/Resolved
1169	[redacted]	MK-3222 100 mg	290	282	Respiratory arrest	Severe	Not Related	Drug Withdrawn	Fatal
1170	[redacted]	MK-3222 200 mg	247	366	Cellulitis	Moderate	Not Related	Dose Not Changed	Recovered/Resolved
1171	[redacted]	MK-3222 200 mg	82	361	Osteonecrosis	Mild	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
3207	[redacted]	MK-3222 200 mg	390	366	Pneumonia	Severe	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
3303	[redacted]	MK-3222 100 mg	29	362	Basal cell carcinoma	Mild	Not Related	Dose Not Changed	Recovered/Resolved
3307	[redacted]	Placebo	10	147	Intervertebral disc protrusion	Moderate	Not Related	Drug Interrupted	Recovered/Resolved
3307	[redacted]	MK-3222 200 mg	218	365	Breast cyst	Moderate	Not Related	Drug Interrupted	Recovered/Resolved
3307	[redacted]	Etanercept 50 mg	123	400	Obesity	Mild	Not Related	Drug Interrupted	Recovered/Resolved

Listing of Subjects with Serious Adverse Events
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated - Based on Updated Base Data

Site Number	Subject ID	Onset Treatment	Rel Day of Onset	Rel Day of Last Recorded Dose of Study Medication	Adverse Event	Intensity	Related	Action Taken	Outcome
3602	[redacted]	MK-3222 200 mg	329	391	Spondylolisthesis	Moderate	Not Related	Drug Interrupted	Recovered/Resolved With Sequelae
3603	[redacted]	MK-3222 100 mg	266	366	Coronary artery stenosis	Moderate	Not Related	Dose Not Changed	Recovered/Resolved
3603	[redacted]	MK-3222 100 mg	353	365	Cholelithiasis	Mild	Not Related	Dose Not Changed	Recovered/Resolved
3906	[redacted]	MK-3222 100 mg	203	190	Basal cell carcinoma	Mild	Not Related	Dose Not Changed	Recovered/Resolved
3906	[redacted]	Etanercept 50 mg	191	222	Lung adenocarcinoma	Severe	Not Related	Drug Withdrawn	Not Recovered/Not Resolved
3906	[redacted]	MK-3222 200 mg	441	222	Sepsis	Severe	Not Related	Not Applicable	Fatal
4302	[redacted]	MK-3222 200 mg	66	364	Abdominal hernia	Severe	Not Related	Drug Interrupted	Recovered/Resolved
4305	[redacted]	Etanercept 50 mg	256	193	Humerus fracture	Severe	Not Related	Not Applicable	Recovered/Resolved
4801	[redacted]	Etanercept 50 mg	18	193	Coronary artery stenosis	Severe	Not Related	Dose Not Changed	Recovered/Resolved
4802	[redacted]	MK-3222 100 mg	155	365	Meniscus injury	Mild	Not Related	Dose Not Changed	Recovered/Resolved
4804	[redacted]	MK-3222 200 mg	121	365	Intervertebral disc disorder	Moderate	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
4804	[redacted]	MK-3222 200 mg	296	366	Abdominal pain upper	Moderate	Not Related	Dose Not Changed	Not Recovered/Not Resolved
4807	[redacted]	MK-3222 200 mg	119	366	Radiculopathy	Moderate	Not Related	Drug Interrupted	Recovered/Resolved With Sequelae

Listing of Subjects with Serious Adverse Events
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated - Based on Updated Base Data

Site Number	Subject ID	Onset Treatment	Rel Day of Onset	Rel Day of Last Recorded Dose of Study Medication	Adverse Event	Intensity	Related	Action Taken	Outcome
4807	[redacted]	MK-3222 200 mg	331	366	Cataract	Moderate	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
4901	[redacted]	MK-3222 100 mg	278	365	Transient ischaemic attack	Severe	Not Related	Dose Not Changed	Recovered/Resolved
4902	[redacted]	MK-3222 100 mg	150	111	Abdominal pain	Severe	Not Related	Dose Not Changed	Recovered/Resolved
4902	[redacted]	Placebo	79	365	Cellulitis	Severe	Not Related	Dose Not Changed	Recovered/Resolved
4904	[redacted]	Etanercept 50 mg	24	191	Seizure	Severe	Not Related	Dose Not Changed	Recovered/Resolved
4905	[redacted]	MK-3222 100 mg	256	256	Bladder transitional cell carcinoma	Severe	Related	Drug Withdrawn	Recovered/Resolved
4906	[redacted]	MK-3222 200 mg	107	103	Herpes zoster	Moderate	Related	Drug Withdrawn	Recovered/Resolved
4907	[redacted]	MK-3222 100 mg	235	227	Atrial fibrillation	Severe	Not Related	Drug Withdrawn	Recovered/Resolved
4907	[redacted]	MK-3222 100 mg	79	227	Peripheral arterial occlusive disease	Moderate	Not Related	Dose Not Changed	Recovered/Resolved
4908	[redacted]	MK-3222 100 mg	376	340	Myocardial infarction	Severe	Not Related	Dose Not Changed	Fatal
4908	[redacted]	MK-3222 100 mg	214	360	Back pain	Severe	Not Related	Dose Not Changed	Recovered/Resolved
4908	[redacted]	MK-3222 100 mg	244	360	Depression	Moderate	Not Related	Dose Not Changed	Recovered/Resolved
4908	[redacted]	MK-3222 100 mg	288	360	Hyperthyroidism	Moderate	Not Related	Dose Not Changed	Recovered/Resolved

Listing of Subjects with Serious Adverse Events
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated - Based on Updated Base Data

Site Number	Subject ID	Onset Treatment	Rel Day of Onset	Rel Day of Last Recorded Dose of Study Medication	Adverse Event	Intensity	Related	Action Taken	Outcome
4908	[redacted]	MK-3222 100 mg	385	360	Thyroid cancer	Moderate	Related	Dose Not Changed	Recovered/Resolved
4909	[redacted]	MK-3222 100 mg	224	365	Erysipelas	Moderate	Not Related	Drug Interrupted	Recovered/Resolved
4911	[redacted]	MK-3222 200 mg	225	364	Tendon rupture	Severe	Not Related	Dose Not Changed	Recovering/Resolving
4911	[redacted]	MK-3222 200 mg	60	364	Basal cell carcinoma	Severe	Not Related	Dose Not Changed	Recovered/Resolved
4911	[redacted]	Etanercept 50 mg	149	189	Sleep apnoea syndrome	Severe	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
4913	[redacted]	MK-3222 100 mg	139	366	Tendon rupture	Severe	Not Related	Dose Not Changed	Recovered/Resolved
4913	[redacted]	MK-3222 100 mg	64	366	Oesophageal polyp	Moderate	Not Related	Dose Not Changed	Recovered/Resolved
4913	[redacted]	MK-3222 100 mg	252	365	Sinusitis	Moderate	Not Related	Dose Not Changed	Recovered/Resolved
4914	[redacted]	MK-3222 200 mg	347	365	Tendon rupture	Severe	Not Related	Dose Not Changed	Recovered/Resolved
4914	[redacted]	Etanercept 50 mg	197	363	Basal cell carcinoma	Moderate	Not Related	Dose Not Changed	Recovered/Resolved
4915	[redacted]	MK-3222 100 mg	214	360	Vertigo	Moderate	Not Related	Dose Not Changed	Recovered/Resolved
4915	[redacted]	MK-3222 100 mg	222	365	Haemorrhoids thrombosed	Moderate	Not Related	Dose Not Changed	Recovered/Resolved
4917	[redacted]	MK-3222 100 mg	114	358	Gastritis	Mild	Not Related	Dose Not Changed	Recovered/Resolved

Listing of Subjects with Serious Adverse Events
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated - Based on Updated Base Data

Site Number	Subject ID	Onset Treatment	Rel Day of Onset	Rel Day of Last Recorded Dose of Study Medication	Adverse Event	Intensity	Related	Action Taken	Outcome
4917	[redacted]	Etanercept 50 mg	50	189	Rotator cuff syndrome	Mild	Not Related	Dose Not Changed	Recovered/Resolved
4918	[redacted]	Etanercept 50 mg	203	199	Psoriasis	Severe	Not Related	Drug Withdrawn	Not Recovered/Not Resolved
4919	[redacted]	Etanercept 50 mg	37	36	Headache	Severe	Related	Drug Withdrawn	Recovered/Resolved
4919	[redacted]	Etanercept 50 mg	195	190	Borderline personality disorder	Moderate	Not Related	Dose Not Changed	Recovered/Resolved
4920	[redacted]	MK-3222 200 mg	76	362	Wound infection	Severe	Related	Drug Interrupted	Recovered/Resolved
4921	[redacted]	MK-3222 200 mg	257	366	Concussion	Moderate	Not Related	Dose Not Changed	Recovered/Resolved
4922	[redacted]	Placebo	42	372	Ureterolithiasis	Moderate	Not Related	Dose Not Changed	Recovered/Resolved
4923	[redacted]	Etanercept 50 mg	312	193	Breast cancer	Severe	Related	Dose Not Changed	Recovered/Resolved With Sequelae
4923	[redacted]	MK-3222 200 mg	248	222	Breast cancer	Moderate	Related	Drug Withdrawn	Not Recovered/Not Resolved
4923	[redacted]	MK-3222 200 mg	226	363	Basal cell carcinoma	Moderate	Not Related	Dose Not Changed	Recovered/Resolved
4924	[redacted]	MK-3222 200 mg	294	374	Atrial fibrillation	Moderate	Not Related	Dose Not Changed	Recovered/Resolved
4924	[redacted]	MK-3222 200 mg	297	374	Mitral valve incompetence	Severe	Not Related	Drug Interrupted	Recovered/Resolved
4924	[redacted]	MK-3222 100 mg	24	362	Tendonitis	Moderate	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae

Listing of Subjects with Serious Adverse Events
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated - Based on Updated Base Data

Site Number	Subject ID	Onset Treatment	Rel Day of Onset	Rel Day of Last Recorded Dose of Study Medication	Adverse Event	Intensity	Related	Action Taken	Outcome
4925	[redacted]	Etanercept 50 mg	150	192	Ankle fracture	Moderate	Not Related	Dose Not Changed	Recovered/Resolved
4925	[redacted]	MK-3222 200 mg	77	366	Osteoarthritis	Mild	Not Related	Dose Not Changed	Recovered/Resolved
4933	[redacted]	Etanercept 50 mg	20	21	Bile duct stone	Severe	Related	Drug Interrupted	Recovered/Resolved
4933	[redacted]	MK-3222 200 mg	449	367	Coronary artery disease	Moderate	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
4933	[redacted]	MK-3222 200 mg	456	367	Atrial flutter	Severe	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
4933	[redacted]	MK-3222 100 mg	192	250	Atrial fibrillation	Mild	Not Related	Dose Not Changed	Recovered/Resolved
4933	[redacted]	MK-3222 100 mg	199	250	Basal cell carcinoma	Moderate	Not Related	Dose Not Changed	Recovered/Resolved
4933	[redacted]	MK-3222 100 mg	199	250	Squamous cell carcinoma of skin	Moderate	Not Related	Drug Withdrawn	Recovered/Resolved
4933	[redacted]	MK-3222 100 mg	259	250	Wound infection	Moderate	Not Related	Dose Not Changed	Recovered/Resolved
4933	[redacted]	MK-3222 100 mg	352	250	Cardiac failure	Severe	Not Related	Dose Not Changed	Recovered/Resolved
4934	[redacted]	MK-3222 200 mg	243	362	Diverticulitis	Moderate	Not Related	Drug Interrupted	Recovered/Resolved
4937	[redacted]	Etanercept 50 mg	108	196	Blood glucose increased	Moderate	Not Related	Drug Interrupted	Recovered/Resolved
4937	[redacted]	Etanercept 50 mg	108	196	Urosepsis	Moderate	Related	Drug Interrupted	Recovered/Resolved

Listing of Subjects with Serious Adverse Events
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated - Based on Updated Base Data

Site Number	Subject ID	Onset Treatment	Rel Day of Onset	Rel Day of Last Recorded Dose of Study Medication	Adverse Event	Intensity	Related	Action Taken	Outcome
4939	[redacted]	MK-3222 100 mg	307	362	Dyspepsia	Moderate	Not Related	Dose Not Changed	Recovered/Resolved
4939	[redacted]	MK-3222 100 mg	247	365	Insomnia	Moderate	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
4939	[redacted]	MK-3222 100 mg	291	196	Psoriasis	Severe	Not Related	Dose Not Changed	Recovered/Resolved
9721	[redacted]	Etanercept 50 mg	165	196	Herpes zoster	Moderate	Related	Drug Interrupted	Recovered/Resolved

Action Taken: None = DOSE NOT CHANGED, Reduced = DOSE REDUCED, Interrupted = DRUG INTERRUPTED, Discontinued = DRUG WITHDRAWN, Increased = DOSE INCREASED, N/A = NOT APPLICABLE.

Outcome: Resolved = RECOVERED/RESOLVED, Resolving = RECOVERING/RESOLVING, Sequelae = RECOVERED/RESOLVED WITH SEQUELAE, Not resolved = NOT RECOVERED/NOT RESOLVED.

Related: Investigator-assessed relationship of the adverse event to study medication.

Note: For the Phase 2 study (P003), the adverse event field of "action/outcome" reported as "None" in the legacy data base was mapped to "Not Applicable" and "Additional Medication, Hospitalization, Disability, Death or Therapeutic Procedure" was mapped to a "blank" field. For the Phase 3 trials (P010 and P011), the "action/outcome" of "Not Applicable" was used for AEs where no study medication was administered or for AEs occurring before the first dose of study medication. The "action/outcome" of "None" applies to AEs occurring in the follow-up period, overdoses in absence of an AE, or where no change was made to study medication.

Results are shown using updated data extracted in June, 2016 after the database lock.

[Source: 5.3.5.3-10]

付録 2.7.4-57
第 III 相試験のベース試験に発現した過敏症反応の記述

Protocol 010: Narratives for Hypersensitivities Reported During Phase 3 Base Study			
Allocation Number	**Treatment Received**	**Reported Term**	**Preferred Term**
[redacted]	Tildrakizumab 100 mg	Urticarial	Urticaria
[redacted]	Tildrakizumab 200 mg	chronic urticarial	Urticaria chronic
[redacted]	Tildrakizumab 200 mg	Whole body hives	Urticaria
[redacted]	Tildrakizumab 100 mg	chronic urticarial	Urticaria chronic
[redacted]	Placebo	chronic urticarial	Urticaria chronic
[redacted]	Tildrakizumab 200 mg	Urticarial	Urticaria
[redacted]	Placebo	Allergic Reaction cause unknown Mild Urticaria	Urticaria
[redacted]	Tildrakizumab 100 mg	Allergic Reaction (Not Yet Diagnosed)	Hypersensitivity
[redacted]	Tildrakizumab 200 mg	Acute Allergic Reaction to NSAID's	Drug hypersensitivity
[redacted]	Tildrakizumab 100 mg	Environmental Allergic Reaction	Hypersensitivity
[redacted]	Tildrakizumab 100 mg	Amoxycillin allergic reaction	Drug hypersensitivity
[redacted]	Tildrakizumab 100 mg	tongue swelling after ingesting clonidine	Drug hypersensitivity
[redacted]	Tildrakizumab 200 mg	allergic reaction to Diclofenac	Drug hypersensitivity

[redacted]-Urticaria

A 5[redacted]-year-old Asian male with no other medical history except psoriasis, ex-tobacco user (17 pack years), and history of no alcohol use had a drug-related hypersensitivity event of urticaria. On Day 1, the subject was randomized to placebo for Part 1. The subject was re-randomized to tildrakizumab 100 mg for Part 2 and continued on this treatment for Part 3. Concomitant therapy included white petrolatum (topical) and bepotastine besylate (+) menthol (topical). On Day 233, the subject experienced a drug-related adverse event of urticaria. The subject reported pruritic skin edema on his hand, foot, and head that often appeared in the evening and occasionally extended to his arm, leg, and body. The subject had no history of urticaria prior to enrolling in the trial and was taking no other medications at the time of the event. The subject received the last dose study medication on Day 226 prior to the event of urticarial. The subject was given bepotastine besylate from Day 254 to Day 366 for treatment of urticaria. The event of urticaria was resolved on Day 394. No action was taken with regard to study medication; the subject's last active dose of tildrakizumab 100 mg during the base study was on Day 450. The event of urticaria was considered to be mild in intensity and was assessed by the investigator to be related to study medication. The subject completed the base study on Day 450 and continued into the extension study.

[redacted] - Urticaria

A 4[redacted]-year-old Asian female with a medical history of migraine, current tobacco user (32 pack years), and no history of alcohol use had a drug-related hypersensitivity event of urticaria. On Day 1, the subject was randomized to tildrakizumab 200 mg for Part 1 and continued on this treatment for Part 2 and Part 3. The concomitant therapy included loxoprofen. On Day 57, the subject experienced urticaria on both upper limbs; the rash was raised and pruritic. The subject did not have a history of similar rashes and had not started any new medications or eaten any new foods. The subject received the last dose of study medication on Day 29 prior to the event. The subject was given fexofenadine hydrochloride starting on Day 57 (ongoing at time of report) for treatment of urticaria. The event of urticaria was recovering/resolving at the last visit of the base study. No action was taken with regard to study medication; the subject's last active dose of tildrakizumab 200 mg during the base study was on Day 449. The event of urticaria was considered to be mild in intensity and was assessed by the investigator to be related to study medication. The subject completed the base study on Day 449 and continued into the extension study.

[redacted]: Urticaria

A 3[redacted]-year-old white female with medical history of osteoarthritis, post-traumatic stress disorder, gastroesophageal reflux disease, cystitis, no history of tobacco usage, and alcohol history of 2 drinks per week had a hypersensitivity event of urticaria. On Day 1, the subject was randomized to placebo in Part 1 and was re-randomized to tildrakizumab 200 mg in Part 2. The subject continued on this therapy for Part 3 and the extension study. The concomitant therapies included escitalopram oxalate (oral), gamma-aminobutric acid, Vitamins, cholecalciferol, camu camu, haematococcus pluvialis, ethinyl estradiol (+) levonorgestril, and ferric pyrophosphate (+) folic acid (+) riboflavin. On Day 111, the subject experienced whole body urticaria (hives). The subject received the last dose of study medication on Day 110. Urticaria was not treated withany medication. The event was resolved on Day 115. The event of urticaria was considered to be mild in intensity and was assessed by the investigator to be not related to study medication. The subject completed the base study on Day 447 and continued into the extension study.

[redacted]: Urticaria

A 4[redacted]-year-old Asian male with no other medical history except psoriasis, current tobacco user (40 pack years), and alcohol use (1 per month) had a hypersensitivity event of urticaria. No concomitant therapy was reported. On Day 1, the subject was randomized to placebo in Part 1 and was re-randomized to tildrakizumab 100 mg in Part 2. The subject continued on this therapy for Part 3 and in the extension study. On Day 106, the subject experienced an adverse event of urticaria. The subject reported wheals and itch over the whole body. The subject had no history of urticaria prior to enrolling in the trial and was taking no other medications at the time of the event. The subject was administered the last dose of study medication on Day 85 prior to the start of the event. The subject was prescribed fexofenadine hydrochloride (Day 113 to Day 181) for treatment of urticaria. The event was resolved on Day 181. The

event of urticaria was considered to be mild in intensity and was assessed by the investigator to be not related to study medication. No action was taken with the study medication. The subject completed the base study on Day 449 and continued into the extension study.

[redacted]: Urticaria

A 3[redacted]-year-old Asian female with medical history of hypertension and asthma and no history of tobacco or alcohol use had a hypersensitivity event of urticaria. The concomitant therapies included mucopolysaccharide polysulfate, petrolatum white, levocetirizine dihydrochloride, carbocysteine, theophylline, pranlukast, tulobuterol hydrochloride, and procaterol hydrochloride. On Day 1, the subject was randomized to tildrakizumab 100 mg in Part 1 and continued to receive this therapy in Part 2. The subject was re-randomized to placebo in Part 3(Day 225). The treatment with tildrakizumab 100 mg was reinitiated upon relapse on Day 309 and the subject continued this therapy in the extension study. On Day 252, the subject experienced an adverse event of urticaria. The subject reported rash over the whole body; the rash was flat. The subject had no history of urticaria prior to enrolling in the trial and was taking no other medications at the time of the event. The subject was administered the last dose of study medication on Day 225 prior to the start of the event. The event was not resolved at the time of the base study database lock. The event of urticaria was considered to be mild in intensity and was assessed by the investigator to be not related to study medication. No action was taken with the study medication. The subject completed the base study on Day 458 and continued into the extension study.

[redacted]: Urticaria

A 4[redacted]-year-old Asian female with medical history of asteatosis, tinea cruris, and blepharitis and history of tobacco use (24 pack-years) and alcohol use (1 drink per month) had a hypersensitivity event of urticaria. The concomitant therapies included rebamipide, candesartan cilexetil, petrolatum, white, mucopolysaccharide polysulfate, and fexofenadine hydrochloride. On Day 1, the subject was randomized to tildrakizumab 200 mg in Part 1. The subject continued on this therapy for Part 2, Part 3 and the extension study. On Day 131, the subject experienced an adverse event of urticaria. The subject reported the slightly raised and pruritic rash over the whole body. The subject had no history of urticaria prior to enrolling in the trial and was taking no other medications at the time of the event. The subject was administered the last dose of study medication on Day 112 prior to the start of the event. The subject was prescribed fexofenadine hydrochloride and the use was ongoing at the time of the base study database lock for treatment of urticaria. The event was resolved on Day 207. The event of urticaria was considered to be mild in intensity and was assessed by the investigator to be not related to study medication. No action was taken with study medication. The subject completed the base study on Day 449 and continued into the extension study.

[redacted]: Urticaria

A 5[redacted]-year-old white male with medical history of Type 2 diabetes mellitus, hypertension, inguinal hernia, iodine allergy, meningitis, and drug hypersensitivity to penicillin, ex-tobacco user (3 pack-years), and alcohol use (20 drinks per year) had a hypersensitivity event of urticaria. On Day 1, the subject was randomized to placebo in Part 1. The subject was re-randomized to tildrakizumab 100 mg in Part 2 (Day 85) of the study and the subject continued on this treatment for Part 3 and during the extension study. The concomitant medications included atenolol, amlodipine, aspirin, irbesartan, insulin glargine, hydrochlorothiazide, glyburide, metformin, and insulin. On Day 45, the subject experienced an adverse event of urticaria. The subject had swelling of tongue and left side of throat after lunch; no rash, itching, and red eyes were reported. The subject was referred to the emergency room. The subject was prescribed to use 50 mg oral diphenhydramine twice a day from Day 45 to Day 47. The event was resolved on Day 46. The discharge diagnosis from emergency room visit was food allergic reaction. The subject was seen by an allergist on Day 87. The skin-prick test was negative and the allergist believed this event was urticaria; cetirizine hydrochloride was prescribed on Day 88 to prevent the events of urticaria in future and was continuing at the time of the base study data base lock. The event of urticaria was considered to be moderate in intensity and was assessed by the investigator to be not related to study medication. The subject completed the base study on Day 450 and continued into the extension study.

[redacted]: Hypersensitivity

A 2[redacted]-year-old white female with medical history of migraine, depression, and talipes correction, no history of tobacco use, and alcohol use (10 drinks per week) had an event of hypersensitivity. The concomitant therapies included norethindrone, fluoxetine, vitamins, iron, and vitamin B complex. On Day 1, the subject was randomized to tildrakizumab 100 mg in Part 1 and continued on this therapy for Part 2. The subject was re-randomized to placebo in Part 3 (Day 238). On Day 87, the subject experienced an adverse event of hypersensitivity. The subject reported rashes, nausea, vomiting, abdominal pain, difficulty, breathing, throat tightness, difficulty swallowing, rashes, hypotension, flushing, and mild rash on face. No additional tests were performed. The subject had no history of hypersensitivity prior to enrolling in the trial and was taking no other medications at the time of the event. The subject was administered the last dose of study medication on Day 85 prior to the start of the event. The subject was prescribed cetirizine hydrochloride on Day 87 for the adverse event. The use of this medication was continuing at the time of base study database lock. The event of hypersensitivity was resolved on Day 88. The event of hypersensitivity was considered to be mild in intensity and was assessed by the investigator to be not related to study medication. No action was taken with the study medication. The subject completed the base study on Day 441 and chose not to continue in the extension study.

[redacted]: Drug Hypersensitivity

A 5[redacted]-year-old white male with medical history of arthralgia and no history of tobacco use and alcohol use had an event of drug hypersensitivity. No concomitant therapies were reported. On Day 1, the subject was randomized to tildrakizumab 200 mg in Part 1 and continued to receive this therapy in Part 2 and Part 3 of the base trial. Subject continued this therapy in the extension study. On Day 359, the subject experienced an adverse event of drug hypersensitivity. The subject had taken acetaminophen(+) diclofenac on the same day for pruritis secondary to psoriasis. The subject was prescribed Pepcid and prednisolone for one day on Day 360. The event was resolved on Day 366. The PI considered allergic reaction attributed to NSAID. The event of drug hypersensitivity was considered to be mild in intensity and was assessed by the investigator to be not related to study medication. No action was taken with the study medication. The subject completed the base study on Day 453 and continued into the extension study.

[redacted]: Hypersensitivity

A 5[redacted]-year-old white male with medical history of hypercholesterolemia, hypertension, appendicectomy, skin papilloma, acne, and arthralgia, history of tobacco use (20 pack-years), and alcohol use (8 drinks per week) had a not drug-related event of hypersensitivity. The concomitant therapy included aspirin. On Day 1, the subject was randomized to tildrakizumab 100 mg in Part 1 and continued to receive the same therapy in Part 2 and Part 3 of the base trial. Subject continued this therapy in the extension study. On Day 156, the subject experienced an adverse event of hypersensitivity. The subject took the last study medication dose on Day 119 prior to the event. The investigator considered the event environmental allergic reaction. The subject was prescribed epinephrine on Day 156, diepinephrine hydrochloride (Days 157 to 159), and prednisolone (Days 157 to 160). The event was resolved on Day 158. The event of hypersensitivity was considered to be mild in intensity and was assessed by the investigator to be not related to study medication. No action was taken with the study medication. The subject completed the base study on Day 450 and continued into the extension study.

[redacted]: Drug hypersensitivity

A 5[redacted]-year-old white female with medical history of hypertension, diabetes mellitus, alopecia, ventricular tachycardia, and microcytic anemia and history of ex-user tobacco use (14 pack- years) and history of no alcohol use had an not drug-related event of drug hypersensitivity. The concomitant therapies included pantopazole, metformin, irbesartan, clonidine hydrochloride, bisoprolol, atorvastatin, aspirin, venlafaxime hydrochloride, repaslinide, levothyroxine sodium hydrochlorothiazide. On Day 1, the subject was randomized to tildrakizumab 100 mg in Part 1 and continued to receive this therapy in Part 2 and Part 3 of the base trial. Subject continued this therapy in the extension study. On Day 287, the subject experienced an adverse event of drug hypersensitivity. The last dose of study medication was taken on Day 282 prior to

the event. The subject was prescribed diphenhydramine hydrochloride and prednisone on Day 287 for the treatment of drug hypersensitivity. The event was resolved within 24 hours on Day 287. The PI considered the allergic reaction attributed to amoxicillin,which was taken for tooth ache from day 287 to Day 291. The event of drug hypersensitivity was considered to be mild in intensity and was assessed by the investigator to be not related to study medication. No action was taken with the study medication. The subject completed the base study on Day 446 and continued into the extension study.

[redacted]: Drug hypersensitivity

A 7[redacted]-year-old white female with medical history of hypertension, onchomycosis, cholecystectomy, brain neoplasm benign, sinus bradycardia, and insomnia, ex-tobacco user (1 pack-year), and history of no alcohol use had an event of drug hypersensitivity. The concomitant therapy included amlodipine On Day 1, the subject was randomized to tildrakizumab 100 mg in Part 1 and continued to receive this therapy in Part 2 and was re-randomized to placebo in Part 3. The treatment with tildrakizumab 100 mg was reinitiated upon relapse. The subject completed the base and was not continuing in the extension study. On Day 7, the subject experienced a not drug-related adverse event of drug hypersensitivity. The subject was prescribed clonidine for hypertension on Day 7 only. The subject had tongue swelling after ingesting clonidine. The investigator attributed the event of drug hypersensitivity to the drug clonidine. The subject was not prescribed any medication for drug hypersensitivity. The event was resolved in 1 hour on the same Day 7. The event of drug hypersensitivity was considered to be moderate in intensity and was assessed by the investigator to be not related to study medication. No action was taken with the study medication. The subject completed the base study on Day 450 and was not continuing in the extension study.

[redacted]: Drug hypersensitivity

A 4[redacted]-year-old Asian female with medical history of hyperlipidaemia, headache, tinea pedis, and tinea cruris, current tobacco user (5 pack-years), and alcohol user (14 drinks per week) had an event of drug hypersensitivity. The concomitant therapy included acetaminophen, diclofenac, and chlorpheniramime. On Day 1, the subject was randomized to tildrakizumab 200 mg in Part 1 and continued to receive this therapy in Part 2. The subject was re-randomized to placebo in Part 3. The subject completed the base and was not continuing in the extension study. On Day 54, the subject experienced an adverse event of drug hypersensitivity. The subject was prescribed diclofenac for the treatment of nerve compression from Day 38 to day 47. The investigator attributed the event of drug hypersensitivity to the drug diclofenac. The subject took the last dose of the study medication on Day 30. The subject was not prescribed any medication for drug hypersensitivity. The event was resolved in 4 hours on the same Day 54. The event of drug hypersensitivity was considered to be mild in intensity and was assessed by the investigator to be not related to study medication. No action was taken with the study medication. The subject completed the base study on Day 464 and was not continuing in the extension study.

Protocol 011: Narratives For Hypersensitivities Reported During Phase 3 Base Study			
Allocation Number	**Treatment Received**	**Reported Term**	**Preferred Term**
[redacted]	Placebo	Angioedema/Urticaria	Angioedema/Urticaria
[redacted]	Tildrakizumab 200 mg	Urticaria	Urticaria
[redacted]	Tildrakizumab 100 mg	Hypersensitivity reaction	Hypersensitivity
[redacted]	Tildrakizumab 100 mg	Swollen tongue, swelling face, and lip swelling	Swollen tongue, swelling face, and lip swelling
[redacted]	Tildrakizumab 100 mg	Swelling face, urticaria	Swelling face, urticaria
[redacted]	Tildrakizumab 100 mg	Injection site urticaria	Injection site urticaria
[redacted]	Etanercept 50 mg	Urticaria	Urticaria
[redacted]	Tildrakizumab 200 mg	Urticaria	Urticaria
[redacted]	Etanercept 50 mg	Hives	Urticaria
[redacted]	Tildrakizumab 100 mg	Urticaria	Urticaria
[redacted]	Tildrakizumab 100 mg	Urticaria	Urticaria
[redacted]	Tildrakizumab 200 mg	Urticaria acute	Urticaria
[redacted]	Tildrakizumab 200 mg	Urticaria	Urticaria
[redacted]	Tildrakizumab 100 mg	Hypersensitivity reaction	Hypersensitivity

[redacted]- Angioedema, Urticaria

A 5[redacted]-year-old Asian female with a relevant medical history of allergies to cats, wool, shellfish, house dust mites, latex, grass, and pollen, headaches, asthma, and hypertension, was reported to have had drug-related hypersensitivity events of angioedema and urticaria. The subject was randomized to placebo and on Day 1; the subject experienced an adverse event of hot flush. The subject stated she had hot flushes all over her body after study medication dosing on Day 1. On Day 5, the subject experienced adverse events of angioedema and urticarial drug eruption. The subject contacted the investigator by phone to inform the site that she had swelling of her arms, ears, legs, and portions of her face after Visit 3 on Day 4. The subject reported wheals, pruritus and confluent skin lesions, and pitting and bleeding of skin lesions. The subject had not started any new medications nor had been exposed to any food or other triggers. The subject was instructed to stop taking the study medication and her early termination visit was scheduled. The subject's last dose of tildrakizumab placebo was on Day 1 and etanercept placebo was on Day 4. The subject was discontinued from the study on Day 7 and completed her early termination visit the same day. On Day 11, the subject was improving and no additional symptoms were present. The subject was given diphenhydramine hydrochloride from Day 6 to Day 25 and methylprednisolone from Day 7 to Day 12 for treatment of these adverse events. On Day 25, the events of angioedema and urticaria resolved. The events of angioedema and urticaria were considered to be severe in intensity and were assessed by the investigator to be related to study medication.

[redacted]- Urticaria

A 3[redacted]-year-old, white male with a relevant medical history of allergy to cats, penicillin allergy, pollinosis, tonsillitis, tobacco usage (21 pack years), and nephrolithiasis had a drug-related hypersensitivity event of urticaria. On Day 1, the subject was randomized to tildrakizumab 200 mg and continued on the same treatment in Part 2 and Part 3 of the study. Concomitant therapy included ibuprofen and clarithromycin. On Day 326, the subject experienced urticaria.

Signs and symptoms included infection and allergic exanthema. The subject was given fluprednidene acetate from Day 327 to Day 329, clemastine fumarate from Day 328 to Day 329, and dimetindene maleate from Day 329 to Day 331 for treatment of urticaria. On Day 332, the event urticaria resolved. The event of urticaria was considered to be moderate in intensity and was assessed by the investigator to be related to study medication. No action was taken with regard to study medication. The subject completed the base study on Day 361 and continued into the extension study.

[redacted]- Hypersensitivity

A 4[redacted]-year-old Native Hawaiian or Pacific Islander female with a relevant medical history of seasonal allergy, sinus headache, and tobacco use (0.2 pack years), had a drug-related event of hypersensitivity. On Day 1, the subject was randomized to placebo. At the Week 12 visit, the subject was re-randomized to tildrakizumab 100 mg. Concomitant therapy included general anesthesia, amoxicillin, and ibuprofen. The subject's last active dose of tildrakizumab 100 mg was on Day 114. On Day 116, the subject experienced facial, neck, and arm itching. The subject denied any mouth or throat swelling and had no previous drug allergies or sensitivities. The subject was not hospitalized. The subject was given hydroxyzine hydrochloride from Day 117 to Day 134 and diphenhydramine hydrochloride and cetirizine hydrochloride from Day 127 to Day 134 for treatment of hypersensitivity. The subject was discontinued from the trial on Day 127 and completed her early termination visit on the same day. On Day 142, the event of hypersensitivity resolved. The event was considered to be moderate in intensity and was assessed by the investigator to be related to study medication.

[redacted]- Hypersensitivity Events

A 6[redacted]-year-old, white female with a relevant medical history of atrioventricular block first degree, fruit allergy, diabetes mellitus, obesity, tobacco usage (66 pack years), and hypertension had drug-related hypersensitivity events of swollen tongue, swelling face, and lip swelling. On Day 1, the subject was randomized to placebo. At the Week 12 visit, she was re-randomized to tildrakizumab 100 mg. Concomitant therapy included ramipril, hydrochlorothiazide, and prednisolone. On Day 124, the subject experienced swollen tongue on the right side; the subject's last active dose prior to the event was on Day 114 (tildrakizumab 100 mg). The subject was given dimetindene maleate and prednisolone on Day 124 and the event resolved the same day. On Day 130, the subject experienced face swelling and lip swelling. The subject was given dimetindene maleate and prednisolone on Day 130 and the events resolved the same day. Study medication was temporarily interrupted due to lip swelling. Study medication resumed on Day 135 (etanercept placebo). The subject's last active dose of tildrakizumab 100 mg was on

Day 142. On Day 143, the subject experienced swollen tongue on the left side. The subject was given prednisolone, ranitidine, and clemastine fumarate on Day 143 and the event resolved the same day. On Day 155, the subject experienced lip swelling which resolved the same day. No further symptoms of swollen tongue, face swelling, and lip swelling were observed and no laboratory tests were done. No new medications were started and no previous events were known. The events of swollen tongue, lip swelling, and swelling face were all considered to be moderate in intensity and were assessed by the investigator to be related to study medication.

The subject withdrew from the study on Day 226.

[redacted]- Urticaria and Face Swelling

A 3[redacted]-year-old, white female with a medical history of intervertebral disc prolapse, and tobacco usage (12 pack years) had drug-related hypersensitivity events of urticaria and face swelling.

There was no history of alcohol substance abuse or allergies. On Day 1, the subject was randomized to tildrakizumab 100 mg and continued on the same treatment in Part 2 and Part 3 of the study. Concomitant therapy included ibuprofen, clemastine fumarate, and fexofenadine hydrochloride. On Day 227, the subject experienced urticaria and face swelling. Urticaria and face swelling started 1 hour after subject had eaten a new ketchup brand and the day after the last injection of study medication (placebo). The subject's last dose of tildrakizumab 100 mg prior to the event of urticarial and face swelling was on Day 226. There was no dyspnoea and no lip or tongue swelling after concomitant medication was given. The subject was given cetirizine hydrochloride on Day 228 for treatment of face swelling and loratadine from Day 229 to

Day 230 and prednisolone from Day 229 to Day 231 for the treatment of urticaria. The event of face swelling resolved on Day 230 and the event of urticaria resolved on Day 240. The events of urticaria and face swelling were both considered to be moderate in intensity and were assessed by the investigator to be related to study medication. On Day 347, the subject experienced another event of urticaria. The subject's last dose of tildrakizumab 100 mg prior to the second event of urticaria was on Day 282. The subject

developed pruritic urticaria on both arms and both legs. The subject was sure that urticaria was related to alcoholic drinks. The subject was given cetirizine hydrochloride on Day 347 for treatment of urticaria and the event resolved the same day. Urticaria did not occur again after the next injection of study medication. No action was taken with regard to study medication. The subject completed the base study on Day 366 and continued into the extension study.

[redacted]- Urticaria

A 3[redacted]-year-old, white female with a medical history of caesarean section had a drug-related hypersensitivity event of injection site urticaria reported on Day 1. On Day 1, the subject was randomized to tildrakizumab 100 mg and continued on the same treatment in Part 2 and Part 3 of the study. Concomitant therapy included ibuprofen. On Day 1, the subject received tildrakizumab 100 mg in the left thigh and right quadrant of the abdomen and etanercept placebo in the right thigh. On the same day, the subject experienced urticaria site reaction on the right thigh with no spreading. Erythema, raising, and pruritus were observed by the subject. The subject did not have a history of similar rashes and did not start any new treatment. The subject was given mequitazine on Day 1 for treatment of the urticaria reaction. The urticaria site reaction resolved on the same day. The event of urticaria site reaction was considered to be mild in intensity and was assessed by the investigator to be related to study medication. No action was taken with regard to study medication. The subject completed the base study on Day 366 and continued into the extension study.

[redacted]- Urticaria

A 3[redacted]-year-old white male with a relevant medical history of psoriasis, depression, psoriatic arthropathy, anxiety, and haematuria, was reported to have had an adverse event of urticaria.

The subject was randomized to etanercept 50 mg on Day 1, was switched to tildrakizumab 200 mg in Part 3 of the base study and continued on the same dose in the extension. On Day 12, the subject experienced an adverse event of urticaria that started in the morning and resolved in the afternoon. The subject reported that hives reappeared on his arms and legs on Day 13 and resolved without any treatment. The last dose of etanercept prior to the onset of the event was on Day 9. The subject did not describe the urticaria as raised or pruritic. The subject took one dose of cetirizine hydrochloride 10 mg after the hives resolved the second time. The subject reported not having taken any new medications or foods prior to or during the course of the event. The investigator suspects that the subject's occupation working with antiques may have triggered the event. The investigator indicated that the adverse event was mild in intensity and was not related to study medication. No action was taken with study medication. The subject completed the base on Day 365 and continued on into the extension.

[redacted]-Urticaria

A 5[redacted]-year-old white male with a medical history of hyperlipidemia and arthralgia was reported to have had an adverse event of urticaria. The subject reported a history of sporadic urticaria, with occurrences once every two to three years and more recently, monthly reoccurrences. The subject was randomized to receive placebo on Day 1 and switched to tildrakizumab 200 mg in Part 2 on Day 109 and remained on tildrakizumab 200 mg in Part 3 on Day 225. The subject's concomitant medications included tolnaftate and omega-3 marine triglycerides. On Day 233, the subject reported lesions on his upper legs and upper arms that were raised, warm to the touch, and pruritic. The lesions were reported to sometimes appear on the lower arms and legs. The lesions were reported to last up to 12 hours and when treated with loratadine would resolve within one to four hours. The subject reported not having taken any new medications or foods prior to or during the course of the event. The investigator indicated that the adverse event was mild in intensity and was not related to study medication. No action was taken with study medication. The subject completed the base study on Day 362 and continued on into the extension.

[redacted]- Pruritus generalized, urticaria

A 5[redacted]-year-old white female with a medical history of hyperglycemia, dyspepsia, pleurisy, and tobacco use (15 packs per year) and alcohol use (4 drinks per year), was reported to have had adverse events of pruritus generalized and urticaria. The subject was randomized to receive etanercept on Day 1, was switched to tildrakizumab 200 mg for Part 3 (Day 233). The subject's concomitant medications included loratadine and milk baths. On Day 148, the subject reported an adverse event of pruritus generalized which resolved on Day 152. The last dose of etanercept before the onset of the generalized pruritus was on Day 205. On Day 235, the subject reported hives on her arms, legs, neck, and back 24 hours after an injection of tildrakizumab 200 mg. The hives resolved on Day 238 and no treatment was required. The investigator indicated that the adverse events of pruritus generalized and urticaria were mild in intensity and were not related to study medication. No action was taken with study medication. The subject completed the base study on Day 367 and continued on into the extension.

[redacted]- Urticaria

A 5[redacted]-year-old white female with a medical history of asthma, headache and gastroesophageal reflux disease was reported to have had an adverse event of urticaria. The subject was randomized to receive tildrakizumab 100 mg on Day 1 and switched to tildrakizumab 100 mg in Part 3 on Day 227. The subject's concomitant medications included fluticasone propionate + salmeterol xinafoate, albuterol, acetaminophen, and rantidine. On Day 200, the subject reported an adverse event of urticaria located on the neck. The urticaria was described as wheals that were slightly raised and pruritic. The subject had not started taking any new medications, food, or any other triggers. The urticaria resolved on Day 207 with diphenhydramine hydrochloride. The last dose of tildrakizumab 100 mg the patient received before the start of the event was on Day 199. The investigator indicated that the adverse event of urticaria was mild in intensity and not related to study medication. No action was taken with study medication. The subject completed the base on Day 367 and continued into the extension.

[redacted]- Urticaria

A 4[redacted]-year-old white male with a medical history of chronic pain of ankle joint was reported to have had an adverse event of urticaria. The subject was randomized to receive tildrakizumab 200 mg on Day 1 and switched to tildrakizumab 100 mg in Part 3 on Day 225. Concomitant medications included dipyrone. On Day 343, the subject reported fleeting urticarial plaques covering their entire body. On Day 366, the subject reported just a few plaques were visible. The subject received desloratadine on Day 359 through Day 369 for the treatment of urticaria. The subject did not have a history of similar rashes and had not started any new medications, food, or other possible triggers. The last dose of tildrakizumab 100 mg taken before the adverse event was given on Day 343. The event of urticaria was considered to be mild in intensity and was assessed by the investigator to be not related to study medication. No action was taken with regard to study medication. The subject completed the base on Day 366 and continued into the extension study.

[redacted]- Urticaria

A 4[redacted]-year-old white female with a medical history of allergic rhinoconjunctivitis, ankylosing spondylitis, and hypertension was reported to have had an adverse event of urticaria. The subject was randomized to receive tildrakizumab 200 mg in Part 1 and continued on the same dose during Parts 2 and 3/ was re-randomized to 100 mg in Part 3. Concomitant medications included metoprolol, pantoprazole, etoricoxib, and diclofenac. On Day 320 the subject was reported to have had pruritic urticaria of the entire body which resolved after 6 hours with no treatment and no sequale. The subject did not have a history of similar symptoms and had not started any new medications, food, or other possible triggers. The last dose of tildrakizumab 200 mg taken before the onset of the event was given on Day 281. The event of urticaria was considered to be mild in intensity and was assessed by the investigator to be not related to study medication. No action was taken with study medication. The subject completed the base on Day 365 and continued into the extension study.

[redacted]- Urticaria

A 3[redacted]-year-old white male with no significant medical history was reported to have had an adverse event of urticaria. The subject was randomized to receive tildrakizumab 200 mg on Day 1 and continued on the same dose in Parts 2 and 3. No concomitant medications were being taken at the time of randomization. On Day 294 the subject was reported to have had an adverse event of urticaria which presented as intermittent small to medium sized urticaria on the trunk and extremities. The subject denied any other symptoms. On Day 300 through Day 377, the subject was prescribed ebastone as needed. On Day 377, the adverse event resolved. No action was taken with regard to study medication. The subject denied having a history of similar rashes and had not started any new medications, food, or other possible triggers. On Day 369 the subject completed the base study and continued to receive tildrakizumab 100 mg in the extension study.

[redacted]- Hypersensitivity

A 6[redacted]-year-old white male with no significant medical history was reported to have had an adverse event of hypersensitivity. The subject was randomized to placebo on Day 1 and the patient was re-randomized to tildrakizumab 100 mg in Part 2 and 3 (Day unknown).

Concomitant medications included saw palmetto. On Day 190, the subject was reported to have had an adverse event of hypersensitivity reaction. The last dose of study medication taken before the start of the adverse event is unknown. The subject indicated that the he had developed an allergy to an unknown agent. On Day 191, the subject was treated with desloratadine, and from Day 192 through Day 193, the subject was treated with betamethasone. The adverse event resolved on Day 201 and was considered to be mild in intensity and not related to study medication. No action was taken with study medication. The subject completed the base study on Day 364 and continued on into the extension.

付録 2.7.4-58
第 III 相試験の延長試験に発現した過敏症反応の記述

Trial 010: Hypersensitivity Events Reported During Phase 3 Extension Study

Allocation Number	Treatment Received	Reported Term	Preferred Term
[redacted]	Tildrakizumab 100 mg	Urticaria	Urticaria
[redacted]	Tildrakizumab 200 mg	Urticaria	Urticaria
[redacted]	Tildrakizumab 100 mg	Urticaria	Urticaria
[redacted]	Tildrakizumab 100 mg	Urticaria	Urticaria

[redacted]: Urticaria

A 5[redacted]-year-old white male with a medical history of hypertension, staphylococcus infection, anogenital warts, seasonal allergies, current tobacco user (18 pack years), and history of no alcohol use had a hypersensitivity event of urticaria. On Day 1, the subject was randomized to tildrakizumab 100 mg group for Part 1 and continued on this treatment in Part 2. In Part 3, the subject was re-randomized to placebo. The treatment with tildrakizumab 100 mg was reinitiated upon relapse and the same treatment was continued in the extension study. The concomitant therapy included lisinopril. On Day 506, the subject experienced a rash that started on the face and neck and was spread to his trunk. The rash was flat, red and pruritic. The subject did not have any history of similar rashes and had not started any new medications or eaten any new foods. The last dose of tildrakizumab 100 mg before the start of the event was on Day 453. The subject was treated with diphenhydramine hydrochloride to relieve the itching. The event of urticaria was resolved on Day 510. On day 527, the subject experienced the 2nd event of urticaria. The second episode was not treated with any medication; the event was resolved 2 days after on Day 529. Both events of urticaria were mild in intensity and the investigator considers them not related to the study medication. No action was taken with regard to study medication. The subject is continuing in the extension study.

[redacted]-Urticaria

A 4[redacted]-year-old Asian female with a medical history of asteatosis, tinea cruris, blepharitis, current tobacco user (24 pack years), and alcohol use (2 drinks per day) had a hypersensitivity event of urticaria. The concomitant medications included candesartan, mucopolysaccharide polysulfate, benidipine hydrochloride, rebamipide, and petrolatum, white. On Day 1, the subject was randomized to tildrakizumab 200 mg group for Part 1 and continued on this treatment in Part 2 and Part 3. The same treatment was continued in the extension study. On Day 497, the subject experienced urticaria. The last dose of tildrakizumab 200 mg before the start of the event was on Day 449. The subject was treated with fexofenadine hydrochloride, epinastine hydrochloride, famotidine, betamethasone, and prednisolone. The event of urticaria was moderate in intensity and the investigator considers this event not to be related to the study medication. The event of urticaria has not been resolved yet. No action was taken with regard to study medication. The subject is continuing in the extension study.

[redacted]– Urticaria

A 4[redacted]-year-old Asian female with a medical history of pneumonia, current tobacco user (10 pack years), and alcohol use (2 drinks per day) had a hypersensitivity event of urticaria. No concomitant medications were reported. On Day 1, the subject was randomized to tildrakizumab 100 mg group for Part 1 and continued on this treatment in Part 2. The subject was re- randomized to placebo in Part 3. The treatment with tildrakizumab 100 mg was reinitiated upon relapse and the same treatment continue in the extension study. On Day 719, the subject experienced urticaria. The last dose of tildrakizumab 100 mg before the start of the event was on Day 677. The subject was treated with bepotastine besylate. The event of urticaria was resolved on Day 726. The event of urticaria was moderate in intensity and the investigator considers this event not to be related to the study medication. No action was taken with regard to study medication. The subject is continuing in the extension study.

[redacted]-Urticaria

A 4[redacted]-year-old Asian male with a no other medical history except psoriasis, ex-tobacco user (10 pack years), and alcohol use (11 drinks per day) had a drug-related hypersensitivity event of urticaria. The concomitant medications included loxoprofen sodium, febuxostat, diclofenac sodium, and rebamipide. On Day 1, the subject was randomized to tildrakizumab 100 mg group for Part 1 and continued on this treatment in Part 2. The subject was re-randomized to placebo in Part 3. The treatment with tildrakizumab 100 mg was reinitiated upon relapse and the same treatment continues in the extension study. On Day 750, the subject experienced urticaria. The rashes appeared and disappeared on the whole body surface; sometimes they appeared on lumbar and both knee on the examination. They were raised and pruritic. The subject has buckwheat allergy; however, the subject did not take buckwheat food at that time. The investigator feels that the subject was very busy and did not sleep enough and it could be a possible trigger. There were no records of similar rashes in the subject's medical records. The last dose of tildrakizumab 100 mg before the start of the event was on Day 750. The subject was treated with bepotastine besylate (+) menthol (Day 750 to day 751), bepotastine besylate (Day 751), and olopatadine hydrochloride (Day 757 to continuing). The event of urticaria was has not been resolved yet. The event of urticaria was moderate in intensity and the investigator considers this event to be related to the study medication. No action was taken with regard to study medication. The subject is continuing in the extension study.

Trial 011: Narratives for Hypersensitivity Reported During Phase 3 Extension Study

Allocation Number	Treatment Received	Reported Term	Preferred Term
[redacted]	Tildrakizumab 200 mg	Urticaria acute	Urticaria
[redacted]	Tildrakizumab 100 mg	Urticaria	Urticaria
[redacted]	Tildrakizumab 100 mg	Drug rash	Drug eruption
[redacted]	Tildrakizumab 100 mg	Drug rash	Drug eruption
[redacted]	Tildrakizumab 100 mg	Urticaria	Urticaria

[redacted]- Urticaria

A 6[redacted]-year-old white male with a medical history of paraplegia and hypothyroidism was reported to have had an adverse event of urticaria. The subject was randomized to receive etanercept 50 mg on Day 1 and switched to tildrakizumab 200 mg in Part 3 on Day 225. Concomitant medications included levothyroxine sodium. The subject was reported to have had adverse events of pruritus on Day 83 through Day 283 which were mild in intensity and not related to study medication. No action was taken with study medication for these two adverse events. On Day 360 completed the base study and continued into the extension study on tildrakizumab 200 mg. On Day 430, the subject reported an adverse event of urticaria with redness, pruritus, and raised areas under both arms and behind both knees. The subject was treated with cetirizin hydrochloride from Day 444 through Day 474. The adverse event resolved on Day 535. The subject denies any new medication, food, or other triggers. The investigator reported the adverse event of urticaria to be mild in intensity and not related to study medication. No action was taken with study medication.

[redacted]- Urticaria

A 3[redacted]-year-old white male with a medical history of asthma was reported to have had an adverse event of urticaria. The subject was randomized to receive tildrakizumab 100 mg on Day 1 and continued on the same dose throughout the base study and into the extension. No concomitant medications were taken at randomization. On Day 361 the subject completed the base study and continued into the extension study on tildrakizumab 100 mg. On Day 780, the subject was reported to have had an adverse event of urticaria which presented as a raised and pruritic area of the right forearm. The subject reports having had a similar rash a few years ago that occurred after egg consumption. The subject reports having eaten “more eggs than usual” prior to the adverse event on Day 780. The adverse event resolved on Day 786 and was reported to be mild and not related to study medication. No treatment was required and no action was taken with study medication.

[redacted]- Drug eruption

A 2[redacted]-year-old white male with a medical history of chronic gastritis, obesity, carpal tunnel syndrome, supraventricular extrasystoles, and hypertonia was reported to have had adverse events of drug eruption and skin exfoliation. The subject was randomized to tildrakizumab 100 mg and continued on the same dose throughout the base study. Concomitant medication included pantoprazole. On Day 334, the subject was reported to have had an adverse event of skin exfoliation of the fingertips that was considered mild in intensity and not related to study medication. No action was taken with study medication and no treatment was necessary. The subject completed the base study on Day 362 and continued on into the extension on tildrakizumab 100 mg. On Day 378, the subject was reported to have had an adverse event of drug eruption on the subject’s bilateral upper arms that was triggered by a nicotine patch. The eruption was reported to have been pruritic. The subject denied any history of similar rashes.

The adverse event of drug eruption was reported as mild in intensity and not related to study medication. No action was taken with study medication and no treatment was necessary.

[redacted]- Drug eruption

A 5[redacted]-year-old white male with a medical history of hypertension and asthma was reported to have had an adverse event of drug eruption. The subject was randomized to tildrakizumab 200 mg on Day 1 and was re-randomized to tildrakizumab 100 mg in Part 3 on Day 230.

Concomitant medications included hydrochlorathiazide + telmisartan, aspirin, budesonide + formoterol fumarate, and cermide + coconut oil +glycerin=medium-chain triglycerides + phospholipids + shea butter. On Day 371 the subject completed the base study and continued on into the extension on tildrakizumab 100 mg. On Day 478, the subject was reported to have had an adverse event of drug eruption which presented as erythematous, papular, and pustular lesions of the face. The drug eruption was thought to be triggered by amoxicillin and/or clarithromycin which were prescribed for erosive gastroduodenitis. The drug eruption was reported to have resolved on Day 480 and be moderate in intensity and not related to study medication. No action was taken with regard to study medication. The drug eruption was treated with an antihistamine (name unknown) on Days 481.

[redacted]- Urticaria

A 3[redacted]-year-old white female with a medical history of insomnia, melanocytic naevus, and psoriatic arthropathy was reported to have had an adverse event of urticaria. The subject was randomized to tildrakizumab 200 mg and re-randomized to tildrakizumab 100 mg in Part 3. Concomitant medications included zopiclone and ibuprofen. On Day 363 the subject completed the base study and continued onto the extension and received tildrakizumab 100 mg. On Day 643, the subject was reported to have had an adverse event of urticaria over the entire body that was pruritic and raised. On Day 644, the subject received cetirizine hydrochloride and the symptoms resolved. The subject denied having a history of any similar rashes and had not started any new medications, food, or other possible triggers. Last dose of tildrakizumab 100 mg was given on Day 615. Study medication was discontinued on Day 671 due to the adverse event of urticaria and thyrotoxic crisis. The event of urticaria was considered mild in intensity and was assessed by the investigator to be not related to study medication.

付録 2.7.4-59
日本人被験者：P06306 試験で 1 回以上投与された全被験者
人口統計学の要約

	SCH 900222 (10 mg/kg IV) Japanese Part 2 n=6	SCH 900222 (50 mg) Japanese n=8	SCH 900222 (200 mg) Japanese n=6	SCH 900222 (400 mg) Japanese n=8	All Japanese Part 1 n=22	SCH 900222 (50 mg) Caucasian n=7
Sex (n,%)						
Female	5 (83)	3 (38)	5 (83)	4 (50)	12 (55)	2 (29)
Male	1 (17)	5 (63)	1 (17)	4 (50)	10 (45)	5 (71)
Ethnicity (n,%)						
Not Hispanic or Latino	6 (100)	8 (100)	6 (100)	8 (100)	22 (100)	7 (100)
Age (yrs)						
Mean (SD)	27.7 (6.7)	21.5 (1.8)	22.7 (3.2)	28.5 (7.0)	24.4 (5.5)	20.3 (1.0)
Median	26.5	21.0	22.0	27.5	22.0	20.0
Range	21 - 38	20 - 25	20 - 29	21 - 41	20 - 41	19 - 22
Age (n,%)						
18 - <65	6 (100)	8 (100)	6 (100)	8 (100)	22 (100)	7 (100)
Weight (kg)						
Mean (SD)	57.30 (9.28)	61.63 (6.20)	56.12 (7.47)	57.56 (5.74)	58.65 (6.54)	59.70 (5.91)
Median	54.55	62.00	56.30	56.10	58.30	59.40
Range	48.0 - 74.5	52.0 - 70.5	47.7 - 63.8	51.5 - 69.0	47.7 - 70.5	52.6 - 70.1
Height (cm)						
Mean (SD)	161.67 (6.69)	169.19 (8.33)	161.33 (7.45)	165.44 (7.87)	165.68 (8.19)	170.93 (7.68)
Median	161.00	170.00	162.00	167.50	167.00	169.00
Range	155.0 - 171.0	158.0 - 182.5	153.0 - 170.0	156.0 - 176.0	153.0 - 182.5	161.0 - 183.0
BMI						
Mean (SD)	21.82 (2.56)	21.48 (1.57)	21.43 (1.42)	21.23 (1.35)	21.37 (1.39)	20.44 (0.88)
Median	21.20	20.65	21.85	21.55	21.25	20.30
Range	19.2 - 25.6	19.8 - 23.7	19.2 - 23.0	18.7 - 22.9	18.7 - 23.7	19.4 - 21.9

[Source: p007: Page 138]

付録 2.7.4-60
日本人被験者：P06306 試験 で 1 回以上投与された全被験者
有害事象の要約

Subject Disposition	SCH 900222 (10 mg/kg IV) Japanese Part 2	SCH 900222 (50 mg) Japanese	SCH 900222 (200 mg) Japanese	SCH 900222 (400 mg) Japanese	SCH 900222 (50 mg) Caucasian	SCH 900222 (200 mg) Caucasian
Randomized	6(100)	8(100)	6(100)	8(100)	7(100)	6(100)
Discontinued Treatment Phase	0	3 (38)	0	3 (38)	2 (29)	0
Adverse Event	0	0	0	1 (13)	0	0
Subject Withdrew Consent	0	3 (38)	0	0	2 (29)	0
Non-Compliance With Protocol	0	0	0	0	0	0
Administrative	0	0	0	2 (25)	0	0
Completed Treatment Phase	6(100)	5 (63)	6(100)	5 (63)	5 (71)	6(100)

[Source: p007: Page 141-142]

付録 2.7.4-61
日本人被験者：被験者の特性
（無作為割付けされた全被験者）
ベース試験

	Placebo n (%)	MK-3222 100 mg n (%)	MK-3222 200 mg n (%)	Total n (%)
Subjects in population	32	64	62	158
Gender				
Male	24 (75.0)	48 (75.0)	52 (83.9)	124 (78.5)
Female	8 (25.0)	16 (25.0)	10 (16.1)	34 (21.5)
Age (years)				
<65	27 (84.4)	61 (95.3)	53 (85.5)	141 (89.2)
≥65	5 (15.6)	3 (4.7)	9 (14.5)	17 (10.8)
Mean	50.5	46.3	49.0	48.2
SD	12.60	11.86	11.55	11.93
Median	48.0	46.0	47.0	47.0
Range	24 to 76	18 to 76	24 to 70	18 to 76

[Source: p010: Page 675]

付録 2.7.4-62
日本人被験者：有効性評価項目のベースライン値の要約
（無作為割付けされた全被験者）
ベース試験

	Placebo n (%)	MK-3222 100 mg n (%)	MK-3222 200 mg n (%)	Total n (%)
Subjects in population	32	64	62	158
PASI Score				
Subjects with data	32	64	62	158
Mean	24.3	26.4	25.6	25.7
SD	9.48	10.30	12.00	10.81
Median	21.1	24.8	23.1	23.2
Range	12.4 to 51.8	12.3 to 59.4	12.0 to 66.0	12.0 to 66.0
PGA Score				
Subjects with data	32	64	62	158
<3	0	0	0	0
3	18 (56.3)	32 (50.0)	29 (46.8)	79 (50.0)
4	13 (40.6)	31 (48.4)	29 (46.8)	73 (46.2)
5	1 (3.1)	1 (1.6)	4 (6.5)	6 (3.8)

PASI = Psoriasis Area Severity Index; PGA = Physician's Global Assessment; SD = Standard deviation.

Data Source: [16.4]
[Source: p010: Page 677]

付録 2.7.4-63
日本人被験者：被験者の既往歴
（1 投与群以上で発現率 > 5%）
（無作為割付けされた全被験者）
ベース試験

	Placebo		MK-3222 100 mg		MK-3222 200 mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	32		64		62		158	
With one or more conditions	32	(100.0)	64	(100.0)	62	(100.0)	158	(100.0)
With no conditions	0		0		0		0	
Cardiac disorders	**4**	**(12.5)**	**3**	**(4.7)**	**5**	**(8.1)**	**12**	**(7.6)**
Angina pectoris	2	(6.3)	0		1	(1.6)	3	(1.9)
Eye disorders	**2**	**(6.3)**	**2**	**(3.1)**	**5**	**(8.1)**	**9**	**(5.7)**
Gastrointestinal disorders	**3**	**(9.4)**	**8**	**(12.5)**	**9**	**(14.5)**	**20**	**(12.7)**
Hepatobiliary disorders	**3**	**(9.4)**	**6**	**(9.4)**	**7**	**(11.3)**	**16**	**(10.1)**
Hepatic steatosis	1	(3.1)	4	(6.3)	5	(8.1)	10	(6.3)
Immune system disorders	**6**	**(18.8)**	**7**	**(10.9)**	**13**	**(21.0)**	**26**	**(16.5)**
Seasonal allergy	5	(15.6)	4	(6.3)	12	(19.4)	21	(13.3)
Infections and infestations	**7**	**(21.9)**	**13**	**(20.3)**	**12**	**(19.4)**	**32**	**(20.3)**
Tinea pedis	2	(6.3)	3	(4.7)	2	(3.2)	7	(4.4)
Injury, poisoning and procedural complications	**3**	**(9.4)**	**4**	**(6.3)**	**2**	**(3.2)**	**9**	**(5.7)**
Metabolism and nutrition disorders	**8**	**(25.0)**	**14**	**(21.9)**	**16**	**(25.8)**	**38**	**(24.1)**

日本人被験者：被験者の既往歴
（1 投与群以上で発現率 > 5%）
（無作為割付けされた全被験者）
ベース試験

	Placebo		MK-3222 100 mg		MK-3222 200 mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Diabetes mellitus	1	(3.1)	1	(1.6)	6	(9.7)	8	(5.1)
Dyslipidaemia	4	(12.5)	2	(3.1)	2	(3.2)	8	(5.1)
Hyperlipidaemia	1	(3.1)	7	(10.9)	6	(9.7)	14	(8.9)
Hyperuricaemia	2	(6.3)	4	(6.3)	6	(9.7)	12	(7.6)
Musculoskeletal and connective tissue disorders	**5**	**(15.6)**	**7**	**(10.9)**	**11**	**(17.7)**	**23**	**(14.6)**
Osteoporosis	2	(6.3)	0		1	(1.6)	3	(1.9)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**3**	**(9.4)**	**3**	**(4.7)**	**4**	**(6.5)**	**10**	**(6.3)**
Nervous system disorders	**1**	**(3.1)**	**6**	**(9.4)**	**4**	**(6.5)**	**11**	**(7.0)**
Psychiatric disorders	**0**		**6**	**(9.4)**	**5**	**(8.1)**	**11**	**(7.0)**
Insomnia	0		4	(6.3)	4	(6.5)	8	(5.1)
Renal and urinary disorders	**3**	**(9.4)**	**1**	**(1.6)**	**1**	**(1.6)**	**5**	**(3.2)**
Nephrolithiasis	2	(6.3)	0		0		2	(1.3)
Reproductive system and breast disorders	**5**	**(15.6)**	**2**	**(3.1)**	**3**	**(4.8)**	**10**	**(6.3)**
Benign prostatic hyperplasia	2	(6.3)	1	(1.6)	1	(1.6)	4	(2.5)

日本人被験者：被験者の既往歴
（1 投与群以上で発現率 > 5%）
（無作為割付けされた全被験者）
ベース試験

	Placebo		MK-3222 100 mg		MK-3222 200 mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Respiratory, thoracic and mediastinal disorders	**4**	**(12.5)**	**10**	**(15.6)**	**12**	**(19.4)**	**26**	**(16.5)**
Asthma	2	(6.3)	1	(1.6)	6	(9.7)	9	(5.7)
Rhinitis allergic	2	(6.3)	7	(10.9)	3	(4.8)	12	(7.6)
Skin and subcutaneous tissue disorders	**32**	**(100.0)**	**64**	**(100.0)**	**62**	**(100.0)**	**158**	**(100.0)**
Psoriasis	32	(100.0)	64	(100.0)	62	(100.0)	158	(100.0)
Vascular disorders	**11**	**(34.4)**	**15**	**(23.4)**	**22**	**(35.5)**	**48**	**(30.4)**
Hypertension	11	(34.4)	15	(23.4)	20	(32.3)	46	(29.1)

Every subject is counted a single time for each applicable specific condition. A subject with multiple conditions within a system organ class is counted a single time for that system organ class.

A system organ class or specific condition appears on this report only if its incidence meets the criterion in the report title, after rounding.

[Source: p010: Page 678 - 680]

付録 2.7.4-64
日本人被験者：特定の併用薬を使用した被験者
（1 投与群以上で発現率 > 5%）
（無作為割付けされた全被験者）
ベース試験

	Placebo		MK-3222 100 mg		MK-3222 200 mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	32		64		62		158	
With one or more concomitant medications	31	(96.9)	56	(87.5)	60	(96.8)	147	(93.0)
With no concomitant medications	1	(3.1)	8	(12.5)	2	(3.2)	11	(7.0)
alimentary tract and metabolism								
antidiarrheals, intestinal antiinflammatory/antiinfective agents	**3**	**(9.4)**	**2**	**(3.1)**	**2**	**(3.2)**	**7**	**(4.4)**
albumin tannate	2	(6.3)	0		0		2	(1.3)
drugs for acid related disorders	**9**	**(28.1)**	**14**	**(21.9)**	**23**	**(37.1)**	**46**	**(29.1)**
rebamipide	2	(6.3)	11	(17.2)	17	(27.4)	30	(19.0)
sodium gualenate	2	(6.3)	2	(3.1)	0		4	(2.5)
teprenone	2	(6.3)	1	(1.6)	1	(1.6)	4	(2.5)
drugs for functional gastrointestinal disorders	**4**	**(12.5)**	**1**	**(1.6)**	**7**	**(11.3)**	**12**	**(7.6)**

日本人被験者：特定の併用薬を服用した被験者
（1 投与群以上で発現率 > 5%）
（無作為割付けされた全被験者）
ベース試験

	Placebo		MK-3222 100 mg		MK-3222 200 mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
butylscopolamine bromide	2	(6.3)	0		1	(1.6)	3	(1.9)
domperidone	2	(6.3)	0		1	(1.6)	3	(1.9)
drugs used in diabetes	**1**	**(3.1)**	**3**	**(4.7)**	**6**	**(9.7)**	**10**	**(6.3)**
vitamins	**3**	**(9.4)**	**4**	**(6.3)**	**5**	**(8.1)**	**12**	**(7.6)**
antiinfectives for systemic use								
antibacterials for systemic use	**8**	**(25.0)**	**15**	**(23.4)**	**23**	**(37.1)**	**46**	**(29.1)**
cefcapene pivoxil hydrochloride	5	(15.6)	7	(10.9)	4	(6.5)	16	(10.1)
cefditoren pivoxil	2	(6.3)	2	(3.1)	2	(3.2)	6	(3.8)
clarithromycin	3	(9.4)	3	(4.7)	7	(11.3)	13	(8.2)
gentamicin sulfate	4	(12.5)	0		2	(3.2)	6	(3.8)
levofloxacin	0		4	(6.3)	7	(11.3)	11	(7.0)

日本人被験者：特定の併用薬を服用した被験者
（1 投与群以上で発現率 > 5%）
（無作為割付けされた全被験者）
ベース試験

	Placebo		MK-3222 100 mg		MK-3222 200 mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
antimycobacterials	**2**	**(6.3)**	**4**	**(6.3)**	**1**	**(1.6)**	**7**	**(4.4)**
antivirals for systemic use	3	(9.4)	**2**	**(3.1)**	4	**(6.5)**	9	**(5.7)**
vaccines	**4**	**(12.5)**	**5**	**(7.8)**	**9**	**(14.5)**	**18**	**(11.4)**
influenza virus split virion 3v vaccine inactivated	1	(3.1)	2	(3.1)	4	(6.5)	7	(4.4)
influenza virus vaccine (unspecified)	2	(6.3)	3	(4.7)	5	(8.1)	10	(6.3)
blood and blood forming organs								
antianemic preparations	**2**	**(6.3)**	**1**	**(1.6)**	3	(4.8)	**6**	**(3.8)**
mecobalamin	2	(6.3)	1	(1.6)	2	(3.2)	5	(3.2)
antihemorrhagics	**4**	**(12.5)**	**3**	**(4.7)**	**5**	**(8.1)**	**12**	**(7.6)**
tranexamic acid	3	(9.4)	3	(4.7)	5	(8.1)	11	(7.0)
blood substitutes and perfusion solutions	**2**	**(6.3)**	**1**	**(1.6)**	**1**	**(1.6)**	**4**	**(2.5)**

日本人被験者：特定の併用薬を服用した被験者
（1 投与群以上で発現率 > 5%）
（無作為割付けされた全被験者）
ベース試験

	Placebo		MK-3222 100 mg		MK-3222 200 mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
cardiovascular system								
agents acting on the renin-angiotensin system	**6**	**(18.8)**	**9**	**(14.1)**	**12**	**(19.4)**	**27**	**(17.1)**
telmisartan	0		2	(3.1)	4	(6.5)	6	(3.8)
beta blocking agents	**3**	**(9.4)**	**1**	**(1.6)**	**3**	**(4.8)**	**7**	**(4.4)**
bisoprolol fumarate	2	(6.3)	0		0		2	(1.3)
calcium channel blockers	**9**	**(28.1)**	**8**	**(12.5)**	**15**	**(24.2)**	**32**	**(20.3)**
amlodipine	2	(6.3)	5	(7.8)	6	(9.7)	13	(8.2)
amlodipine besylate	5	(15.6)	2	(3.1)	5	(8.1)	12	(7.6)
cardiac therapy	**3**	**(9.4)**	**0**		**3**	**(4.8)**	**6**	**(3.8)**
lipid modifying agents	**4**	**(12.5)**	**7**	**(10.9)**	**8**	**(12.9)**	**19**	**(12.0)**
rosuvastatin calcium	1	(3.1)	1	(1.6)	4	(6.5)	6	(3.8)

日本人被験者：特定の併用薬を服用した被験者
（1 投与群以上で発現率 > 5%）
（無作為割付けされた全被験者）
ベース試験

	Placebo		MK-3222 100 mg		MK-3222 200 mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
dermatologicals								
antibiotics and chemotherapeutics for dermatological use	**1**	**(3.1)**	**4**	**(6.3)**	**3**	**(4.8)**	**8**	**(5.1)**
antifungals for dermatological use	**3**	**(9.4)**	**5**	**(7.8)**	**7**	**(11.3)**	**15**	**(9.5)**
luliconazole	2	(6.3)	3	(4.7)	5	(8.1)	10	(6.3)
antipruritics, incl. antihistamines, anesthetics, etc.	**0**		**1**	**(1.6)**	**4**	**(6.5)**	**5**	**(3.2)**
antiseptics and disinfectants	**7**	**(21.9)**	**7**	**(10.9)**	**4**	**(6.5)**	**18**	**(11.4)**
guaiazulene	2	(6.3)	1	(1.6)	0		3	(1.9)
zinc oxide	2	(6.3)	3	(4.7)	1	(1.6)	6	(3.8)
corticosteroids, dermatological preparations	**3**	**(9.4)**	**4**	**(6.3)**	**4**	**(6.5)**	**11**	**(7.0)**
emollients and protectives	**17**	**(53.1)**	**30**	**(46.9)**	**28**	**(45.2)**	**75**	**(47.5)**
petrolatum, white	17	(53.1)	30	(46.9)	28	(45.2)	75	(47.5)

日本人被験者：特定の併用薬を服用した被験者
（1 投与群以上で発現率 > 5%）
（無作為割付けされた全被験者）
ベース試験

	Placebo		MK-3222 100 mg		MK-3222 200 mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
genitourinary system and sex hormones								
urologicals	**3**	**(9.4)**	**0**		**2**	**(3.2)**	**5**	**(3.2)**
silodosin	2	(6.3)	0		1	(1.6)	3	(1.9)
musculoskeletal system								
antigout preparations	**2**	**(6.3)**	**3**	**(4.7)**	**5**	**(8.1)**	**10**	**(6.3)**
allopurinol	2	(6.3)	0		1	(1.6)	3	(1.9)
antiinflammatory and antirheumatic products	**19**	**(59.4)**	**34**	**(53.1)**	**44**	**(71.0)**	**97**	**(61.4)**
diclofenac sodium	1	(3.1)	1	(1.6)	5	(8.1)	7	(4.4)
ketoprofen	2	(6.3)	1	(1.6)	3	(4.8)	6	(3.8)
loxoprofen	0		2	(3.1)	4	(6.5)	6	(3.8)
loxoprofen sodium	5	(15.6)	13	(20.3)	20	(32.3)	38	(24.1)

日本人被験者：特定の併用薬を服用した被験者
（1 投与群以上で発現率 > 5%）
（無作為割付けされた全被験者）
ベース試験

	Placebo		MK-3222 100 mg		MK-3222 200 mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
mucopolysaccharide polysulfate	15	(46.9)	22	(34.4)	25	(40.3)	62	(39.2)
other drugs for disorders of musculo-skeletal system	**4**	**(12.5)**	**2**	**(3.1)**	**5**	**(8.1)**	**11**	**(7.0)**
hyaluronate sodium	2	(6.3)	0		2	(3.2)	4	(2.5)
pronase	2	(6.3)	2	(3.1)	3	(4.8)	7	(4.4)
topical products for joint and muscular pain	**0**		**3**	**(4.7)**	**5**	**(8.1)**	**8**	**(5.1)**
nervous system								
analgesics	**10**	**(31.3)**	**26**	**(40.6)**	**17**	**(27.4)**	**53**	**(33.5)**
acetaminophen	6	(18.8)	6	(9.4)	5	(8.1)	17	(10.8)
acetaminophen (+) caffeine (+) promethazine methylenedisalicylate (+) salicylamide	4	(12.5)	12	(18.8)	4	(6.5)	20	(12.7)
aspirin	3	(9.4)	6	(9.4)	6	(9.7)	15	(9.5)
anesthetics	**7**	**(21.9)**	**1**	**(1.6)**	**6**	**(9.7)**	**14**	**(8.9)**

日本人被験者：特定の併用薬を服用した被験者
（1 投与群以上で発現率 > 5%）
（無作為割付けされた全被験者）
ベース試験

	Placebo		MK-3222 100 mg		MK-3222 200 mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
lidocaine	3	(9.4)	0		2	(3.2)	5	(3.2)
lidocaine hydrochloride	4	(12.5)	1	(1.6)	3	(4.8)	8	(5.1)
psychoanaleptics	**2**	**(6.3)**	**3**	**(4.7)**	**1**	**(1.6)**	**6**	**(3.8)**
psycholeptics	**0**		**4**	**(6.3)**	**8**	**(12.9)**	**12**	**(7.6)**
respiratory system								
antihistamines for systemic use	**13**	**(40.6)**	**30**	**(46.9)**	**31**	**(50.0)**	**74**	**(46.8)**
bepotastine besylate	1	(3.1)	6	(9.4)	5	(8.1)	12	(7.6)
bepotastine besylate (+) menthol	1	(3.1)	2	(3.1)	4	(6.5)	7	(4.4)
epinastine hydrochloride	3	(9.4)	5	(7.8)	3	(4.8)	11	(7.0)
fexofenadine hydrochloride	9	(28.1)	8	(12.5)	12	(19.4)	29	(18.4)
levocetirizine dihydrochloride	1	(3.1)	6	(9.4)	6	(9.7)	13	(8.2)

日本人被験者：特定の併用薬を服用した被験者
（1 投与群以上で発現率 > 5%）
（無作為割付けされた全被験者）
ベース試験

	Placebo		MK-3222 100 mg		MK-3222 200 mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
cough and cold preparations	**6**	**(18.8)**	**13**	**(20.3)**	**12**	**(19.4)**	**31**	**(19.6)**
carbocysteine	4	(12.5)	7	(10.9)	8	(12.9)	19	(12.0)
dextromethorphan hydrobromide	2	(6.3)	2	(3.1)	1	(1.6)	5	(3.2)
drugs for obstructive airway diseases	**6**	**(18.8)**	**7**	**(10.9)**	**8**	**(12.9)**	**21**	**(13.3)**
fluticasone propionate	2	(6.3)	0		1	(1.6)	3	(1.9)
montelukast sodium	2	(6.3)	2	(3.1)	3	(4.8)	7	(4.4)
nasal preparations	**2**	**(6.3)**	**5**	**(7.8)**	**6**	**(9.7)**	**13**	**(8.2)**
sensory organs								
ophthalmologicals	**10**	**(31.3)**	**9**	**(14.1)**	**14**	**(22.6)**	**33**	**(20.9)**
olopatadine hydrochloride	10	(31.3)	8	(12.5)	9	(14.5)	27	(17.1)
systemic hormonal preparations, excl. sex hormones and insulins								

日本人被験者：特定の併用薬を服用した被験者
（1 投与群以上で発現率 > 5%）
（無作為割付けされた全被験者）
ベース試験

	Placebo		MK-3222 100 mg		MK-3222 200 mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
lidocaine	3	(9.4)	0		2	(3.2)	5	(3.2)
lidocaine hydrochloride	4	(12.5)	1	(1.6)	3	(4.8)	8	(5.1)
psychoanaleptics	**2**	**(6.3)**	**3**	**(4.7)**	**1**	**(1.6)**	**6**	**(3.8)**
psycholeptics	**0**		**4**	**(6.3)**	**8**	**(12.9)**	**12**	**(7.6)**
respiratory system								
antihistamines for systemic use	**13**	**(40.6)**	**30**	**(46.9)**	**31**	**(50.0)**	**74**	**(46.8)**
bepotastine besylate	1	(3.1)	6	(9.4)	5	(8.1)	12	(7.6)
bepotastine besylate (+) menthol	1	(3.1)	2	(3.1)	4	(6.5)	7	(4.4)
epinastine hydrochloride	3	(9.4)	5	(7.8)	3	(4.8)	11	(7.0)
fexofenadine hydrochloride	9	(28.1)	8	(12.5)	12	(19.4)	29	(18.4)
levocetirizine dihydrochloride	1	(3.1)	6	(9.4)	6	(9.7)	13	(8.2)

日本人被験者：特定の併用薬を服用した被験者
（1 投与群以上で発現率 > 5%）
（無作為割付けされた全被験者）
ベース試験

	Placebo		MK-3222 100 mg		MK-3222 200 mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
corticosteroids for systemic use	**2**	**(6.3)**	**4**	**(6.3)**	**6**	**(9.7)**	**12**	**(7.6)**
betamethasone butyrate propionate	1	(3.1)	4	(6.3)	1	(1.6)	6	(3.8)
various								
all other therapeutic products	**2**	**(6.3)**	**9**	**(14.1)**	**6**	**(9.7)**	**17**	**(10.8)**

Every subject is counted a single time for each applicable specific prior medication. A subject with multiple prior medication within a medication category is counted a single time for that category.

A medication class or specific medication appears on this report only if its incidence meets the criterion in the report title, after rounding.

[Source: p010: Page 732 – 741]

付録 2.7.4-65
日本人被験者：治験治療下で発現した有害事象（TEAE）の要約（降順）

Protocol No. P06306

	SCH 900222 (10 mg/kg IV) Japanese Part 2 n=6		All Japanese Part 1 n=22		All Caucasian n=19		All Chinese n=12		Total n=59	
SUBJECTS REPORTING ANY ADVERSE EVENT	5	(83)	17	(77)	17	(89)	11	(92)	50	(85)
HEADACHE	2	(33)	5	(23)	5	(26)	2	(17)	14	(24)
UPPER RESPIRATORY TRACT INFECTION	1	(17)	3	(14)	7	(37)	0		11	(19)
INJECTION SITE HAEMATOMA	0		4	(18)	3	(16)	2	(17)	9	(15)
CONTUSION	3	(50)	3	(14)	2	(11)	0		8	(14)
INJECTION SITE PAIN	0		2	(9)	3	(16)	2	(17)	7	(12)
DYSMENORRHOEA	1	(17)	1	(5)	3	(16)	1	(8)	6	(10)
MYALGIA	1	(17)	2	(9)	2	(11)	1	(8)	6	(10)
DIARRHOEA	0		2	(9)	3	(16)	0		5	(8)
INJECTION SITE ERYTHEMA	0		3	(14)	0		2	(17)	5	(8)
NAUSEA	0		2	(9)	3	(16)	0		5	(8)
DIZZINESS	0		1	(5)	3	(16)	0		4	(7)
OROPHARYNGEAL PAIN	0		1	(5)	0		3	(25)	4	(7)
ABDOMINAL PAIN	1	(17)	2	(9)	0		0		3	(5)
MIGRAINE	0		0		3	(16)	0		3	(5)
RASH	0		1	(5)	1	(5)	1	(8)	3	(5)
VOMITING	0		0		3	(16)	0		3	(5)
BACK PAIN	0		1	(5)	1	(5)	0		2	(3)
COUGH	0		1	(5)	1	(5)	0		2	(3)

日本人被験者：
日本人被験者：試験治療下で発現した有害事象（TEAE）の要約（降順）

Protocol No. P06306

	SCH 900222 (10 mg/kg IV) Japanese Part 2 n=6		All Japanese Part 1 n=22		All Caucasian n=19		All Chinese n=12		Total n=59	
HYPOAESTHESIA	0		1	(5)	1	(5)	0		2	(3)
INFUSION SITE THROMBOSIS	1	(17)	0		1	(5)	0		2	(3)
INJECTION SITE REACTION	0		0		1	(5)	1	(8)	2	(3)
NEUTROPENIA	1	(17)	0		1	(5)	0		2	(3)
ABDOMINAL PAIN UPPER	0		0		1	(5)	0		1	(2)
ALANINE AMINOTRANSFERASE INCREASED	0		1	(5)	0		0		1	(2)
APPENDICITIS	0		0		1	(5)	0		1	(2)
ARTHROPOD BITE	0		0		1	(5)	0		1	(2)
BLOOD TRIGLYCERIDES INCREASED	0		1	(5)	0		0		1	(2)
BODY TEMPERATURE INCREASED	1	(17)	0		0		0		1	(2)
CATHETER SITE HAEMATOMA	0		0		0		1	(8)	1	(2)
CATHETER SITE PAIN	1	(17)	0		0		0		1	(2)
COLD SWEAT	0		0		1	(5)	0		1	(2)
DEPRESSION	0		0		1	(5)	0		1	(2)
DISTURBANCE IN ATTENTION	0		0		1	(5)	0		1	(2)
DYSPEPSIA	0		1	(5)	0		0		1	(2)
ENTEROBIASIS	0		0		1	(5)	0		1	(2)
EOSINOPHIL COUNT INCREASED	0		1	(5)	0		0		1	(2)
EPISTAXIS	0		0		0		1	(8)	1	(2)

日本人被験者：
日本人被験者：試験治療下で発現した有害事象（TEAE）の要約（降順）

Protocol No. P06306

	SCH 900222 (10 mg/kg IV) Japanese Part 2 n=6		All Japanese Part 1 n=22		All Caucasian n=19		All Chinese n=12		Total n=59	
ERYTHEMA	0		0		1	(5)	0		1	(2)
EXCORIATION	0		0		1	(5)	0		1	(2)
FACE INJURY	0		0		1	(5)	0		1	(2)
GINGIVAL BLEEDING	0		0		0		1	(8)	1	(2)
HAEMATOMA	0		1	(5)	0		0		1	(2)
HYPERHIDROSIS	0		0		0		1	(8)	1	(2)
JOINT STIFFNESS	0		1	(5)	0		0		1	(2)
LACERATION	0		1	(5)	0		0		1	(2)
LETHARGY	0		0		1	(5)	0		1	(2)
MUSCULOSKELETAL CHEST PAIN	0		0		0		1	(8)	1	(2)
NASAL CONGESTION	0		1	(5)	0		0		1	(2)
NASOPHARYNGITIS	0		0		1	(5)	0		1	(2)
NECK PAIN	0		0		1	(5)	0		1	(2)
PAIN IN EXTREMITY	0		1	(5)	0		0		1	(2)
PARAESTHESIA	0		0		1	(5)	0		1	(2)
PLATELET COUNT DECREASED	0		0		0		1	(8)	1	(2)
POLLAKIURIA	0		1	(5)	0		0		1	(2)
PRESYNCOPE	0		0		1	(5)	0		1	(2)
PRURITUS	0		1	(5)	0		0		1	(2)

日本人被験者：
日本人被験者：試験治療下で発現した有害事象（TEAE）の要約（降順）

Protocol No. P06306

	SCH 900222 (10 mg/kg IV) Japanese Part 2 n=6		All Japanese Part 1 n=22		All Caucasian n=19		All Chinese n=12		Total n=59	
RASH ERYTHEMATOUS	0		1	(5)	0		0		1	(2)
RASH MACULO-PAPULAR	0		1	(5)	0		0		1	(2)
RASH PRURITIC	0		1	(5)	0		0		1	(2)
SCRATCH	0		1	(5)	0		0		1	(2)
SEASONAL ALLERGY	0		1	(5)	0		0		1	(2)
SINUSITIS	0		0		1	(5)	0		1	(2)
SKIN IRRITATION	0		0		1	(5)	0		1	(2)
SOMNOLENCE	0		0		0		1	(8)	1	(2)
SUICIDAL IDEATION	0		1	(5)	0		0		1	(2)
SWELLING FACE	0		0		1	(5)	0		1	(2)
SYNCOPE	0		0		1	(5)	0		1	(2)
THROAT IRRITATION	1	(17)	0		0		0		1	(2)
TOOTHACHE	0		0		1	(5)	0		1	(2)
URINARY TRACT INFECTION	0		0		1	(5)	0		1	(2)
VENOMOUS STING	0		1	(5)	0		0		1	(2)
VESSEL PUNCTURE SITE HAEMATOMA	0		0		0		1	(8)	1	(2)

[Source: p007: Section 12.2.2 Table 16]

付録 2.7.4-66
日本人被験者：治験薬との因果関係を否定できない
試験治療下で発現した有害事象（TEAE）の要約（降順）

Protocol No. P06306

	SCH 900222 (10 mg/kg IV) Japanese Part 2 n=6		All Japanese Part 1 n=22		All Caucasian n=19		All Chinese n=12		Total n=59	
SUBJECTS REPORTING ANY ADVERSE EVENT	0		9	(41)	10	(53)	5	(42)	24	(41)
INJECTION SITE HAEMATOMA	0		4	(18)	3	(16)	2	(17)	9	(15)
INJECTION SITE PAIN	0		2	(9)	2	(11)	2	(17)	6	(10)
INJECTION SITE ERYTHEMA	0		3	(14)	0		2	(17)	5	(8)
HEADACHE	0		2	(9)	1	(5)	0		3	(5)
NAUSEA	0		0		3	(16)	0		3	(5)
INJECTION SITE REACTION	0		0		1	(5)	1	(8)	2	(3)
MYALGIA	0		0		2	(11)	0		2	(3)
ABDOMINAL PAIN	0		1	(5)	0		0		1	(2)
COLD SWEAT	0		0		1	(5)	0		1	(2)
DISTURBANCE IN ATTENTION	0		0		1	(5)	0		1	(2)
DIZZINESS	0		0		1	(5)	0		1	(2)
LETHARGY	0		0		1	(5)	0		1	(2)
NECK PAIN	0		0		1	(5)	0		1	(2)

[Source: p007: Section 12.2.2 Table 17]

付録 2.7.4-67
日本人被験者：有害事象の要約
（1 回以上投与された被験者）
Part 1

	Placebo		MK-3222 100 mg		MK-3222 200 mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population[†]	32		64		62		158	
with one or more adverse events	17	(53.1)	31	(48.4)	23	(37.1)	71	(44.9)
with no adverse events	15	(46.9)	33	(51.6)	39	(62.9)	87	(55.1)
with drug-related[‡] adverse events	5	(15.6)	7	(10.9)	6	(9.7)	18	(11.4)
with serious adverse events	0		1	(1.6)	2	(3.2)	3	(1.9)
with serious drug-related[‡] adverse events	0		0		1	(1.6)	1	(0.6)
who died	0		0		0		0	
discontinued[§] due to an adverse event	0		0		1	(1.6)	1	(0.6)
discontinued[§] due to a drug-related[‡] adverse event	0		0		0		0	
discontinued[§] due to a serious adverse event	0		0		1	(1.6)	1	(0.6)
discontinued[§] due to a serious drug-related[‡] adverse event	0		0		0		0	

[†]Subjects who took at least one dose of Part 1 study medication based on the treatment actually received.
[‡]Determined by the investigator to be related to the drug.
[§]Study medication withdrawn.

[Source: p010: Table 14.3.2-6]

付録 2.7.4-68
日本人被験者：有害事象の要約
（1 回以上投与された被験者）
Part 2

	MK-3222 100 mg‖		MK-3222 200 mg‖		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population†	77		74		151	
with one or more adverse events	32	(41.6)	28	(37.8)	60	(39.7)
with no adverse events	45	(58.4)	46	(62.2)	91	(60.3)
with drug-related‡ adverse events	6	(7.8)	12	(16.2)	18	(11.9)
with serious adverse events	0		1	(1.4)	1	(0.7)
with serious drug-related‡ adverse events	0		0		0	
who died	0		0		0	
discontinued§ due to an adverse event	0		0		0	
discontinued§ due to a drug-related‡ adverse event	0		0		0	
discontinued§ due to a serious adverse event	0		0		0	
discontinued§ due to a serious drug-related‡ adverse event	0		0		0	

†Subjects who took at least one dose of Part 2 study medication based on the treatment actually received.
‡Determined by the investigator to be related to the drug.
§Study medication withdrawn.
‖Includes placebo subjects re-randomized at Week 12 to receive either MK-3222 100 mg or MK-3222 200 mg.

[Source: p010: Table 14.3.2-7]

付録 2.7.4-69
日本人被験者：有害事象の要約
（1 回以上投与された被験者）
Part 3

	MK-3222 100 mg		MK-3222 200 mg		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population†	65		80		145	
with one or more adverse events††	47	(72.3)	54	(67.5)	101	(69.7)
with no adverse events	18	(27.7)	26	(32.5)	44	(30.3)
with drug-related‡ adverse events	12	(18.5)	15	(18.8)	27	(18.6)
with serious adverse events	1	(1.5)	1	(1.3)	2	(1.4)
with serious drug-related‡ adverse events	0		0		0	
who died	0		0		0	
discontinued§ due to an adverse event	2	(3.1)	0		2	(1.4)
discontinued§ due to a drug-related‡ adverse event	1	(1.5)	0		1	(0.7)
discontinued§ due to a serious adverse event	0		0		0	
discontinued§ due to a serious drug-related‡ adverse event	0		0		0	

†Subjects who took at least one dose of Part 3 study medication based on the treatment actually received. Includes subjects re-randomized to placebo.
‡Determined by the investigator to be related to the drug.
§Study medication withdrawn.
††12 (63.2%) out of 19 subjects who were randomized to MK-3222 100 mg in Part 1 and re-randomized to placebo in Part 3 had an adverse event while they took placebo.
11 (52.4%) out of 21 subjects who were randomized to MK-3222 200 mg in Part 1 and re-randomized to placebo in Part 3 had an adverse event while they took placebo.

[Source: p010: Table 14.3.2-10]

付録 2.7.4-70
日本人被験者：特に注目すべき有害事象を発現した被験者
（1 投与群以上で発現率 ≥ 5%）
（1 回以上投与された被験者）
Part 1

	Placebo		MK-3222 100 mg		MK-3222 200 mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population[1]	32		64		62		158	
With one or more specific adverse events	17	(53.1)	31	(48.4)	23	(37.1)	71	(44.9)
With no specific adverse events	15	(46.9)	33	(51.6)	39	(62.9)	87	(55.1)
General disorders and administration site conditions	**2**	**(6.3)**	**1**	**(1.6)**	**2**	**(3.2)**	**5**	**(3.2)**
Infections and infestations	**4**	**(12.5)**	**16**	**(25.0)**	**14**	**(22.6)**	**34**	**(21.5)**
Nasopharyngitis	1	(3.1)	13	(20.3)	6	(9.7)	20	(12.7)
Investigations	**0**		**5**	**(7.8)**	**0**		**5**	**(3.2)**
Musculoskeletal and connective tissue disorders	**2**	**(6.3)**	**4**	**(6.3)**	**4**	**(6.5)**	**10**	**(6.3)**
Arthralgia	2	(6.3)	1	(1.6)	0		3	(1.9)
Renal and urinary disorders	**2**	**(6.3)**	**1**	**(1.6)**	**0**		**3**	**(1.9)**
Hypertonic bladder	2	(6.3)	0		0		2	(1.3)
Skin and subcutaneous tissue disorders	**12**	**(37.5)**	**4**	**(6.3)**	**3**	**(4.8)**	**19**	**(12.0)**
Pruritus	4	(12.5)	4	(6.3)	0		8	(5.1)
Psoriasis	7	(21.9)	1	(1.6)	0		8	(5.1)

[1] Subjects who took at least one dose of Part 1 study medication based on the treatment actually received.
Subjects are counted only once in the overall category. The same subject may appear in different categories.
A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns is greater than or equal to the percent incidence specified in the report title, after rounding.
MedDRA Version: Merck T2-MedDRA.

[Source: p010: Table 14.3.2-15]

付録 2.7.4-71
日本人被験者：特に注目すべき有害事象を発現した被験者
（1 投与群以上で発現率 ≥ 5%）
（1 回以上投与された被験者）
Part 2

	MK-3222 100 mg[2]		MK-3222 200 mg[2]		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population[1]	77		74		151	
With one or more specific adverse events	32	(41.6)	28	(37.8)	60	(39.7)
With no specific adverse events	45	(58.4)	46	(62.2)	91	(60.3)
Gastrointestinal disorders	**4**	**(5.2)**	**2**	**(2.7)**	**6**	**(4.0)**
Infections and infestations	**11**	**(14.3)**	**12**	**(16.2)**	**23**	**(15.2)**
Nasopharyngitis	7	(9.1)	6	(8.1)	13	(8.6)
Injury, poisoning and procedural complications	**4**	**(5.2)**	**4**	**(5.4)**	**8**	**(5.3)**
Musculoskeletal and connective tissue disorders	**2**	**(2.6)**	**7**	**(9.5)**	**9**	**(6.0)**
Skin and subcutaneous tissue disorders	**8**	**(10.4)**	**6**	**(8.1)**	**14**	**(9.3)**

[1]Subjects who took at least one dose of Part 2 study medication based on the treatment actually received.
[2]Includes placebo subjects re-randomized at Week 12 to receive either MK-3222 200 mg or MK-3222 100 mg.
Subjects are counted only once in the overall category. The same subject may appear in different categories.
A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns is greater than or equal to the percent incidence specified in the report title, after rounding.
MedDRA Version: Merck T2-MedDRA.

[Source: p010: Table 14.3.2-17]

付録 2.7.4-72
日本人被験者：特に注目すべき有害事象を発現した被験者
（1 投与群以上で発現率 ≥ 5%）
（1 回以上投与された被験者）
Part 3

	MK-3222 100 mg		MK-3222 200 mg		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population[†]	65		80		145	
With one or more specific adverse events	47	(72.3)	54	(67.5)	101	(69.7)
With no specific adverse events	18	(27.7)	26	(32.5)	44	(30.3)
Gastrointestinal disorders	**4**	**(6.2)**	**4**	**(5.0)**	**8**	**(5.5)**
Infections and infestations	**28**	**(43.1)**	**31**	**(38.8)**	**59**	**(40.7)**
Influenza	1	(1.5)	4	(5.0)	5	(3.4)
Nasopharyngitis	19	(29.2)	19	(23.8)	38	(26.2)
Injury, poisoning and procedural complications	**4**	**(6.2)**	**5**	**(6.3)**	**9**	**(6.2)**
Musculoskeletal and connective tissue disorders	**7**	**(10.8)**	**11**	**(13.8)**	**18**	**(12.4)**
Respiratory, thoracic and mediastinal disorders	**5**	**(7.7)**	**2**	**(2.5)**	**7**	**(4.8)**
Skin and subcutaneous tissue disorders	**17**	**(26.2)**	**20**	**(25.0)**	**37**	**(25.5)**
Eczema	4	(6.2)	3	(3.8)	7	(4.8)

	MK-3222 100 mg n (%)	MK-3222 200 mg n (%)	Total n (%)
Pruritus	0	5 (6.3)	5 (3.4)
Psoriasis	5 (7.7)	6 (7.5)	11 (7.6)

[†]Subjects who took at least one dose of Part 3 study medication based on the treatment actually received. Includes subjects re-randomized to placebo.

12 (63.2%) out of 19 subjects who were randomized to MK-3222 100 mg in Part 1 and re-randomized to placebo in Part 3 had an adverse event while they took placebo.

11 (52.4%) out of 21 subjects who were randomized to MK-3222 200 mg in Part 1 and re-randomized to placebo in Part 3 had an adverse event while they took placebo.

Subjects are counted only once in the overall category. The same subject may appear in different categories.

A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns is greater than or equal to the percent incidence specified in the report title, afterrounding.

MedDRA Version: Merck T 2-MedDRA.

[Source: p010: Table 14.3.2-23]

付録 2.7.4-73
日本人被験者：治験薬との因果関係を否定できない有害事象発現被験者
（1 回以上投与された被験者）
Part 1

	Placebo		MK-3222 100 mg		MK-3222 200 mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population[1]	32		64		62		158	
With one or more drug-related adverse events	5	(15.6)	7	(10.9)	6	(9.7)	18	(11.4)
With no drug-related adverse events	27	(84.4)	57	(89.1)	56	(90.3)	140	(88.6)
Cardiac disorders	**1**	**(3.1)**	**0**		**0**		**1**	**(0.6)**
Palpitations	1	(3.1)	0		0		1	(0.6)
General disorders and administration site conditions	**1**	**(3.1)**	**1**	**(1.6)**	**1**	**(1.6)**	**3**	**(1.9)**
Malaise	0		1	(1.6)	0		1	(0.6)
Pyrexia	1	(3.1)	0		1	(1.6)	2	(1.3)
Infections and infestations	**2**	**(6.3)**	**2**	**(3.1)**	**5**	**(8.1)**	**9**	**(5.7)**
Bronchitis	0		1	(1.6)	0		1	(0.6)
Epiglottitis	0		0		1	(1.6)	1	(0.6)
Folliculitis	0		0		1	(1.6)	1	(0.6)
Influenza	1	(3.1)	0		0		1	(0.6)
Nasopharyngitis	0		2	(3.1)	1	(1.6)	3	(1.9)
Oral herpes	0		0		1	(1.6)	1	(0.6)
Sinusitis	1	(3.1)	0		0		1	(0.6)
Skin candida	0		0		1	(1.6)	1	(0.6)

日本人被験者：治験薬との因果関係を否定できない有害事象発現被験者
（実際に投薬を受けた被験者）
Part 1

	Placebo		MK-3222 100 mg		MK-3222 200 mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Investigations	**0**		**4**	**(6.3)**	**0**		**4**	**(2.5)**
Alanine aminotransferase increased	0		2	(3.1)	0		2	(1.3)
Aspartate aminotransferase increased	0		1	(1.6)	0		1	(0.6)
Blood triglycerides increased	0		1	(1.6)	0		1	(0.6)
Blood urine present	0		1	(1.6)	0		1	(0.6)
Gamma-glutamyltransferase increased	0		1	(1.6)	0		1	(0.6)
Musculoskeletal and connective tissue disorders	**1**	**(3.1)**	**1**	**(1.6)**	**0**		**2**	**(1.3)**
Arthralgia	1	(3.1)	0		0		1	(0.6)
Psoriatic arthropathy	0		1	(1.6)	0		1	(0.6)
Nervous system disorders	**1**	**(3.1)**	**0**		**0**		**1**	**(0.6)**
Paraesthesia	1	(3.1)	0		0		1	(0.6)
Renal and urinary disorders	**0**		**1**	**(1.6)**	**0**		**1**	**(0.6)**
Proteinuria	0		1	(1.6)	0		1	(0.6)
Skin and subcutaneous tissue disorders	**1**	**(3.1)**	**0**		**1**	**(1.6)**	**2**	**(1.3)**
Psoriasis	1	(3.1)	0		0		1	(0.6)
Urticaria	0		0		1	(1.6)	1	(0.6)

[1]Subjects who took at least one dose of Part 1 study medication based on the treatment actually received.
Subjects are counted only once in the overall category. The same subject may appear in different categories.
MedDRA Version: Merck T2-MedDRA.

[Source: p010: Table 14.3.2-33]

付録 2.7.4-74
日本人被験者：治験薬との因果関係を否定できない有害事象発現被験者
（1 回以上投与された被験者）
Part 2

	MK-3222 100 mg[1]		MK-3222 200 mg[1]		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population[1]	77		74		151	
With one or more drug-related adverse events	6	(7.8)	12	(16.2)	18	(11.9)
With no drug-related adverse events	71	(92.2)	62	(83.8)	133	(88.1)
Cardiac disorders	**0**		**1**	**(1.4)**	**1**	**(0.7)**
Ventricular extrasystoles	0		1	(1.4)	1	(0.7)
Eye disorders	**0**		**1**	**(1.4)**	**1**	**(0.7)**
Conjunctivitis allergic	0		1	(1.4)	1	(0.7)
Gastrointestinal disorders	**1**	**(1.3)**	**1**	**(1.4)**	**2**	**(1.3)**
Abdominal pain	1	(1.3)	0		1	(0.7)
Diarrhoea	0		1	(1.4)	1	(0.7)
General disorders and administration site conditions	**0**		**2**	**(2.7)**	**2**	**(1.3)**
Fatigue	0		1	(1.4)	1	(0.7)
Injection site reaction	0		1	(1.4)	1	(0.7)
Hepatobiliary disorders	**1**	**(1.3)**	**0**		**1**	**(0.7)**
Hepatic function abnormal	1	(1.3)	0		1	(0.7)
Infections and infestations	**2**	**(2.6)**	**4**	**(5.4)**	**6**	**(4.0)**

日本人被験者：治験薬との因果関係を否定できない有害事象発現被験者
（実際に投薬を受けた被験者）
Part 2

	MK-3222 100 mg		MK-3222 200 mg		Total	
	n	(%)	n	(%)	n	(%)
Nasopharyngitis	0		2	(2.7)	2	(1.3)
Oral herpes	1	(1.3)	0		1	(0.7)
Paronychia	0		1	(1.4)	1	(0.7)
Pharyngitis	1	(1.3)	0		1	(0.7)
Tinea pedis	0		1	(1.4)	1	(0.7)
Investigations	**0**		**1**	**(1.4)**	**1**	**(0.7)**
Blood urine present	0		1	(1.4)	1	(0.7)
Protein urine	0		1	(1.4)	1	(0.7)
Metabolism and nutrition disorders	**0**		**2**	**(2.7)**	**2**	**(1.3)**
Diabetes mellitus	0		1	(1.4)	1	(0.7)
Hyperlipidaemia	0		1	(1.4)	1	(0.7)
Musculoskeletal and connective tissue disorders	**0**		**1**	**(1.4)**	**1**	**(0.7)**
Psoriatic arthropathy	0		1	(1.4)	1	(0.7)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**1**	**(1.3)**	**0**		**1**	**(0.7)**
Gastrointestinal submucosal tumour	1	(1.3)	0		1	(0.7)
Respiratory, thoracic and mediastinal disorders	**1**	**(1.3)**	**0**		**1**	**(0.7)**
Oropharyngeal pain	1	(1.3)	0		1	(0.7)

日本人被験者：治験薬との因果関係を否定できない有害事象発現被験者
（実際に投薬を受けた被験者）
Part 2

	MK-3222 100 mg†		MK-3222 200 mg‡		Total	
	n	(%)	n	(%)	n	(%)
Skin and subcutaneous tissue disorders	**1**	**(1.3)**	**2**	**(2.7)**	**3**	**(2.0)**
Dermal cyst	1	(1.3)	0		1	(0.7)
Prurigo	0		1	(1.4)	1	(0.7)
Psoriasis	0		1	(1.4)	1	(0.7)
Vascular disorders	**0**		**1**	**(1.4)**	**1**	**(0.7)**
Hypertension	0		1	(1.4)	1	(0.7)

†Subjects who took at least one dose of Part 2 study medication based on the treatment actually received.
‡Includes placebo subjects re-randomized at Week 12 to receive either MK-3222 200 mg or MK-3222 100 mg.
Subjects are counted only once in the overall category. The same subject may appear in different categories.
MedDRA Version: Merck T2-MedDRA.

[Source: p010: Table 14.3.2-34]

付録 2.7.4-75
日本人被験者：治験薬との因果関係を否定できない有害事象発現被験者
（1 回以上投与された被験者）
Part 3

	MK-3222 100 mg		MK-3222 200 mg		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population[†]	65		80		145	
With one or more drug-related adverse events	12	(18.5)	15	(18.8)	27	(18.6)
With no drug-related adverse events	53	(81.5)	65	(81.3)	118	(81.4)
Gastrointestinal disorders	**0**		**1**	**(1.3)**	**1**	**(0.7)**
Dental caries	0		1	(1.3)	1	(0.7)
General disorders and administration site conditions	**0**		**1**	**(1.3)**	**1**	**(0.7)**
Injection site erythema	0		1	(1.3)	1	(0.7)
Infections and infestations	**5**	**(7.7)**	**11**	**(13.8)**	**16**	**(11.0)**
Cellulitis	0		1	(1.3)	1	(0.7)
Conjunctivitis	0		1	(1.3)	1	(0.7)
Folliculitis	1	(1.5)	0		1	(0.7)
Gastroenteritis	0		1	(1.3)	1	(0.7)
Influenza	0		2	(2.5)	2	(1.4)
Mumps	0		1	(1.3)	1	(0.7)
Nasopharyngitis	2	(3.1)	6	(7.5)	8	(5.5)
Oral herpes	1	(1.5)	0		1	(0.7)
Otitis media	1	(1.5)	0		1	(0.7)
Pharyngitis	0		1	(1.3)	1	(0.7)
Tinea versicolour	0		1	(1.3)	1	(0.7)
Injury, poisoning and procedural complications	**0**		**1**	**(1.3)**	**1**	**(0.7)**
Skin injury	0		1	(1.3)	1	(0.7)
Renal and urinary disorders	**1**	**(1.5)**	**0**		**1**	**(0.7)**
Ureterolithiasis	1	(1.5)	0		1	(0.7)
Respiratory, thoracic and mediastinal disorders	**1**	**(1.5)**	**0**		**1**	**(0.7)**

日本人被験者：治験薬との因果関係を否定できない有害事象発現被験者
（実際に投薬を受けた被験者）
Part 3

	MK-3222 100 mg		MK-3222 200 mg		Total	
	n	(%)	n	(%)	n	(%)
Oropharyngeal pain	1	(1.5)	0		1	(0.7)
Skin and subcutaneous tissue disorders	**6**	**(9.2)**	**6**	**(7.5)**	**12**	**(8.3)**
Eczema	0		1	(1.3)	1	(0.7)
Erythema	0		1	(1.3)	1	(0.7)
Onychoclasis	1	(1.5)	0		1	(0.7)
Pruritus	0		2	(2.5)	2	(1.4)
Psoriasis	4	(6.2)	4	(5.0)	8	(5.5)
Urticaria	1	(1.5)	0		1	(0.7)

[1] Subjects who took at least one dose of Part 3 study medication based on the treatment actually received. Includes subjects re-randomized to placebo.

5 (26.3%) out of 19 subjects who were randomized to MK-3222 100 mg in Part 1 and re-randomized to placebo in Part 3 had an adverse event while they took placebo.

4 (19%) out of 21 subjects who were randomized to MK-3222 200 mg in Part 1 and re-randomized to placebo in Part 3 had an adverse event while they took placebo.

Subjects are counted only once in the overall category. The same subject may appear in different categories.

MedDRA Version: Merck T2-MedDRA.

[Source: p010: Table 14.3.2-37]

付録 2.7.4-76
日本人被験者：治験薬との因果関係を否定できない重篤な有害事象発現被験者
（1 回以上投与された被験者）
Part 1

	Placebo		MK-3222 100 mg		MK-3222 200 mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population[†]	32		64		62		158	
With one or more serious drug-related adverse events	0		0		1	(1.6)	1	(0.6)
With no serious drug-related adverse events	32	(100.0)	64	(100.0)	61	(98.4)	157	(99.4)
Infections and infestations	**0**		**0**		**1**	**(1.6)**	**1**	**(0.6)**
Epiglottitis	0		0		1	(1.6)	1	(0.6)

[†]Subjects who took at least one dose of Part 1 study medication based on the treatment actually received.
Subjects are counted only once in the overall category. The same subject may appear in different categories.
MedDRA Version: Merck T2-MedDRA.

[Source: p010: Table 14.3.2-43]

付録 2.7.4-77
日本人被験者：重篤な有害事象発現被験者
（1 回以上投与された被験者）
Part 2

	MK-3222 100 mg‡		MK-3222 200 mg‡		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population†	77		74		151	
With one or more serious adverse events	0		1	(1.4)	1	(0.7)
With no serious adverse events	77	(100.0)	73	(98.6)	150	(99.3)
Nervous system disorders	**0**		**1**	**(1.4)**	**1**	**(0.7)**
Lacunar infarction	0		1	(1.4)	1	(0.7)

†Subjects who took at least one dose of Part 2 study medication based on the treatment actually received.
‡Includes placebo subjects re-randomized at Week 12 to receive either MK-3222 200 mg or MK-3222 100 mg.
Subjects are counted only once in the overall category. The same subject may appear in different categories.
MedDRA Version: Merck T2-MedDRA.

[Source: p010: Table 14.3.2-44]

付録 2.7.4-78
日本人被験者：重篤な有害事象発現被験者
（1 回以上投与された被験者）
Part 3

	MK-3222 100 mg		MK-3222 200 mg		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population[†]	65		80		145	
With one or more serious adverse events	1	(1.5)	1	(1.3)	2	(1.4)
With no serious adverse events	64	(98.5)	79	(98.8)	143	(98.6)
Eye disorders	**0**		**1**	**(1.3)**	**1**	**(0.7)**
Cataract	0		1	(1.3)	1	(0.7)
Macular fibrosis	0		1	(1.3)	1	(0.7)
Respiratory, thoracic and mediastinal disorders	**1**	**(1.5)**	**0**		**1**	**(0.7)**
Sleep apnoea syndrome	1	(1.5)	0		1	(0.7)

[†]Subjects who took at least one dose of Part 3 study medication based on the treatment actually received. Includes subjects re-randomized to placebo.

0 out of 19 subjects who were randomized to MK-3222 100 mg in Part 1 and re-randomized to placebo in Part 3 had an adverse event while they took placebo.

0 out of 21 subjects who were randomized to MK-3222 200 mg in Part 1 and re-randomized to placebo in Part 3 had an adverse event while they took placebo.

Subjects are counted only once in the overall category. The same subject may appear in different categories.

MedDRA Version: Merck T2-MedDRA.

[Source: p010: Table 14.3.2-50]

付録 2.7.4-79
日本人被験者：治験薬との因果関係を否定できない有害事象を発現し，投与中止に至った被験者
（1 回以上投与された被験者）
Part 1

	Placebo n (%)	MK-3222 100 mg n (%)	MK-3222 200 mg n (%)	Total n (%)
Subjects in population[†]	32	64	62	158
With one or more drug-related adverse events resulting in discontinuation of study medication	0	0	0	0
With no drug-related adverse events resulting in discontinuation of study medication	32 (	64 (100	62 (100.0)	158 (100.0)

[†]Subjects who took at least one dose of Part 1 study medication based on the treatment actually received.
Subjects are counted only once in the overall category. The same subject may appear in different categories.
MedDRA Version: Merck T2-MedDRA.

[Source: p010: Table 14.3.2-61]

付録 2.7.4-80
日本人被験者：治験薬との因果関係を否定できない有害事象を発現し，投与中止に至った被験者
（1 回以上投与された被験者）
Part 2

	MK-3222 100 mg‡ n	(%)	MK-3222 200 mg‡ n	(%)	Total n	(%)
Subjects in population†	77		74		151	
With one or more drug-related adverse events resulting in discontinuation of study medication	0		0		0	
With no drug-related adverse events resulting in discontinuation of study medication	77	(100.0)	74	(100.0)	151	(100.0)

†Subjects who took at least one dose of Part 2 study medication based on the treatment actually received.
‡Includes placebo subjects re-randomized at Week 12 to receive either MK-3222 200 mg or MK-3222 100 mg.
Subjects are counted only once in the overall category. The same subject may appear in different categories.
MedDRA Version: Merck T2-MedDRA.

[Source: p010: Table 14.3.2-64]

付録 2.7.4-81
日本人被験者：治験薬との因果関係を否定できない有害事象を発現し，投与中止に至った被験者
（1 回以上投与された被験者）
Part 3

	MK-3222 100 mg		MK-3222 200 mg		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population[†]	65		80		145	
With one or more adverse events resulting in discontinuation of study medication	2	(3.1)	0		2	(1.4)
With no adverse events resulting in discontinuation of study medication	63	(96.9)	80	(100.0)	143	(98.6)
Musculoskeletal and connective tissue disorders	**1**	**(1.5)**	**0**		**1**	**(0.7)**
Arthritis	1	(1.5)	0		1	(0.7)
Skin and subcutaneous tissue disorders	**1**	**(1.5)**	**0**		**1**	**(0.7)**
Psoriasis	1	(1.5)	0		1	(0.7)

[†]Subjects who took at least one dose of Part 3 study medication based on the treatment actually received. Includes subjects re-randomized to placebo.
0 out of 19 subjects who were randomized to MK-3222 100 mg in Part 1 and re-randomized to placebo in Part 3 had an adverse event while they took placebo.
0 out of 21 subjects who were randomized to MK-3222 200 mg in Part 1 and re-randomized to placebo in Part 3 had an adverse event while they took placebo.
Subjects are counted only once in the overall category. The same subject may appear in different categories.
MedDRA Version: Merck T2-MedDRA.

[Source: p010: Table 14.3.2-68]

付録 2.7.4-82
日本人被験者：ADA を発現した被験者で認められた特に注目すべき有害事象
（1 回以上投与された被験者）
ベース試験：曝露期間で調整済み

	Placebo†			MK-3222 100 mg‡			MK-3222 200 mg‡		
	n	M§	Expo. Adj.‖	n	M§	Expo. Adj.‖	n	M§	Expo. Adj.‖
Subjects in population††	10	156		11	568		12	792	
With one or more adverse events	2		(66.9)	8		(73.5)	10		(65.9)
With no adverse events	8		(267.6)	3		(27.6)	2		(13.2)
Gastrointestinal disorders	**0**			**1**		**(9.2)**	**1**		**(6.6)**
Chronic gastritis	0			1		(9.2)	0		
Dental caries	0			0			1		(6.6)
Gastrooesophageal reflux disease	0			1		(9.2)	0		
Hiatus hernia	0			1		(9.2)	0		
Infections and infestations	**1**		**(33.4)**	**5**		**(45.9)**	**6**		**(39.5)**
Cellulitis	0			0			1		(6.6)
Nasopharyngitis	0			5		(45.9)	5		(32.9)
Otitis media	1		(33.4)	0			0		
Tinea pedis	0			0			1		(6.6)
Injury, poisoning and procedural complications	**0**			**0**			**2**		**(13.2)**

日本人被験者：ADA を発現した被験者で認められた
特に注目すべき有害事象
（1 回以上投与された被験者）
ベース試験：曝露期間で調整済み

	Placebo†			MK-3222 100 mg‡			MK-3222 200 mg‡		
	n	M§	Expo. Adj.‖	n	M§	Expo. Adj.‖	n	M§	Expo. Adj.‖
Contusion	0			0			1		(6.6)
Skin injury	0			0			1		(6.6)
Investigations	**0**			**1**		**(9.2)**	**0**		
Alanine aminotransferase increased	0			1		(9.2)	0		
Aspartate aminotransferase increased	0			1		(9.2)	0		
Musculoskeletal and connective tissue disorders	**0**			**1**		**(9.2)**	**2**		**(13.2)**
Arthritis	0			1		(9.2)	0		
Back pain	0			0			1		(6.6)
Spinal osteoarthritis	0			0			1		(6.6)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**0**			**1**		**(9.2)**	**1**		**(6.6)**
Acrochordon	0			0			1		(6.6)
Seborrhoeic keratosis	0			1		(9.2)	0		
Nervous system disorders	**0**			**1**		**(9.2)**	**1**		**(6.6)**
Headache	0			1		(9.2)	1		(6.6)
Psychiatric disorders	**0**			**0**			**1**		**(6.6)**

日本人被験者：ADA を発現した被験者で認められた
特に注目すべき有害事象
（1 回以上投与された被験者）
ベース試験：曝露期間で調整済み

	Placebo†			MK-3222 100 mg‡			MK-3222 200 mg‡		
	n	M§	Expo. Adj.‖	n	M§	Expo. Adj.‖	n	M§	Expo. Adj.‖
Insomnia	0			0			1		(6.6)
Respiratory, thoracic and mediastinal disorders	**0**			**2**		**(18.4)**	**0**		
Cough	0			1		(9.2)	0		
Nasal congestion	0			1		(9.2)	0		
Skin and subcutaneous tissue disorders	**1**		**(33.4)**	**4**		**(36.7)**	**6**		**(39.5)**
Dermatitis contact	0			1		(9.2)	2		(13.2)
Hyperkeratosis	0			1		(9.2)	0		
Miliaria	0			0			1		(6.6)
Pruritus	0			0			1		(6.6)
Psoriasis	1		(33.4)	1		(9.2)	2		(13.2)
Solar dermatitis	0			1		(9.2)	0		
Urticaria	0			0			1		(6.6)
Vascular disorders	**0**			**0**			**1**		**(6.6)**
Hypertension	0			0			1		(6.6)

†Includes placebo subjects who took at least one dose of placebo in Part 1 or during placebo period in Part 3.
‡Includes subjects who received MK-3222 100 mg or MK-3222 200 mg anytime during the study.
§M = person-time (person-weeks) exposure to treatment (start of treatment to end of treatment).
‖Exposure adjustment is calculated as (52.17857143 weeks * n/M)*100.
††Subjects with anti-drug antibodies and who took at least one dose of Part 1 study medication based on the treatment actually received. Subjects are counted only once in the overall category. The same subject may appear in different categories. Events were counted in each treatment group based on the treatment the subject actually received when the event occurred.
MedDRA Version: Merck T2-MedDRA.

[Source: p010: Table 14.3.2-105]

付録 2.7.4-83
Subjects With Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Applicati				SUR				Cumulati			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	621		616		574		586		620		616	
with one or more adverse events	399	(64.3)	398	(64.6)	328	(57.1)	352	(60.1)	474	(76.5)	480	(77.9)
with no adverse events	222	(35.7)	218	(35.4)	246	(42.9)	234	(39.9)	146	(23.5)	136	(22.1)
Blood and lymphatic system disorders	8	(1.3)	7	(1.1)	7	(1.2)	7	(1.2)	15	(2.4)	14	(2.3)
Anaemia	2	(0.3)	2	(0.3)	2	(0.3)	3	(0.5)	6	(1.0)	5	(0.8)
Bone marrow oedema	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Eosinophilia	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Haemorrhagic anaemia	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)
Hypochromic anaemia	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Iron deficiency anaemia	2	(0.3)	1	(0.2)	1	(0.2)	0	(0.0)	2	(0.3)	1	(0.2)
Leukopenia	2	(0.3)	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)	0	(0.0)
Lymphadenopathy	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Lymphadenopathy mediastinal	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Lymphopenia	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Pernicious anaemia	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)
Polycythaemia	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Splenic cyst	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Splenomegaly	1	(0.2)	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)
Thrombocytopenia	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Cardiac disorders	14	(2.3)	10	(1.6)	13	(2.3)	20	(3.4)	26	(4.2)	25	(4.1)
Acute myocardial infarction	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.3)	0	(0.0)	4	(0.6)
Angina pectoris	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)	1	(0.2)
Aortic valve calcification	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)

Subjects With Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Applicatio				SUR				Cumulativ			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Cardiac disorders	14	(2.3)	10	(1.6)	13	(2.3)	20	(3.4)	26	(4.2)	25	(4.1)
Arteriosclerosis coronary artery	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Atrial fibrillation	2	(0.3)	2	(0.3)	2	(0.3)	2	(0.3)	4	(0.6)	3	(0.5)
Atrioventricular block	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Atrioventricular block first degree	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)
Atrioventricular block second degree	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Bundle branch block left	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Bundle branch block right	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)	0	(0.0)
Congestive cardiomyopathy	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Coronary artery disease	0	(0.0)	0	(0.0)	2	(0.3)	3	(0.5)	2	(0.3)	3	(0.5)
Coronary artery stenosis	0	(0.0)	0	(0.0)	0	(0.0)	3	(0.5)	0	(0.0)	3	(0.5)
Extrasystoles	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)	1	(0.2)
Left atrial dilatation	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Mitral valve calcification	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Mitral valve incompetence	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)
Myocardial infarction	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Myocardial ischaemia	2	(0.3)	0	(0.0)	0	(0.0)	2	(0.3)	1	(0.2)	2	(0.3)
Palpitations	2	(0.3)	1	(0.2)	0	(0.0)	2	(0.3)	2	(0.3)	2	(0.3)
Sinus arrhythmia	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.3)
Sinus bradycardia	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Sinus tachycardia	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Supraventricular tachycardia	0	(0.0)	1	(0.2)	2	(0.3)	0	(0.0)	2	(0.3)	1	(0.2)
Tachycardia	3	(0.5)	0	(0.0)	2	(0.3)	1	(0.2)	4	(0.6)	1	(0.2)
Tricuspid valve incompetence	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Ventricular dysfunction	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)

Subjects With Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Cardiac disorders	14	(2.3)	10	(1.6)	13	(2.3)	20	(3.4)	26	(4.2)	25	(4.1)
Ventricular extrasystoles	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)	0	(0.0)	4	(0.6)
Ventricular tachycardia	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Congenital, familial and genetic disorders	1	(0.2)	0	(0.0)	1	(0.2)	1	(0.2)	3	(0.5)	2	(0.3)
Atrial septal defect	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Hypertrophic cardiomyopathy	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Keratosis follicular	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Phimosis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Thalassaemia alpha	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Ear and labyrinth disorders	10	(1.6)	6	(1.0)	4	(0.7)	5	(0.9)	12	(1.9)	11	(1.8)
Cerumen impaction	1	(0.2)	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)
Deafness	0	(0.0)	2	(0.3)	0	(0.0)	1	(0.2)	0	(0.0)	3	(0.5)
Ear discomfort	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)
Ear haemorrhage	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Ear pain	4	(0.6)	0	(0.0)	2	(0.3)	1	(0.2)	5	(0.8)	2	(0.3)
Ear pruritus	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Meniere's disease	2	(0.3)	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)	0	(0.0)
Sudden hearing loss	0	(0.0)	2	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Tinnitus	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.3)
Tympanic membrane perforation	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Vertigo	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)

Subjects With Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Endocrine disorders	3	(0.5)	3	(0.5)	1	(0.2)	4	(0.7)	3	(0.5)	6	(1.0)
Androgen deficiency	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Hyperthyroidism	1	(0.2)	1	(0.2)	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)
Hypothyroidism	1	(0.2)	2	(0.3)	1	(0.2)	1	(0.2)	2	(0.3)	3	(0.5)
Inappropriate antidiuretic hormone secretion	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Thyroid mass	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Thyrotoxic crisis	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Eye disorders	8	(1.3)	13	(2.1)	4	(0.7)	11	(1.9)	16	(2.6)	21	(3.4)
Amaurosis fugax	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Blepharitis	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)
Blepharochalasis	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Cataract	0	(0.0)	3	(0.5)	0	(0.0)	2	(0.3)	1	(0.2)	4	(0.6)
Cataract nuclear	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Chalazion	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Conjunctivitis allergic	0	(0.0)	2	(0.3)	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)
Corneal disorder	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Corneal erosion	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Diabetic eye disease	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Diabetic retinopathy	1	(0.2)	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)
Dry eye	1	(0.2)	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)
Eye allergy	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Eye haemorrhage	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Eye inflammation	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Giant papillary conjunctivitis	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)

Subjects With Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Eye disorders	8	(1.3)	13	(2.1)	4	(0.7)	11	(1.9)	16	(2.6)	21	(3.4)
Glaucoma	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Hypermetropia	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Keratitis	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Macular fibrosis	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)
Meibomian gland dysfunction	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Myopia	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Photopsia	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Pterygium	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Retinal detachment	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Retinal haemorrhage	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Vision blurred	2	(0.3)	0	(0.0)	0	(0.0)	1	(0.2)	2	(0.3)	1	(0.2)
Visual impairment	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Vitreous detachment	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Gastrointestinal disorders	59	(9.5)	64	(10.4)	48	(8.4)	67	(11.4)	95	(15.3)	104	(16.9)
Abdominal discomfort	1	(0.2)	1	(0.2)	1	(0.2)	2	(0.3)	2	(0.3)	2	(0.3)
Abdominal distension	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Abdominal hernia	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Abdominal pain	4	(0.6)	5	(0.8)	0	(0.0)	4	(0.7)	5	(0.8)	9	(1.5)
Abdominal pain lower	1	(0.2)	1	(0.2)	0	(0.0)	2	(0.3)	1	(0.2)	2	(0.3)
Abdominal pain upper	4	(0.6)	6	(1.0)	4	(0.7)	5	(0.9)	6	(1.0)	9	(1.5)
Abdominal tenderness	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Acquired oesophageal web	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Anal fissure	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)

Subjects With Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Gastrointestinal disorders	59	(9.5)	64	(10.4)	48	(8.4)	67	(11.4)	95	(15.3)	104	(16.9)
Anal pruritus	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Anorectal discomfort	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Aphthous ulcer	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Barrett's oesophagus	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)
Cheilitis	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Colitis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Colitis ischaemic	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Constipation	6	(1.0)	1	(0.2)	5	(0.9)	1	(0.2)	10	(1.6)	3	(0.5)
Crohn's disease	0	(0.0)	1	(0.2)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Dental caries	3	(0.5)	4	(0.6)	1	(0.2)	0	(0.0)	6	(1.0)	4	(0.6)
Dental necrosis	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Diarrhoea	16	(2.6)	9	(1.5)	11	(1.9)	10	(1.7)	26	(4.2)	18	(2.9)
Diverticulum	2	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)
Diverticulum intestinal	3	(0.5)	0	(0.0)	1	(0.2)	1	(0.2)	3	(0.5)	1	(0.2)
Duodenal polyp	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Dyspepsia	3	(0.5)	2	(0.3)	2	(0.3)	2	(0.3)	4	(0.6)	4	(0.6)
Dysphagia	2	(0.3)	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)	0	(0.0)
Enterocolitis	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)
Food poisoning	1	(0.2)	1	(0.2)	2	(0.3)	2	(0.3)	2	(0.3)	3	(0.5)
Gastric polyps	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)
Gastric ulcer	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)
Gastritis	1	(0.2)	6	(1.0)	0	(0.0)	3	(0.5)	4	(0.6)	8	(1.3)
Gastritis erosive	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Gastrointestinal angiodysplasia	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)

Subjects With Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Gastrointestinal disorders	59	(9.5)	64	(10.4)	48	(8.4)	67	(11.4)	95	(15.3)	104	(16.9)
Gastrointestinal disorder	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Gastrointestinal haemorrhage	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Gastrointestinal inflammation	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Gastrooesophageal reflux disease	3	(0.5)	6	(1.0)	0	(0.0)	5	(0.9)	4	(0.6)	11	(1.8)
Gingival pain	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Haematochezia	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)
Haemorrhoids	2	(0.3)	0	(0.0)	1	(0.2)	3	(0.5)	3	(0.5)	4	(0.6)
Haemorrhoids thrombosed	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Hiatus hernia	1	(0.2)	1	(0.2)	0	(0.0)	1	(0.2)	2	(0.3)	1	(0.2)
Hyperchlorhydria	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Hypoaesthesia oral	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Inguinal hernia	2	(0.3)	2	(0.3)	0	(0.0)	4	(0.7)	2	(0.3)	4	(0.6)
Intestinal mucosal atrophy	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Intestinal polyp	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Irritable bowel syndrome	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Large intestine polyp	1	(0.2)	1	(0.2)	1	(0.2)	2	(0.3)	1	(0.2)	4	(0.6)
Lip blister	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Loose tooth	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Malocclusion	1	(0.2)	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)
Melaena	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Mesenteric artery thrombosis	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Mouth ulceration	0	(0.0)	2	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Nausea	3	(0.5)	7	(1.1)	3	(0.5)	4	(0.7)	6	(1.0)	8	(1.3)
Oesophageal ulcer	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)

Subjects With Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Gastrointestinal disorders	59	(9.5)	64	(10.4)	48	(8.4)	67	(11.4)	95	(15.3)	104	(16.9)
Oral pain	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.3)
Pancreatic steatosis	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Pancreatitis chronic	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Peptic ulcer	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Periodontal disease	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Portal hypertensive gastropathy	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Proctitis	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Rectal haemorrhage	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)	0	(0.0)
Reflux gastritis	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Salivary gland calculus	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Stomatitis	0	(0.0)	1	(0.2)	1	(0.2)	0	(0.0)	1	(0.2)	1	(0.2)
Tooth impacted	1	(0.2)	1	(0.2)	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)
Tooth loss	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Toothache	9	(1.4)	4	(0.6)	4	(0.7)	5	(0.9)	11	(1.8)	8	(1.3)
Umbilical hernia	1	(0.2)	1	(0.2)	3	(0.5)	0	(0.0)	3	(0.5)	1	(0.2)
Vomiting	1	(0.2)	7	(1.1)	1	(0.2)	7	(1.2)	2	(0.3)	10	(1.6)
General disorders and administration site conditions	36	(5.8)	31	(5.0)	20	(3.5)	27	(4.6)	47	(7.6)	48	(7.8)
Accidental death	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Application site pain	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Asthenia	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Chest discomfort	1	(0.2)	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)
Chest pain	1	(0.2)	3	(0.5)	0	(0.0)	0	(0.0)	1	(0.2)	2	(0.3)

Subjects With Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
General disorders and administration site conditions	36	(5.8)	31	(5.0)	20	(3.5)	27	(4.6)	47	(7.6)	48	(7.8)
Chills	2	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)
Cyst	4	(0.6)	0	(0.0)	0	(0.0)	0	(0.0)	4	(0.6)	0	(0.0)
Cyst rupture	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Death	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Fat necrosis	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Fatigue	4	(0.6)	5	(0.8)	1	(0.2)	3	(0.5)	4	(0.6)	7	(1.1)
Influenza like illness	7	(1.1)	4	(0.6)	2	(0.3)	2	(0.3)	7	(1.1)	5	(0.8)
Injection site bruising	3	(0.5)	0	(0.0)	2	(0.3)	1	(0.2)	3	(0.5)	1	(0.2)
Injection site discomfort	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Injection site erythema	0	(0.0)	2	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.3)
Injection site haematoma	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)
Injection site haemorrhage	3	(0.5)	0	(0.0)	0	(0.0)	0	(0.0)	3	(0.5)	0	(0.0)
Injection site laceration	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Injection site pain	2	(0.3)	1	(0.2)	1	(0.2)	3	(0.5)	3	(0.5)	4	(0.6)
Injection site pruritus	0	(0.0)	2	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.3)
Injection site reaction	0	(0.0)	1	(0.2)	1	(0.2)	0	(0.0)	2	(0.3)	1	(0.2)
Injection site swelling	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Malaise	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)
Mass	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Non-cardiac chest pain	3	(0.5)	0	(0.0)	3	(0.5)	3	(0.5)	6	(1.0)	5	(0.8)
Oedema peripheral	2	(0.3)	0	(0.0)	2	(0.3)	3	(0.5)	2	(0.3)	3	(0.5)
Peripheral swelling	4	(0.6)	3	(0.5)	4	(0.7)	3	(0.5)	5	(0.8)	4	(0.6)
Polyp	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)

Subjects With Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
General disorders and administration site conditions	36	(5.8)	31	(5.0)	20	(3.5)	27	(4.6)	47	(7.6)	48	(7.8)
Pyrexia	3	(0.5)	4	(0.6)	3	(0.5)	3	(0.5)	5	(0.8)	6	(1.0)
Vaccination site bruising	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Hepatobiliary disorders	7	(1.1)	4	(0.6)	7	(1.2)	8	(1.4)	14	(2.3)	13	(2.1)
Bile duct obstruction	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Cholecystitis	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Cholecystitis chronic	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Cholelithiasis	4	(0.6)	0	(0.0)	3	(0.5)	2	(0.3)	6	(1.0)	2	(0.3)
Gallbladder polyp	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Hepatic cirrhosis	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Hepatic fibrosis	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Hepatic steatosis	2	(0.3)	2	(0.3)	3	(0.5)	4	(0.7)	6	(1.0)	6	(1.0)
Hepatomegaly	1	(0.2)	1	(0.2)	1	(0.2)	1	(0.2)	2	(0.3)	2	(0.3)
Liver disorder	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Non-alcoholic steatohepatitis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Immune system disorders	7	(1.1)	6	(1.0)	2	(0.3)	8	(1.4)	8	(1.3)	9	(1.5)
Allergy to animal	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Allergy to arthropod bite	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Allergy to arthropod sting	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Drug hypersensitivity	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Food allergy	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Mite allergy	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)	0	(0.0)

Subjects With Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Immune system disorders	7	(1.1)	6	(1.0)	2	(0.3)	8	(1.4)	8	(1.3)	9	(1.5)
Seasonal allergy	4	(0.6)	5	(0.8)	1	(0.2)	5	(0.9)	5	(0.8)	6	(1.0)
Infections and infestations	260	(41.9)	265	(43.0)	178	(31.0)	199	(34.0)	327	(52.7)	330	(53.6)
Abdominal abscess	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)
Abscess jaw	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Abscess limb	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Acute sinusitis	1	(0.2)	2	(0.3)	0	(0.0)	0	(0.0)	2	(0.3)	4	(0.6)
Anal fungal infection	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Appendicitis	3	(0.5)	0	(0.0)	1	(0.2)	1	(0.2)	4	(0.6)	1	(0.2)
Arthritis infective	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)
Asymptomatic bacteriuria	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Bacterial infection	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Bacterial prostatitis	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Bacterial rhinitis	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Bacteriuria	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	1	(0.2)	2	(0.3)
Body tinea	2	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)
Bronchitis	14	(2.3)	19	(3.1)	7	(1.2)	10	(1.7)	24	(3.9)	26	(4.2)
Bronchitis bacterial	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Bronchitis viral	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Candida infection	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Cellulitis	2	(0.3)	3	(0.5)	4	(0.7)	1	(0.2)	7	(1.1)	4	(0.6)
Cellulitis of male external genital organ	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Chlamydial infection	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Chronic sinusitis	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	3	(0.5)

Subjects With Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Applicatio				SUR				Cumulativ			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Infections and infestations	260	(41.9)	265	(43.0)	178	(31.0)	199	(34.0)	327	(52.7)	330	(53.6)
Citrobacter infection	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Conjunctivitis	4	(0.6)	8	(1.3)	4	(0.7)	2	(0.3)	7	(1.1)	8	(1.3)
Corneal infection	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Cystitis	2	(0.3)	5	(0.8)	2	(0.3)	2	(0.3)	5	(0.8)	6	(1.0)
Dermatophytosis of nail	1	(0.2)	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)	1	(0.2)
Device related sepsis	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Diarrhoea infectious	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Diverticulitis	2	(0.3)	2	(0.3)	4	(0.7)	2	(0.3)	6	(1.0)	3	(0.5)
Ear infection	2	(0.3)	3	(0.5)	1	(0.2)	1	(0.2)	3	(0.5)	5	(0.8)
Erysipelas	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)	1	(0.2)
Eye infection	1	(0.2)	1	(0.2)	1	(0.2)	2	(0.3)	1	(0.2)	2	(0.3)
Folliculitis	0	(0.0)	5	(0.8)	0	(0.0)	2	(0.3)	0	(0.0)	6	(1.0)
Fungal infection	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Fungal skin infection	2	(0.3)	2	(0.3)	3	(0.5)	0	(0.0)	3	(0.5)	1	(0.2)
Furuncle	1	(0.2)	2	(0.3)	1	(0.2)	1	(0.2)	3	(0.5)	2	(0.3)
Gangrene	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Gastritis viral	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Gastroenteritis	13	(2.1)	16	(2.6)	9	(1.6)	10	(1.7)	23	(3.7)	24	(3.9)
Gastroenteritis bacterial	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Gastroenteritis viral	6	(1.0)	2	(0.3)	5	(0.9)	2	(0.3)	8	(1.3)	2	(0.3)
Gastrointestinal infection	5	(0.8)	5	(0.8)	3	(0.5)	2	(0.3)	7	(1.1)	7	(1.1)
Gastrointestinal viral infection	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Genital candidiasis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Gingivitis	3	(0.5)	1	(0.2)	2	(0.3)	1	(0.2)	7	(1.1)	2	(0.3)

Subjects With Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Infections and infestations	260	(41.9)	265	(43.0)	178	(31.0)	199	(34.0)	327	(52.7)	330	(53.6)
Groin abscess	2	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)
Haemorrhoid infection	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Helicobacter infection	2	(0.3)	2	(0.3)	2	(0.3)	2	(0.3)	4	(0.6)	3	(0.5)
Hepatitis E	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Herpes simplex	0	(0.0)	2	(0.3)	0	(0.0)	1	(0.2)	0	(0.0)	3	(0.5)
Herpes zoster	4	(0.6)	1	(0.2)	3	(0.5)	4	(0.7)	7	(1.1)	5	(0.8)
Hordeolum	2	(0.3)	2	(0.3)	1	(0.2)	1	(0.2)	2	(0.3)	2	(0.3)
Impetigo	0	(0.0)	2	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.3)
Infected bite	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Infection	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Infectious colitis	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Influenza	18	(2.9)	22	(3.6)	14	(2.4)	18	(3.1)	28	(4.5)	38	(6.2)
Laryngitis	0	(0.0)	2	(0.3)	1	(0.2)	0	(0.0)	1	(0.2)	2	(0.3)
Localised infection	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)
Lower respiratory tract infection	2	(0.3)	2	(0.3)	0	(0.0)	1	(0.2)	1	(0.2)	2	(0.3)
Lower respiratory tract infection viral	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Lymph gland infection	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Nail candida	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Nail infection	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Nasopharyngitis	8	(1.3)	4	(0.6)	5	(0.9)	8	(1.4)	15	(2.4)	11	(1.8)
Nematodiasis	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Oesophageal candidiasis	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Onychomycosis	0	(0.0)	5	(0.8)	0	(0.0)	0	(0.0)	0	(0.0)	5	(0.8)
Ophthalmic herpes simplex	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)

Subjects With Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Infections and infestations	260	(41.9)	265	(43.0)	178	(31.0)	199	(34.0)	327	(52.7)	330	(53.6)
Ophthalmic herpes zoster	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Oral bacterial infection	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Oral candidiasis	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)	0	(0.0)
Oral herpes	5	(0.8)	6	(1.0)	2	(0.3)	3	(0.5)	7	(1.1)	9	(1.5)
Oropharyngeal candidiasis	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Osteomyelitis	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Otitis externa	2	(0.3)	0	(0.0)	2	(0.3)	0	(0.0)	3	(0.5)	0	(0.0)
Otitis media	1	(0.2)	3	(0.5)	1	(0.2)	2	(0.3)	1	(0.2)	4	(0.6)
Otitis media acute	2	(0.3)	2	(0.3)	0	(0.0)	1	(0.2)	2	(0.3)	2	(0.3)
Parotitis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Periodontitis	2	(0.3)	1	(0.2)	1	(0.2)	1	(0.2)	2	(0.3)	1	(0.2)
Peritonitis	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Pertussis	0	(0.0)	2	(0.3)	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)
Pharyngitis	8	(1.3)	7	(1.1)	4	(0.7)	4	(0.7)	9	(1.5)	11	(1.8)
Pharyngitis streptococcal	3	(0.5)	1	(0.2)	3	(0.5)	2	(0.3)	4	(0.6)	3	(0.5)
Pneumonia	5	(0.8)	3	(0.5)	4	(0.7)	3	(0.5)	8	(1.3)	6	(1.0)
Pneumonia mycoplasmal	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Postoperative wound infection	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)
Pseudomonas infection	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Pulpitis dental	7	(1.1)	2	(0.3)	6	(1.0)	1	(0.2)	10	(1.6)	2	(0.3)
Pyelonephritis	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Pyoderma	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Rash pustular	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	1	(0.2)
Respiratory tract infection	1	(0.2)	1	(0.2)	0	(0.0)	1	(0.2)	2	(0.3)	2	(0.3)

Subjects With Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Infections and infestations	260	(41.9)	265	(43.0)	178	(31.0)	199	(34.0)	327	(52.7)	330	(53.6)
Rhinitis	6	(1.0)	7	(1.1)	5	(0.9)	8	(1.4)	8	(1.3)	10	(1.6)
Rhinovirus infection	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Root canal infection	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Scrotal abscess	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Sepsis	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Septic arthritis staphylococcal	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Sialoadenitis	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Sinusitis	16	(2.6)	14	(2.3)	11	(1.9)	10	(1.7)	23	(3.7)	16	(2.6)
Skin bacterial infection	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	2	(0.3)	1	(0.2)
Skin candida	0	(0.0)	2	(0.3)	1	(0.2)	0	(0.0)	1	(0.2)	2	(0.3)
Skin infection	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Soft tissue infection	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Staphylococcal infection	3	(0.5)	1	(0.2)	0	(0.0)	1	(0.2)	2	(0.3)	1	(0.2)
Subcutaneous abscess	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Tinea cruris	1	(0.2)	0	(0.0)	1	(0.2)	1	(0.2)	2	(0.3)	1	(0.2)
Tinea infection	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Tinea pedis	3	(0.5)	4	(0.6)	3	(0.5)	4	(0.7)	5	(0.8)	5	(0.8)
Tinea versicolour	1	(0.2)	2	(0.3)	0	(0.0)	2	(0.3)	1	(0.2)	2	(0.3)
Tonsillitis	1	(0.2)	4	(0.6)	2	(0.3)	1	(0.2)	3	(0.5)	4	(0.6)
Tooth abscess	9	(1.4)	6	(1.0)	1	(0.2)	2	(0.3)	9	(1.5)	8	(1.3)
Tooth infection	3	(0.5)	6	(1.0)	1	(0.2)	3	(0.5)	4	(0.6)	8	(1.3)
Tracheitis	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Upper respiratory tract infection	26	(4.2)	43	(7.0)	32	(5.6)	37	(6.3)	46	(7.4)	64	(10.4)
Upper respiratory tract infection bacterial	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)

Subjects With Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Infections and infestations	260	(41.9)	265	(43.0)	178	(31.0)	199	(34.0)	327	(52.7)	330	(53.6)
Urethritis	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)
Urinary tract infection	20	(3.2)	10	(1.6)	19	(3.3)	12	(2.0)	29	(4.7)	20	(3.2)
Urinary tract infection fungal	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Vaginal infection	0	(0.0)	2	(0.3)	1	(0.2)	1	(0.2)	1	(0.2)	2	(0.3)
Varicella	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Viraemia	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Viral infection	3	(0.5)	0	(0.0)	1	(0.2)	0	(0.0)	3	(0.5)	0	(0.0)
Viral pharyngitis	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Viral rhinitis	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Viral tonsillitis	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Viral upper respiratory tract infection	111	(17.9)	121	(19.6)	56	(9.8)	69	(11.8)	148	(23.9)	164	(26.6)
Vulvovaginal mycotic infection	3	(0.5)	1	(0.2)	3	(0.5)	1	(0.2)	4	(0.6)	1	(0.2)
Wound infection	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Injury, poisoning and procedural complications	63	(10.1)	49	(8.0)	42	(7.3)	50	(8.5)	87	(14.0)	85	(13.8)
Acetabulum fracture	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Alcohol poisoning	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Anaesthetic complication	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Anastomotic ulcer	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Animal bite	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Ankle fracture	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Arthropod bite	1	(0.2)	3	(0.5)	2	(0.3)	3	(0.5)	2	(0.3)	6	(1.0)
Arthropod sting	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)

Subjects With Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Injury, poisoning and procedural complications	63	(10.1)	49	(8.0)	42	(7.3)	50	(8.5)	87	(14.0)	85	(13.8)
Bone contusion	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)	2	(0.3)
Brain contusion	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Burns second degree	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Chest injury	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Clavicle fracture	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)	0	(0.0)
Contusion	7	(1.1)	5	(0.8)	3	(0.5)	1	(0.2)	11	(1.8)	8	(1.3)
Corneal abrasion	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Electric shock	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Epicondylitis	3	(0.5)	2	(0.3)	2	(0.3)	2	(0.3)	4	(0.6)	3	(0.5)
Eye burns	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Eye contusion	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Eye injury	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)	1	(0.2)
Facial bones fracture	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	1	(0.2)
Fall	0	(0.0)	2	(0.3)	2	(0.3)	0	(0.0)	2	(0.3)	2	(0.3)
Foot fracture	3	(0.5)	0	(0.0)	1	(0.2)	0	(0.0)	3	(0.5)	0	(0.0)
Foreign body in eye	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)	0	(0.0)
Fracture	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Hand fracture	2	(0.3)	2	(0.3)	1	(0.2)	2	(0.3)	4	(0.6)	3	(0.5)
Head injury	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Hip fracture	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Incisional hernia	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Joint dislocation	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)
Joint injury	2	(0.3)	1	(0.2)	3	(0.5)	2	(0.3)	4	(0.6)	2	(0.3)

Subjects With Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Injury, poisoning and procedural complications	63	(10.1)	49	(8.0)	42	(7.3)	50	(8.5)	87	(14.0)	85	(13.8)
Laceration	2	(0.3)	5	(0.8)	1	(0.2)	2	(0.3)	3	(0.5)	8	(1.3)
Ligament injury	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.3)
Ligament rupture	1	(0.2)	0	(0.0)	1	(0.2)	3	(0.5)	1	(0.2)	3	(0.5)
Ligament sprain	5	(0.8)	6	(1.0)	6	(1.0)	4	(0.7)	10	(1.6)	7	(1.1)
Limb injury	2	(0.3)	3	(0.5)	1	(0.2)	5	(0.9)	4	(0.6)	5	(0.8)
Lower limb fracture	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Meniscus injury	4	(0.6)	3	(0.5)	1	(0.2)	1	(0.2)	3	(0.5)	4	(0.6)
Muscle injury	1	(0.2)	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)
Muscle rupture	1	(0.2)	2	(0.3)	0	(0.0)	2	(0.3)	1	(0.2)	3	(0.5)
Muscle strain	3	(0.5)	5	(0.8)	0	(0.0)	4	(0.7)	2	(0.3)	7	(1.1)
Musculoskeletal injury	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Nerve injury	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Pelvic fracture	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Post-traumatic neck syndrome	1	(0.2)	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)	1	(0.2)
Post-traumatic pain	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Procedural haemorrhage	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Procedural pain	7	(1.1)	2	(0.3)	4	(0.7)	1	(0.2)	8	(1.3)	3	(0.5)
Pubis fracture	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Pulmonary contusion	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Radiation skin injury	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Radius fracture	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Rib fracture	1	(0.2)	1	(0.2)	0	(0.0)	1	(0.2)	2	(0.3)	2	(0.3)
Road traffic accident	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)

Subjects With Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Injury, poisoning and procedural complications	63	(10.1)	49	(8.0)	42	(7.3)	50	(8.5)	87	(14.0)	85	(13.8)
Scar	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Skin abrasion	3	(0.5)	0	(0.0)	0	(0.0)	0	(0.0)	3	(0.5)	0	(0.0)
Skin injury	0	(0.0)	2	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.3)
Skull fracture	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Soft tissue injury	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.3)
Sports injury	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Sunburn	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Superficial injury of eye	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Tendon injury	1	(0.2)	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)
Tendon rupture	2	(0.3)	1	(0.2)	3	(0.5)	1	(0.2)	3	(0.5)	1	(0.2)
Thermal burn	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)	0	(0.0)	3	(0.5)
Thoracic vertebral fracture	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Tooth fracture	4	(0.6)	1	(0.2)	0	(0.0)	3	(0.5)	4	(0.6)	3	(0.5)
Toxicity to various agents	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Venomous sting	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Wound	2	(0.3)	0	(0.0)	0	(0.0)	1	(0.2)	2	(0.3)	1	(0.2)
Wound dehiscence	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Wound secretion	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Wrist fracture	1	(0.2)	1	(0.2)	1	(0.2)	0	(0.0)	2	(0.3)	1	(0.2)
Investigations	23	(3.7)	22	(3.6)	13	(2.3)	22	(3.8)	37	(6.0)	41	(6.7)
Alanine aminotransferase increased	1	(0.2)	4	(0.6)	0	(0.0)	1	(0.2)	2	(0.3)	4	(0.6)
Arthroscopy	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

Subjects With Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Investigations	23	(3.7)	22	(3.6)	13	(2.3)	22	(3.8)	37	(6.0)	41	(6.7)
Aspartate aminotransferase increased	1	(0.2)	1	(0.2)	1	(0.2)	0	(0.0)	3	(0.5)	3	(0.5)
Bacterial test	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Bacterial test positive	0	(0.0)	0	(0.0)	0	(0.0)	3	(0.5)	0	(0.0)	3	(0.5)
Blood alkaline phosphatase increased	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Blood bilirubin increased	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Blood cholesterol increased	0	(0.0)	1	(0.2)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Blood glucose increased	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Blood iron increased	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Blood lactate dehydrogenase increased	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Blood potassium increased	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Blood pressure increased	1	(0.2)	2	(0.3)	0	(0.0)	0	(0.0)	1	(0.2)	2	(0.3)
Blood thyroid stimulating hormone decreased	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Blood thyroid stimulating hormone increased	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Blood triglycerides increased	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.3)	1	(0.2)	2	(0.3)
Blood urine present	2	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)
C-reactive protein increased	8	(1.3)	2	(0.3)	0	(0.0)	2	(0.3)	8	(1.3)	4	(0.6)
Electrocardiogram PR prolongation	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Electrocardiogram QT prolonged	1	(0.2)	1	(0.2)	2	(0.3)	1	(0.2)	3	(0.5)	1	(0.2)
Electrocardiogram abnormal	1	(0.2)	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Electrocardiogram repolarisation abnormality	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Fungal test positive	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Gamma-glutamyltransferase increased	3	(0.5)	2	(0.3)	2	(0.3)	2	(0.3)	6	(1.0)	4	(0.6)
Heart rate irregular	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Helicobacter test positive	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)

Subjects With Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Investigations	23	(3.7)	22	(3.6)	13	(2.3)	22	(3.8)	37	(6.0)	41	(6.7)
Intraocular pressure increased	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Lipase increased	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Liver function test increased	1	(0.2)	3	(0.5)	1	(0.2)	2	(0.3)	2	(0.3)	5	(0.8)
Neutrophil count increased	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Platelet count decreased	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)
Prostatic specific antigen increased	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)
Protein urine	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Protein urine present	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)	0	(0.0)
Transaminases increased	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Urinary sediment present	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)
Urine analysis abnormal	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Weight decreased	3	(0.5)	1	(0.2)	0	(0.0)	1	(0.2)	3	(0.5)	2	(0.3)
Weight increased	2	(0.3)	1	(0.2)	2	(0.3)	1	(0.2)	2	(0.3)	1	(0.2)
White blood cell count increased	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
White blood cells urine	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Metabolism and nutrition disorders	18	(2.9)	22	(3.6)	20	(3.5)	28	(4.8)	40	(6.5)	47	(7.6)
Decreased appetite	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Dehydration	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Diabetes mellitus	1	(0.2)	4	(0.6)	0	(0.0)	4	(0.7)	2	(0.3)	7	(1.1)
Diabetes mellitus inadequate control	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Electrolyte imbalance	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Fluid retention	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Folate deficiency	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)

Subjects With Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Metabolism and nutrition disorders	18	(2.9)	22	(3.6)	20	(3.5)	28	(4.8)	40	(6.5)	47	(7.6)
Glucose tolerance impaired	2	(0.3)	1	(0.2)	1	(0.2)	0	(0.0)	2	(0.3)	0	(0.0)
Gout	2	(0.3)	4	(0.6)	1	(0.2)	5	(0.9)	4	(0.6)	6	(1.0)
Histamine intolerance	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Hypercalcaemia	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)	1	(0.2)
Hypercholesterolaemia	1	(0.2)	4	(0.6)	3	(0.5)	4	(0.7)	4	(0.6)	8	(1.3)
Hyperglycaemia	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	2	(0.3)	2	(0.3)
Hyperkalaemia	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Hyperlipidaemia	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)	1	(0.2)	5	(0.8)
Hypertriglyceridaemia	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	1	(0.2)
Hyperuricaemia	1	(0.2)	0	(0.0)	2	(0.3)	2	(0.3)	2	(0.3)	2	(0.3)
Hypocalcaemia	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Hypoglycaemia	1	(0.2)	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)	1	(0.2)
Hypokalaemia	4	(0.6)	1	(0.2)	3	(0.5)	2	(0.3)	7	(1.1)	3	(0.5)
Hypomagnesaemia	1	(0.2)	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)
Hyponatraemia	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)	1	(0.2)
Lactose intolerance	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Malnutrition	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Obesity	2	(0.3)	1	(0.2)	1	(0.2)	1	(0.2)	3	(0.5)	2	(0.3)
Type 1 diabetes mellitus	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Type 2 diabetes mellitus	3	(0.5)	4	(0.6)	3	(0.5)	2	(0.3)	7	(1.1)	8	(1.3)
Vitamin D deficiency	4	(0.6)	2	(0.3)	4	(0.7)	1	(0.2)	7	(1.1)	3	(0.5)

Subjects With Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Musculoskeletal and connective tissue disorders	82	(13.2)	87	(14.1)	63	(11.0)	88	(15.0)	120	(19.4)	148	(24.0)
Ankle impingement	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Arthralgia	23	(3.7)	26	(4.2)	13	(2.3)	16	(2.7)	32	(5.2)	34	(5.5)
Arthritis	3	(0.5)	1	(0.2)	3	(0.5)	0	(0.0)	5	(0.8)	0	(0.0)
Arthritis reactive	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Arthropathy	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Articular calcification	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Back pain	15	(2.4)	14	(2.3)	10	(1.7)	11	(1.9)	24	(3.9)	31	(5.0)
Bone pain	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Bursitis	4	(0.6)	5	(0.8)	1	(0.2)	0	(0.0)	4	(0.6)	8	(1.3)
Chondrodynia	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Chondropathy	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Costochondritis	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Enthesopathy	1	(0.2)	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)	1	(0.2)
Exostosis	0	(0.0)	1	(0.2)	1	(0.2)	2	(0.3)	1	(0.2)	3	(0.5)
Fibromyalgia	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Flank pain	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)
Foot deformity	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Gouty arthritis	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Haemarthrosis	1	(0.2)	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)
Intervertebral disc degeneration	1	(0.2)	2	(0.3)	1	(0.2)	0	(0.0)	3	(0.5)	2	(0.3)
Intervertebral disc disorder	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Intervertebral disc protrusion	4	(0.6)	2	(0.3)	2	(0.3)	5	(0.9)	8	(1.3)	7	(1.1)
Jaw cyst	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)

Subjects With Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Musculoskeletal and connective tissue disorders	82	(13.2)	87	(14.1)	63	(11.0)	88	(15.0)	120	(19.4)	148	(24.0)
Joint effusion	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Joint stiffness	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Joint swelling	2	(0.3)	0	(0.0)	2	(0.3)	2	(0.3)	3	(0.5)	2	(0.3)
Kyphosis	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Limb discomfort	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Lumbar spinal stenosis	1	(0.2)	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)
Muscle spasms	4	(0.6)	4	(0.6)	3	(0.5)	3	(0.5)	4	(0.6)	4	(0.6)
Muscle tightness	0	(0.0)	2	(0.3)	0	(0.0)	1	(0.2)	0	(0.0)	3	(0.5)
Muscular weakness	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Musculoskeletal chest pain	1	(0.2)	0	(0.0)	2	(0.3)	1	(0.2)	3	(0.5)	1	(0.2)
Musculoskeletal pain	7	(1.1)	7	(1.1)	4	(0.7)	7	(1.2)	11	(1.8)	10	(1.6)
Musculoskeletal stiffness	2	(0.3)	2	(0.3)	1	(0.2)	1	(0.2)	3	(0.5)	2	(0.3)
Myalgia	0	(0.0)	3	(0.5)	1	(0.2)	6	(1.0)	1	(0.2)	8	(1.3)
Neck pain	2	(0.3)	3	(0.5)	1	(0.2)	4	(0.7)	4	(0.6)	9	(1.5)
Osteoarthritis	9	(1.4)	5	(0.8)	6	(1.0)	4	(0.7)	12	(1.9)	9	(1.5)
Osteochondrosis	1	(0.2)	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)
Osteonecrosis	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Pain in extremity	4	(0.6)	2	(0.3)	7	(1.2)	7	(1.2)	7	(1.1)	10	(1.6)
Pain in jaw	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Patellofemoral pain syndrome	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Periarthritis	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.3)
Plantar fasciitis	0	(0.0)	3	(0.5)	0	(0.0)	1	(0.2)	0	(0.0)	3	(0.5)
Psoriatic arthropathy	9	(1.4)	4	(0.6)	6	(1.0)	5	(0.9)	11	(1.8)	8	(1.3)

Subjects With Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Musculoskeletal and connective tissue disorders	82	(13.2)	87	(14.1)	63	(11.0)	88	(15.0)	120	(19.4)	148	(24.0)
Rhabdomyolysis	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Rheumatoid arthritis	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.3)
Rotator cuff syndrome	1	(0.2)	1	(0.2)	3	(0.5)	1	(0.2)	3	(0.5)	2	(0.3)
Sacroiliitis	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Spinal column stenosis	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Spinal disorder	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Spinal osteoarthritis	3	(0.5)	2	(0.3)	2	(0.3)	1	(0.2)	5	(0.8)	3	(0.5)
Spinal pain	2	(0.3)	2	(0.3)	2	(0.3)	1	(0.2)	3	(0.5)	4	(0.6)
Spondylitis	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)	0	(0.0)
Spondylolisthesis	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)
Synovial cyst	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)	0	(0.0)
Synovial disorder	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Synovitis	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.3)	0	(0.0)	3	(0.5)
Tendon calcification	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Tendon pain	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Tendonitis	2	(0.3)	3	(0.5)	1	(0.2)	4	(0.7)	2	(0.3)	5	(0.8)
Tenosynovitis	1	(0.2)	2	(0.3)	1	(0.2)	3	(0.5)	1	(0.2)	4	(0.6)
Tenosynovitis stenosans	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Trigger finger	1	(0.2)	1	(0.2)	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	17	(2.7)	14	(2.3)	16	(2.8)	15	(2.6)	36	(5.8)	28	(4.5)
Acanthoma	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)

Subjects With Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	17	(2.7)	14	(2.3)	16	(2.8)	15	(2.6)	36	(5.8)	28	(4.5)
Acrochordon	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)	3	(0.5)
Adenoma benign	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Anogenital warts	1	(0.2)	1	(0.2)	0	(0.0)	1	(0.2)	1	(0.2)	2	(0.3)
Basal cell carcinoma	1	(0.2)	0	(0.0)	0	(0.0)	2	(0.3)	1	(0.2)	4	(0.6)
Basosquamous carcinoma	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Benign breast neoplasm	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Benign lung neoplasm	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Benign neoplasm of thyroid gland	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Benign pancreatic neoplasm	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Bladder transitional cell carcinoma	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Breast cancer	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Breast cancer metastatic	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Cervix carcinoma	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Clear cell renal cell carcinoma	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Colon adenoma	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.3)
Diffuse large B-cell lymphoma	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Dysplastic naevus	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	2	(0.3)
Fibroadenoma of breast	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Fibrous histiocytoma	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)	0	(0.0)
Intraductal proliferative breast lesion	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Invasive lobular breast carcinoma	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Leiomyoma	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Leiomyosarcoma	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)

Subjects With Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	17	(2.7)	14	(2.3)	16	(2.8)	15	(2.6)	36	(5.8)	28	(4.5)
Lipoma	1	(0.2)	2	(0.3)	0	(0.0)	1	(0.2)	2	(0.3)	2	(0.3)
Lobular breast carcinoma in situ	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Malignant melanoma in situ	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Melanocytic naevus	2	(0.3)	2	(0.3)	2	(0.3)	1	(0.2)	3	(0.5)	3	(0.5)
Metastatic carcinoma of the bladder	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Monoclonal gammopathy	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Nasal neoplasm benign	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Non-Hodgkin's lymphoma	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Ovarian cancer	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Papillary thyroid cancer	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)	1	(0.2)
Prostate cancer	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Prostatic adenoma	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Rectal adenocarcinoma	1	(0.2)	1	(0.2)	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)
Seborrhoeic keratosis	2	(0.3)	0	(0.0)	2	(0.3)	1	(0.2)	4	(0.6)	1	(0.2)
Skin papilloma	4	(0.6)	1	(0.2)	4	(0.7)	1	(0.2)	7	(1.1)	1	(0.2)
Uterine leiomyoma	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)	0	(0.0)
Nervous system disorders	55	(8.9)	40	(6.5)	37	(6.4)	34	(5.8)	79	(12.7)	61	(9.9)
Aphonia	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Arachnoid cyst	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Burning sensation	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)
Carotid arteriosclerosis	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Carotid artery stenosis	1	(0.2)	0	(0.0)	3	(0.5)	0	(0.0)	3	(0.5)	0	(0.0)

Subjects With Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Nervous system disorders	55	(8.9)	40	(6.5)	37	(6.4)	34	(5.8)	79	(12.7)	61	(9.9)
Carpal tunnel syndrome	1	(0.2)	3	(0.5)	1	(0.2)	2	(0.3)	2	(0.3)	5	(0.8)
Cerebral arteriosclerosis	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Cerebral haemorrhage	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Cerebral infarction	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Cerebrovascular accident	1	(0.2)	0	(0.0)	1	(0.2)	1	(0.2)	2	(0.3)	1	(0.2)
Cervical radiculopathy	0	(0.0)	2	(0.3)	1	(0.2)	0	(0.0)	1	(0.2)	2	(0.3)
Cervicobrachial syndrome	2	(0.3)	3	(0.5)	1	(0.2)	0	(0.0)	2	(0.3)	3	(0.5)
Cubital tunnel syndrome	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Diabetic neuropathy	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)	1	(0.2)	2	(0.3)
Dizziness	5	(0.8)	3	(0.5)	1	(0.2)	4	(0.7)	7	(1.1)	8	(1.3)
Dysgeusia	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Epilepsy	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Facial paralysis	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Facial paresis	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Formication	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Haemorrhage intracranial	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Headache	16	(2.6)	16	(2.6)	10	(1.7)	12	(2.0)	23	(3.7)	24	(3.9)
Hypertonia	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Hypoaesthesia	1	(0.2)	2	(0.3)	4	(0.7)	3	(0.5)	4	(0.6)	3	(0.5)
Hyposmia	2	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)
Intensive care unit acquired weakness	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Intracranial aneurysm	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Ischaemic cerebral infarction	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Lethargy	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)

Subjects With Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Nervous system disorders	55	(8.9)	40	(6.5)	37	(6.4)	34	(5.8)	79	(12.7)	61	(9.9)
Loss of consciousness	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Lumbar radiculopathy	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Memory impairment	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Meralgia paraesthetica	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Migraine	5	(0.8)	4	(0.6)	2	(0.3)	4	(0.7)	7	(1.1)	5	(0.8)
Monoparesis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Myelopathy	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Nerve compression	0	(0.0)	2	(0.3)	1	(0.2)	0	(0.0)	1	(0.2)	2	(0.3)
Nerve root compression	2	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)
Neuropathy peripheral	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Paraesthesia	3	(0.5)	1	(0.2)	4	(0.7)	1	(0.2)	5	(0.8)	1	(0.2)
Paresis	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Perineurial cyst	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Presyncope	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Sciatica	4	(0.6)	4	(0.6)	4	(0.7)	5	(0.9)	7	(1.1)	7	(1.1)
Spinal cord compression	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Syncope	3	(0.5)	0	(0.0)	2	(0.3)	2	(0.3)	3	(0.5)	2	(0.3)
Tension headache	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)	0	(0.0)
Thrombotic cerebral infarction	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Transient ischaemic attack	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	1	(0.2)
Visual field defect	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Product issues	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Device failure	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)

Subjects With Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Psychiatric disorders	20	(3.2)	15	(2.4)	21	(3.7)	16	(2.7)	38	(6.1)	27	(4.4)
Adjustment disorder with depressed mood	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Affective disorder	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Alcoholism	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Anxiety	5	(0.8)	4	(0.6)	8	(1.4)	0	(0.0)	14	(2.3)	5	(0.8)
Anxiety disorder	1	(0.2)	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)
Attention deficit/hyperactivity disorder	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Breathing-related sleep disorder	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Bruxism	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Burnout syndrome	1	(0.2)	1	(0.2)	0	(0.0)	1	(0.2)	1	(0.2)	2	(0.3)
Completed suicide	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Delirium	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Depressed mood	0	(0.0)	1	(0.2)	2	(0.3)	1	(0.2)	2	(0.3)	1	(0.2)
Depression	7	(1.1)	2	(0.3)	4	(0.7)	5	(0.9)	10	(1.6)	7	(1.1)
Drug use disorder	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Generalised anxiety disorder	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Insomnia	4	(0.6)	3	(0.5)	4	(0.7)	4	(0.7)	7	(1.1)	6	(1.0)
Major depression	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)	1	(0.2)
Mental disorder	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Nervousness	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Obsessive-compulsive disorder	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Seasonal affective disorder	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Sleep disorder	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)
Stress	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Suicidal ideation	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)	3	(0.5)	0	(0.0)

Subjects With Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Renal and urinary disorders	16	(2.6)	18	(2.9)	15	(2.6)	19	(3.2)	26	(4.2)	31	(5.0)
Acute kidney injury	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)
Bladder pain	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Calculus urinary	1	(0.2)	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.3)	0	(0.0)
Chronic kidney disease	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)
Diabetic nephropathy	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Dysuria	1	(0.2)	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)
Glycosuria	1	(0.2)	3	(0.5)	0	(0.0)	2	(0.3)	1	(0.2)	6	(1.0)
Haematuria	4	(0.6)	5	(0.8)	5	(0.9)	4	(0.7)	7	(1.1)	7	(1.1)
Leukocyturia	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Micturition disorder	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Nephrolithiasis	2	(0.3)	3	(0.5)	3	(0.5)	3	(0.5)	4	(0.6)	4	(0.6)
Nocturia	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Pollakiuria	2	(0.3)	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)	0	(0.0)
Proteinuria	4	(0.6)	2	(0.3)	2	(0.3)	5	(0.9)	5	(0.8)	5	(0.8)
Renal colic	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Renal cyst	1	(0.2)	1	(0.2)	1	(0.2)	1	(0.2)	1	(0.2)	2	(0.3)
Renal failure	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Renal glycosuria	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Renal impairment	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Renal vein thrombosis	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Ureteric obstruction	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Ureterolithiasis	1	(0.2)	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)
Urethral stenosis	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Urinary incontinence	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)

Subjects With Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Renal and urinary disorders	16	(2.6)	18	(2.9)	15	(2.6)	19	(3.2)	26	(4.2)	31	(5.0)
Urinary retention	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)
Urine abnormality	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Reproductive system and breast disorders	10	(1.6)	12	(1.9)	4	(0.7)	6	(1.0)	18	(2.9)	18	(2.9)
Adenomyosis	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Adnexa uteri pain	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Benign prostatic hyperplasia	4	(0.6)	2	(0.3)	2	(0.3)	1	(0.2)	5	(0.8)	4	(0.6)
Breast cyst	0	(0.0)	2	(0.3)	0	(0.0)	1	(0.2)	1	(0.2)	2	(0.3)
Breast enlargement	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Breast tenderness	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Dysfunctional uterine bleeding	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Dysmenorrhoea	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Endometrial thickening	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Erectile dysfunction	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)
Fibrocystic breast disease	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Genital rash	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Menopausal symptoms	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Oligomenorrhoea	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Ovarian cyst	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Pelvic pain	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Polymenorrhoea	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Postmenopausal haemorrhage	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Prostatitis	1	(0.2)	2	(0.3)	0	(0.0)	3	(0.5)	2	(0.3)	4	(0.6)
Uterovaginal prolapse	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)

Subjects With Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Reproductive system and breast disorders	10	(1.6)	12	(1.9)	4	(0.7)	6	(1.0)	18	(2.9)	18	(2.9)
Vulvovaginal dryness	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Vulvovaginal pruritus	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Respiratory, thoracic and mediastinal disorders	45	(7.2)	43	(7.0)	34	(5.9)	37	(6.3)	65	(10.5)	72	(11.7)
Acquired diaphragmatic eventration	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Allergic sinusitis	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Asphyxia	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Asthma	3	(0.5)	3	(0.5)	5	(0.9)	0	(0.0)	7	(1.1)	5	(0.8)
Chronic obstructive pulmonary disease	1	(0.2)	0	(0.0)	1	(0.2)	1	(0.2)	2	(0.3)	1	(0.2)
Cough	11	(1.8)	17	(2.8)	8	(1.4)	9	(1.5)	16	(2.6)	24	(3.9)
Dysphonia	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	1	(0.2)
Dyspnoea	3	(0.5)	2	(0.3)	2	(0.3)	3	(0.5)	4	(0.6)	5	(0.8)
Dyspnoea exertional	2	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)
Epistaxis	3	(0.5)	1	(0.2)	0	(0.0)	0	(0.0)	3	(0.5)	1	(0.2)
Haemoptysis	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Hyperventilation	2	(0.3)	1	(0.2)	0	(0.0)	0	(0.0)	2	(0.3)	1	(0.2)
Laryngeal granuloma	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Laryngeal oedema	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Nasal congestion	2	(0.3)	2	(0.3)	3	(0.5)	2	(0.3)	5	(0.8)	3	(0.5)
Nasal septum deviation	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Nasal turbinate hypertrophy	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.3)
Oropharyngeal discomfort	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)
Oropharyngeal pain	9	(1.4)	8	(1.3)	9	(1.6)	10	(1.7)	12	(1.9)	13	(2.1)

Subjects With Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Respiratory, thoracic and mediastinal disorders	45	(7.2)	43	(7.0)	34	(5.9)	37	(6.3)	65	(10.5)	72	(11.7)
Paranasal cyst	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Pharyngeal mass	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Pleural effusion	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Pleurisy	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Productive cough	3	(0.5)	2	(0.3)	1	(0.2)	1	(0.2)	4	(0.6)	2	(0.3)
Pulmonary embolism	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)
Pulmonary mass	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)	1	(0.2)
Respiratory failure	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Respiratory tract congestion	2	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)
Respiratory tract irritation	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Rhinitis allergic	0	(0.0)	3	(0.5)	0	(0.0)	0	(0.0)	0	(0.0)	3	(0.5)
Rhinorrhoea	0	(0.0)	3	(0.5)	0	(0.0)	0	(0.0)	0	(0.0)	3	(0.5)
Sinus congestion	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)
Sinus pain	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Sleep apnoea syndrome	3	(0.5)	1	(0.2)	3	(0.5)	4	(0.7)	7	(1.1)	5	(0.8)
Throat irritation	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Upper-airway cough syndrome	1	(0.2)	1	(0.2)	1	(0.2)	1	(0.2)	2	(0.3)	1	(0.2)
Skin and subcutaneous tissue disorders	65	(10.5)	52	(8.4)	39	(6.8)	44	(7.5)	90	(14.5)	77	(12.5)
Acne	1	(0.2)	2	(0.3)	0	(0.0)	0	(0.0)	1	(0.2)	3	(0.5)
Actinic keratosis	6	(1.0)	4	(0.6)	1	(0.2)	3	(0.5)	7	(1.1)	5	(0.8)
Alopecia	1	(0.2)	1	(0.2)	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)
Alopecia areata	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)

Subjects With Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Skin and subcutaneous tissue disorders	65	(10.5)	52	(8.4)	39	(6.8)	44	(7.5)	90	(14.5)	77	(12.5)
Asteatosis	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Blister	0	(0.0)	2	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.3)
Blood blister	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Cold sweat	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Dermal cyst	2	(0.3)	0	(0.0)	2	(0.3)	1	(0.2)	3	(0.5)	1	(0.2)
Dermatitis	2	(0.3)	3	(0.5)	1	(0.2)	1	(0.2)	2	(0.3)	5	(0.8)
Dermatitis allergic	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Dermatitis atopic	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)
Dermatitis contact	7	(1.1)	4	(0.6)	3	(0.5)	3	(0.5)	7	(1.1)	7	(1.1)
Diffuse alopecia	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Drug eruption	3	(0.5)	0	(0.0)	1	(0.2)	0	(0.0)	3	(0.5)	0	(0.0)
Dry skin	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	1	(0.2)
Dyshidrotic eczema	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	3	(0.5)	0	(0.0)
Eczema	6	(1.0)	6	(1.0)	5	(0.9)	6	(1.0)	10	(1.6)	11	(1.8)
Eczema asteatotic	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Eczema nummular	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Erythema	1	(0.2)	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)
Excessive granulation tissue	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Guttate psoriasis	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)
Hidradenitis	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Hyperkeratosis	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.3)
Ingrowing nail	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)
Intertrigo	3	(0.5)	2	(0.3)	1	(0.2)	2	(0.3)	4	(0.6)	3	(0.5)
Keratosis pilaris	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)

Subjects With Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Skin and subcutaneous tissue disorders	65	(10.5)	52	(8.4)	39	(6.8)	44	(7.5)	90	(14.5)	77	(12.5)
Lichen sclerosus	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Lichenoid keratosis	0	(0.0)	2	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.3)
Miliaria	1	(0.2)	3	(0.5)	0	(0.0)	2	(0.3)	2	(0.3)	3	(0.5)
Myxoid cyst	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Neurodermatitis	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Night sweats	1	(0.2)	1	(0.2)	1	(0.2)	1	(0.2)	2	(0.3)	1	(0.2)
Onychoclasis	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Palmoplantar keratoderma	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Papule	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Photosensitivity reaction	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	2	(0.3)	2	(0.3)
Polymorphic light eruption	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Pruritus	3	(0.5)	4	(0.6)	3	(0.5)	3	(0.5)	7	(1.1)	5	(0.8)
Pruritus generalised	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Psoriasis	8	(1.3)	6	(1.0)	7	(1.2)	5	(0.9)	11	(1.8)	9	(1.5)
Rash	0	(0.0)	1	(0.2)	2	(0.3)	0	(0.0)	2	(0.3)	1	(0.2)
Rash erythematous	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Rash generalised	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Rosacea	1	(0.2)	1	(0.2)	1	(0.2)	0	(0.0)	2	(0.3)	1	(0.2)
Seborrhoeic dermatitis	0	(0.0)	2	(0.3)	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)
Skin burning sensation	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Skin erosion	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Skin hyperpigmentation	1	(0.2)	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)
Skin lesion	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Skin mass	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)

Subjects With Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Skin and subcutaneous tissue disorders	65	(10.5)	52	(8.4)	39	(6.8)	44	(7.5)	90	(14.5)	77	(12.5)
Skin odour abnormal	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Skin striae	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Skin ulcer	1	(0.2)	0	(0.0)	1	(0.2)	2	(0.3)	1	(0.2)	2	(0.3)
Solar dermatitis	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Stasis dermatitis	2	(0.3)	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)	0	(0.0)
Transient acantholytic dermatosis	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Urticaria	5	(0.8)	2	(0.3)	3	(0.5)	4	(0.7)	8	(1.3)	4	(0.6)
Vitiligo	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)	2	(0.3)	1	(0.2)
Xanthelasma	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Xeroderma	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Social circumstances	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Alcohol use	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Surgical and medical procedures	3	(0.5)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Endodontic procedure	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Gastrectomy	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Peripheral nerve decompression	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Tooth extraction	2	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Vascular disorders	23	(3.7)	27	(4.4)	24	(4.2)	24	(4.1)	43	(6.9)	53	(8.6)
Aortic aneurysm	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Aortic arteriosclerosis	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Aortic dissection	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)

Subjects With Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Vascular disorders	23	(3.7)	27	(4.4)	24	(4.2)	24	(4.1)	43	(6.9)	53	(8.6)
Arterial occlusive disease	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Arteriosclerosis	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)
Deep vein thrombosis	1	(0.2)	1	(0.2)	0	(0.0)	1	(0.2)	1	(0.2)	2	(0.3)
Essential hypertension	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Flushing	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Haematoma	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Hot flush	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Hypertension	17	(2.7)	17	(2.8)	22	(3.8)	19	(3.2)	35	(5.6)	40	(6.5)
Hypertensive crisis	1	(0.2)	0	(0.0)	1	(0.2)	1	(0.2)	2	(0.3)	1	(0.2)
Hypotension	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)
Peripheral arterial occlusive disease	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)	0	(0.0)
Peripheral artery aneurysm	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Peripheral coldness	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.3)
Subgaleal haematoma	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Thrombophlebitis	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Thrombosis	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Varicose vein	1	(0.2)	1	(0.2)	2	(0.3)	0	(0.0)	2	(0.3)	1	(0.2)
Venous thrombosis	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
NULL	5	(0.8)	0	(0.0)	3	(0.5)	4	(0.7)	4	(0.6)	4	(0.6)

Every subject is counted a single time for each applicable row and column.
A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.
[Source: 5.3.5.3-8]

付録 2.7.4-84
Unencoded Adverse Event Terms in the Phase 3 Extension Safety Pool for the SUR

Study Number	Subject Allocation Number	Treatment Group Assignment	AE Reported Term	AE Severity	AE Serious (Y / N)
3222-010	[redacted]	MK-3222 200mg	Aphasia episode w/ seizure like activity	Severe	Y
3222-010	[redacted]	MK-3222 100mg	Exacerbation of Joint Pains (Shoulders, hips, knees, elbows) - (psoriasis worsening due to interruption of IP)	Mild	N
3222-010	[redacted]	MK-3222 200mg	Possible Cellulitis to Right testicle	Severe	Y
3222-011	[redacted]	MK-3222 200mg	Root Canal #19	Moderate	N
3222-011	[redacted]	MK-3222 100mg	Burn on stomach	Moderate	N
3222-011	[redacted]	MK-3222 100mg	Abnormal urinalysis Bacteria test- result "3+ #/HPF"	Mild	N
3222-011	[redacted]	MK-3222 100mg	Abnormal urinalysis RBC test - result " 3-5 #/HPF"	Mild	N
3222-011	[redacted]	MK-3222 100mg	Abnormal urinalysis Squamous Epithelial Cells test- result "30-49#/HPF"	Mild	N
3222-011	[redacted]	MK-3222 100mg	Abnormal urinalysis WBC test - result " 16-29 #/HPF"	Mild	N
3222-011	[redacted]	MK-3222 100mg	abnormal urinalysis Protein test - result "trace"	Mild	N
3222-011	[redacted]	MK-3222 200mg	INTERCOSTAL MUSCLE STRAIN	Moderate	N
3222-011	[redacted]	MK-3222 200mg	suspected hyperuricemia	Mild	N
3222-011	[redacted]	MK-3222 100mg	suspicious looking naevus right lower back	Mild	N

[Source: 5.3.5.3-8]

付録 2.7.4-85
Listing of Subjects with Adverse Events that Worsened
Phase 3: Extension Safety Pool (SUR) All Subjects as Treated

Site Number	Subject ID	Onset Treatment	Rel Day of Onset†	Adverse Event	Intensity	Serious	Related	Action Taken	Outcome
Trial Number = 3222-010									
0101	[redacted]	MK-3222 200 mg	815	Influenza	Moderate	N	Not Related	Dose Not Changed	Recovered/Resolved
0107	[redacted]	MK-3222 100 mg	1328	Sinusitis	Mild	N	Not Related	Dose Not Changed	Recovered/Resolved
0107	[redacted]	MK-3222 100 mg	1349	Otitis media acute	Mild	N	Not Related	Dose Not Changed	Recovered/Resolved
0107	[redacted]	MK-3222 100 mg	892	Pneumonia	Mild	N	Not Related	Dose Not Changed	Recovered/Resolved
0107	[redacted]	MK-3222 100 mg	923	Otitis media acute	Mild	N	Not Related	Dose Not Changed	Recovered/Resolved
0111	[redacted]	MK-3222 100 mg	944	Osteoarthritis	Mild	Y	Not Related	Dose Not Changed	Recovered/Resolved
0113	[redacted]	MK-3222 200 mg	843	Pruritus	Mild	N	Not Related	Dose Not Changed	Recovered/Resolved
0115	[redacted]	MK-3222 100 mg	449	Hypertension	Mild	N	Related	Dose Not Changed	Not Recovered/Not Resolved
0117	[redacted]	MK-3222 100 mg	971	Hypertension	Mild	N	Not Related	Dose Not Changed	Not Recovered/Not Resolved
0122	[redacted]	MK-3222 100 mg	1196	Pneumonia	Severe	Y	Related	Dose Not Changed	Recovered/Resolved
0127	[redacted]	MK-3222 200 mg	1186	Depression	Moderate	N	Not Related	Dose Not Changed	Recovering/Resolving
0127	[redacted]	MK-3222 100 mg	982	Hypokalaemia	Mild	N	Not Related	Dose Not Changed	Recovered/Resolved
0137	[redacted]	MK-3222 100 mg	760	Haemorrhoids	Mild	N	Not Related	Dose Not Changed	Unknown
0141	[redacted]	MK-3222 200 mg	1289	Dermatitis contact	Mild	N	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
0141	[redacted]	MK-3222 200 mg	1359	Back pain	Moderate	N	Not Related	Dose Not Changed	Not Recovered/Not Resolved

Listing of Subjects with Adverse Events that Worsened
Phase 3: Extension Safety Pool (SUR) All Subjects as Treated

Site Number	Subject ID	Onset Treatment	Rel Day of Onset†	Adverse Event	Intensity	Serious	Related	Action Taken	Outcome
0141	[redacted]	MK-3222 200 mg	888	Diabetic eye disease	Mild	N	Not Related	Dose Not Changed	Recovered/Resolved
0141	[redacted]	MK-3222 200 mg	952	Hypoaesthesia	Mild	N	Not Related	Dose Not Changed	Not Recovered/Not Resolved
1101	[redacted]	MK-3222 100 mg	1186	Proctitis	Mild	N	Not Related	Dose Not Changed	Recovered/Resolved
1101	[redacted]	MK-3222 200 mg	1197	Urinary tract infection	Moderate	N	Not Related	Dose Not Changed	Recovered/Resolved
1101	[redacted]	MK-3222 100 mg	1192	Urticaria	Moderate	N	Not Related	Dose Not Changed	Recovered/Resolved
1101	[redacted]	MK-3222 200 mg	1266	Uncoded	Severe	Y	Not Related	Dose Not Changed	Recovering/Resolving
1101	[redacted]	MK-3222 200 mg	927	Myalgia	Moderate	N	Not Related	Dose Not Changed	Recovered/Resolved
1102	[redacted]	MK-3222 100 mg	673	Papillary thyroid cancer	Moderate	Y	Not Related	Drug Interrupted	Recovered/Resolved
1108	[redacted]	MK-3222 200 mg	1038	Asthma	Moderate	N	Not Related	Dose Not Changed	Recovered/Resolved
1108	[redacted]	MK-3222 100 mg	513	Headache	Mild	N	Not Related	Dose Not Changed	Recovered/Resolved
1112	[redacted]	MK-3222 200 mg	1050	Vomiting	Moderate	N	Not Related	Dose Not Changed	Recovered/Resolved
6101	[redacted]	MK-3222 200 mg	1029	Lichenoid keratosis	Moderate	N	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
6101	[redacted]	MK-3222 200 mg	1379	Pain in extremity	Mild	N	Not Related	Dose Not Changed	Unknown
6101	[redacted]	MK-3222 200 mg	1221	Psoriatic arthropathy	Severe	Y	Not Related	Dose Not Changed	Not Recovered/Not Resolved
6101	[redacted]	MK-3222 100 mg	1222	Dental caries	Mild	N	Not Related	Dose Not Changed	Recovered/Resolved
6101	[redacted]	MK-3222 200 mg	246	Sciatica	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved

Listing of Subjects with Adverse Events that Worsened
Phase 3: Extension Safety Pool (SUR) All Subjects as Treated

Site Number	Subject ID	Onset Treatment	Rel Day of Onset†	Adverse Event	Intensity	Serious	Related	Action Taken	Outcome
6101	[redacted]	MK-3222 200 mg	246	Sciatica	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
6102	[redacted]	MK-3222 100 mg	407	Cholelithiasis	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
6103	[redacted]	MK-3222 200 mg	1262	Food poisoning	Moderate	N	Not Related	Dose Not Changed	Recovered/Resolved
6104	[redacted]	MK-3222 100 mg	1353	Upper respiratory tract infection	Mild	N	Not Related	Dose Not Changed	Recovered/Resolved
8101	[redacted]	MK-3222 100 mg	778	Psoriatic arthropathy	Moderate	N	Not Related	Dose Not Changed	Not Recovered/Not Resolved
8103	[redacted]	MK-3222 100 mg	719	Urticaria	Moderate	N	Not Related	Dose Not Changed	Recovered/Resolved
8103	[redacted]	MK-3222 100 mg	1007	Miliaria	Moderate	N	Not Related	Dose Not Changed	Not Recovered/Not Resolved
8103	[redacted]	MK-3222 100 mg	852	Gastroenteritis	Severe	Y	Related	Dose Not Changed	Recovered/Resolved
8109	[redacted]	MK-3222 200 mg	720	Upper respiratory tract infection	Mild	N	Not Related	Dose Not Changed	Recovered/Resolved
8109	[redacted]	MK-3222 100 mg	422	Eczema	Mild	N	Not Related	Dose Not Changed	Recovered/Resolved
8109	[redacted]	MK-3222 100 mg	422	Eczema	Mild	N	Not Related	Dose Not Changed	Recovering/Resolving
8114	[redacted]	MK-3222 200 mg	232	Arthralgia	Moderate	N	Not Related	Dose Not Changed	Not Recovered/Not Resolved
8133	[redacted]	MK-3222 200 mg	405	Back pain	Moderate	N	Not Related	Dose Not Changed	Recovered/Resolved
8135	[redacted]	MK-3222 100 mg	449	Iron deficiency anaemia	Moderate	N	Not Related	Dose Not Changed	Recovered/Resolved
8145	[redacted]	MK-3222 200 mg	526	Viral upper respiratory tract infection	Mild	N	Not Related	Dose Not Changed	Recovered/Resolved

Trial Number = 3222-011

Listing of Subjects with Adverse Events that Worsened
Phase 3: Extension Safety Pool (SUR) All Subjects as Treated

Site Number	Subject ID	Onset Treatment	Rel Day of Onset†	Adverse Event	Intensity	Serious	Related	Action Taken	Outcome
0163	[redacted]	MK-3222 100 mg	1044	Upper respiratory tract infection	Moderate	N	Not Related	Dose Not Changed	Recovered/Resolved
0163	[redacted]	MK-3222 200 mg	700	Psoriasis	Moderate	N	Not Related	Drug Withdrawn	Recovered/Resolved
0168	[redacted]	MK-3222 200 mg	1101	Uncoded	Moderate	N	Not Related	Dose Not Changed	Recovered/Resolved
0169	[redacted]	MK-3222 200 mg	746	Intervertebral disc degeneration	Mild	N	Not Related	Dose Not Changed	Recovered/Resolved
0171	[redacted]	MK-3222 100 mg	763	Skin ulcer	Moderate	N	Not Related	Drug Interrupted	Not Recovered/Not Resolved
0172	[redacted]	MK-3222 200 mg	749	Urinary tract infection	Moderate	N	Not Related	Dose Not Changed	Recovered/Resolved
0172	[redacted]	MK-3222 100 mg	413	Pain in extremity	Moderate	N	Not Related	Dose Not Changed	Recovered/Resolved
0172	[redacted]	MK-3222 100 mg	510	Adenomyosis	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
0172	[redacted]	MK-3222 200 mg	763	Acute sinusitis	Mild	N	Not Related	Dose Not Changed	Recovered/Resolved
0172	[redacted]	MK-3222 200 mg	763	Otitis media acute	Mild	N	Not Related	Dose Not Changed	Recovered/Resolved
0172	[redacted]	MK-3222 200 mg	54	Back pain	Moderate	N	Not Related	Dose Not Changed	Not Recovered/Not Resolved
0178	[redacted]	MK-3222 100 mg	1287	Headache	Moderate	N	Not Related	Dose Not Changed	Recovered/Resolved
0179	[redacted]	MK-3222 200 mg	794	Pharyngitis streptococcal	Moderate	N	Not Related	Dose Not Changed	Recovered/Resolved
1163	[redacted]	MK-3222 100 mg	1056	Gout	Moderate	N	Not Related	Dose Not Changed	Recovered/Resolved
1164	[redacted]	MK-3222 100 mg	677	Migraine	Severe	N	Not Related	Dose Not Changed	Recovered/Resolved
1164	[redacted]	MK-3222 100 mg	779	Urticaria	Mild	N	Not Related	Dose Not Changed	Recovered/Resolved

Listing of Subjects with Adverse Events that Worsened
Phase 3: Extension Safety Pool (SUR) All Subjects as Treated

Site Number	Subject ID	Onset Treatment	Rel Day of Onset†	Adverse Event	Intensity	Serious	Related	Action Taken	Outcome
1164	[redacted]	MK-3222 200 mg	768	Acute myocardial infarction	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
1164	[redacted]	MK-3222 100 mg	434	Cyst	Mild	N	Not Related	Dose Not Changed	Recovered/Resolved
1171	[redacted]	MK-3222 100 mg	482	Influenza	Moderate	N	Not Related	Dose Not Changed	Recovered/Resolved
1171	[redacted]	MK-3222 100 mg	1017	Keratosis follicular	Severe	Y	Not Related	Drug Interrupted	Recovered/Resolved
1171	[redacted]	MK-3222 100 mg	1027	Cellulitis of male external genital organ	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
1171	[redacted]	MK-3222 100 mg	1027	Scrotal abscess	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
3101	[redacted]	MK-3222 200 mg	7	Pruritus	Mild	N	Related	Dose Not Changed	Not Recovered/Not Resolved
3203	[redacted]	MK-3222 100 mg	633	Perineurial cyst	Moderate	N	Not Related	Dose Not Changed	Recovered/Resolved
3206	[redacted]	MK-3222 200 mg	452	Anxiety	Moderate	N	Not Related	Dose Not Changed	Not Recovered/Not Resolved
3306	[redacted]	MK-3222 100 mg	1146	Wrist fracture	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
3307	[redacted]	MK-3222 200 mg	856	Dizziness	Mild	N	Not Related	Dose Not Changed	Recovered/Resolved
3601	[redacted]	MK-3222 100 mg	525	Viral upper respiratory tract infection	Mild	N	Not Related	Dose Not Changed	Recovered/Resolved
3603	[redacted]	MK-3222 100 mg	489	Abdominal pain	Mild	N	Not Related	Dose Not Changed	Recovered/Resolved
3603	[redacted]	MK-3222 100 mg	701	Electrocardiogram QT prolonged	Mild	N	Not Related	Dose Not Changed	Recovered/Resolved
3603	[redacted]	MK-3222 100 mg	353	Cholelithiasis	Mild	Y	Not Related	Dose Not Changed	Recovered/Resolved
3904	[redacted]	MK-3222 200 mg	519	Toothache	Mild	N	Related	Dose Not Changed	Recovered/Resolved

Listing of Subjects with Adverse Events that Worsened
Phase 3: Extension Safety Pool (SUR) All Subjects as Treated

Site Number	Subject ID	Onset Treatment	Rel Day of Onset†	Adverse Event	Intensity	Serious	Related	Action Taken	Outcome
3905	[redacted]	MK-3222 200 mg	1121	Hypercholesterolaemia	Mild	N	Not Related	Dose Not Changed	Not Recovered/Not Resolved
4202	[redacted]	MK-3222 100 mg	856	Diverticulitis	Severe	Y	Not Related	Drug Withdrawn	Recovered/Resolved
4301	[redacted]	MK-3222 100 mg	754	Carotid artery stenosis	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
4304	[redacted]	MK-3222 200 mg	530	Muscle spasms	Mild	N	Not Related	Dose Not Changed	Recovering/Resolving
4802	[redacted]	MK-3222 100 mg	939	Hiatus hernia	Moderate	Y	Not Related	Dose Not Changed	Recovering/Resolving
4805	[redacted]	MK-3222 200 mg	990	Bronchitis	Mild	N	Related	Dose Not Changed	Recovered/Resolved
4807	[redacted]	MK-3222 100 mg	1	Hypertriglyceridaemia	Mild	N	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
4904	[redacted]	MK-3222 200 mg	517	Viral upper respiratory tract infection	Moderate	N	Not Related	Dose Not Changed	Recovered/Resolved
4905	[redacted]	MK-3222 100 mg	1087	Gastrointestinal infection	Mild	N	Related	Dose Not Changed	Recovered/Resolved
4905	[redacted]	MK-3222 100 mg	1142	Viral upper respiratory tract infection	Moderate	N	Related	Dose Not Changed	Recovered/Resolved With Sequelae
4905	[redacted]	MK-3222 100 mg	925	Viral upper respiratory tract infection	Moderate	N	Related	Dose Not Changed	Recovered/Resolved
4906	[redacted]	MK-3222 100 mg	541	Herpes zoster	Mild	N	Not Related	Dose Not Changed	Not Recovered/Not Resolved
4908	[redacted]	MK-3222 200 mg	583	Intervertebral disc protrusion	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
4909	[redacted]	MK-3222 100 mg	1027	Periodontitis	Moderate	N	Not Related	Dose Not Changed	Recovered/Resolved
4911	[redacted]	MK-3222 200 mg	225	Tendon rupture	Severe	Y	Not Related	Dose Not Changed	Recovering/Resolving
4911	[redacted]	MK-3222 200 mg	708	Carpal tunnel syndrome	Mild	N	Not Related	Dose Not Changed	Recovered/Resolved

Listing of Subjects with Adverse Events that Worsened
Phase 3: Extension Safety Pool (SUR) All Subjects as Treated

Site Number	Subject ID	Onset Treatment	Rel Day of Onset†	Adverse Event	Intensity	Serious	Related	Action Taken	Outcome
4911	[redacted]	MK-3222 100 mg	942	Intervertebral disc protrusion	Severe	Y	Not Related	Dose Not Changed	Not Recovered/Not Resolved
4911	[redacted]	MK-3222 100 mg	893	Diverticulitis	Severe	Y	Related	Dose Not Changed	Recovered/Resolved
4913	[redacted]	MK-3222 100 mg	703	Viral upper respiratory tract infection	Moderate	N	Not Related	Dose Not Changed	Recovered/Resolved
4914	[redacted]	MK-3222 100 mg	1267	Gingivitis	Moderate	N	Not Related	Dose Not Changed	Recovered/Resolved
4914	[redacted]	MK-3222 200 mg	865	Cold sweat	Moderate	N	Not Related	Dose Not Changed	Recovered/Resolved
4914	[redacted]	MK-3222 200 mg	865	Dyspnoea	Mild Mild	N	Not Related	Dose Not Changed	Recovered/Resolved
4914	[redacted]	MK-3222 200 mg	865	Musculoskeletal chest pain	Severe	N	Not Related	Dose Not Changed	Recovered/Resolved
4915	[redacted]	MK-3222 100 mg	575	Depression	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
4916	[redacted]	MK-3222 100 mg	706	Non-cardiac chest pain	Mild Mild	Y	Not Related	Dose Not Changed	Recovered/Resolved
4917	[redacted]	MK-3222 100 mg	609	Viral upper respiratory tract infection	Mild	N	Not Related	Dose Not Changed	Recovered/Resolved
4918	[redacted]	MK-3222 100 mg	1189	Viral upper respiratory tract infection	Moderate	N	Not Related	Dose Not Changed	Recovered/Resolved
4919	[redacted]	MK-3222 100 mg	947	Viral upper respiratory tract infection	Severe	N	Not Related	Dose Not Changed	Recovered/Resolved
4920	[redacted]	MK-3222 100 mg	876	Gamma-glutamyltransferase increased	Severe	N	Not Related	Dose Not Changed	Recovered/Resolved
4921	[redacted]	MK-3222 100 mg	594	Peripheral arterial occlusive disease	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
4923	[redacted]	MK-3222 100 mg	639	Bronchitis		N	Related	Dose Not Changed	Recovered/Resolved
4923	[redacted]	MK-3222 100 mg	670	Viral upper respiratory tract infection		N	Not Related	Dose Not Changed	Recovered/Resolved

Listing of Subjects with Adverse Events that Worsened
Phase 3: Extension Safety Pool (SUR) All Subjects as Treated

Site Number	Subject ID	Onset Treatment	Rel Day of Onset†	Adverse Event	Intensity	Serious	Related	Action Taken	Outcome
4923	[redacted]	MK-3222 100 mg	652	Dyspnoea	Moderate	N	Not Related	Dose Not Changed	Recovered/Resolved
4923	[redacted]	MK-3222 100 mg	615	Dizziness	Mild	N	Not Related	Dose Not Changed	Recovered/Resolved
4923	[redacted]	MK-3222 100 mg	892	Psoriatic arthropathy	Moderate	N	Not Related	Dose Not Changed	Not Recovered/Not Resolved
4924	[redacted]	MK-3222 200 mg	1222	Viral upper respiratory tract infection	Mild	N	Related	Dose Not Changed	Recovered/Resolved With Sequelae
4924	[redacted]	MK-3222 200 mg	911	Hidradenitis	Moderate	N	Not Related	Dose Not Changed	Recovered/Resolved
4925	[redacted]	MK-3222 100 mg	894	Umbilical hernia	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
4926	[redacted]	MK-3222 100 mg	876	Diarrhoea	Moderate	N	Not Related	Dose Not Changed	Recovered/Resolved
4926	[redacted]	MK-3222 200 mg	386	Umbilical hernia	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
4926	[redacted]	MK-3222 200 mg	758	Pneumonia mycoplasmal	Severe	Y	Related	Drug Interrupted	Recovered/Resolved
4928	[redacted]	MK-3222 200 mg	778	Spinal pain	Mild	N	Not Related	Dose Not Changed	Recovered/Resolved
4930	[redacted]	MK-3222 200 mg	898	Viral upper respiratory tract infection	Moderate	N	Related	Drug Interrupted	Recovered/Resolved
4934	[redacted]	MK-3222 200 mg	709	Malocclusion	Mild	Y	Not Related	Dose Not Changed	Recovered/Resolved
4936	[redacted]	MK-3222 200 mg	1060	Cough	Mild	N	Not Related	Dose Not Changed	Recovered/Resolved
4937	[redacted]	MK-3222 200 mg	869	Liver function test increased	Mild	N	Not Related	Dose Not Changed	Not Recovered/Not Resolved
4939	[redacted]	MK-3222 100 mg	247	Insomnia	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
4939	[redacted]	MK-3222 100 mg	1112	Diverticulitis	Moderate	N	Not Related	Dose Not Changed	Not Recovered/Not Resolved

Listing of Subjects with Adverse Events that Worsened
Phase 3: Extension Safety Pool (SUR) All Subjects as Treated

Site Number	Subject ID	Onset Treatment	Rel Day of Onset†	Adverse Event	Intensity	Serious	Related	Action Taken	Outcome
4939	[redacted]	MK-3222 200 mg	660	Otitis media acute	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
4939	[redacted]	MK-3222 100 mg	467	Gastritis erosive	Moderate	Y	Related	Dose Not Changed	Recovered/Resolved

Action Taken: None = DOSE NOT CHANGED, Reduced = DOSE REDUCED, Interrupted = DRUG INTERRUPTED, Discontinued = DRUG WITHDRAWN, Increased = DOSE INCREASED, N/A = NOT APPLICABLE.

Outcome: Resolved = RECOVERED/RESOLVED, Resolving = RECOVERING/RESOLVING, Sequelae = RECOVERED/RESOLVED WITH SEQUELAE, Not resolved = NOT RECOVERED/NOT RESOLVED.

Related: Investigator-assessed relationship of the adverse event to study medication.

† Relative to start of Base Period

Note: For the Phase 2 study (P003), the adverse event field of "action/outcome" reported as "None" in the legacy data base was mapped to "Not Applicable" and "Additional Medication, Hospitalization, Disability, Death or Therapeutic Procedure" was mapped to a "blank" field. For the Phase 3 trials (P010 and P011), the "action/outcome" of "Not Applicable" was used for AEs where no study medication was administered or for AEs occurring before the first dose of study medication. The "action /outcome" of "None" applies to AEs occurring in the follow-up period, overdoses in absence of an AE, or where no change was made to study medication.

[Source: 5.3.5.3-8]

付録 2.7.4-86
Subjects With Serious Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	621		616		575		586		620		616	
with one or more serious adverse events	46	(7.4)	31	(5.0)	65	(11.3)	61	(10.4)	89	(14.4)	75	(12.2)
with no serious adverse events	575	(92.6)	585	(95.0)	510	(88.7)	525	(89.6)	531	(85.6)	541	(87.8)
Blood and lymphatic system disorders	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Haemorrhagic anaemia	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Cardiac disorders	1	(0.2)	4	(0.6)	5	(0.9)	7	(1.2)	6	(1.0)	8	(1.3)
Acute myocardial infarction	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.3)	0	(0.0)	3	(0.5)
Angina pectoris	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Atrial fibrillation	0	(0.0)	1	(0.2)	2	(0.3)	1	(0.2)	2	(0.3)	1	(0.2)
Atrioventricular block second degree	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Congestive cardiomyopathy	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Coronary artery disease	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)	1	(0.2)
Coronary artery stenosis	0	(0.0)	0	(0.0)	0	(0.0)	3	(0.5)	0	(0.0)	3	(0.5)
Myocardial infarction	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Supraventricular tachycardia	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Ventricular tachycardia	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Congenital, familial and genetic disorders	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Keratosis follicular	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Endocrine disorders	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)
Inappropriate antidiuretic hormone secretion	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Thyrotoxic crisis	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)

Subjects With Serious Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Eye disorders	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Cataract	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Gastrointestinal disorders	4	(0.6)	4	(0.6)	5	(0.9)	11	(1.9)	8	(1.3)	12	(1.9)
Anal fissure	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Colitis ischaemic	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Diverticulum	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Diverticulum intestinal	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Duodenal polyp	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Enterocolitis	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Gastric polyps	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Gastric ulcer	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Gastritis erosive	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Gastrointestinal haemorrhage	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Hiatus hernia	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Inguinal hernia	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.3)
Large intestine polyp	1	(0.2)	0	(0.0)	1	(0.2)	3	(0.5)	1	(0.2)	3	(0.5)
Malocclusion	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Mesenteric artery thrombosis	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Peptic ulcer	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Portal hypertensive gastropathy	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Umbilical hernia	0	(0.0)	1	(0.2)	1	(0.2)	0	(0.0)	1	(0.2)	1	(0.2)

Subjects With Serious Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
General disorders and administration site conditions	3	(0.5)	1	(0.2)	0	(0.0)	1	(0.2)	3	(0.5)	1	(0.2)
Accidental death	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Chest pain	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Death	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Non-cardiac chest pain	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)
Hepatobiliary disorders	3	(0.5)	1	(0.2)	3	(0.5)	1	(0.2)	4	(0.6)	2	(0.3)
Bile duct obstruction	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Cholelithiasis	3	(0.5)	0	(0.0)	3	(0.5)	1	(0.2)	4	(0.6)	1	(0.2)
Infections and infestations	6	(1.0)	7	(1.1)	9	(1.6)	8	(1.4)	15	(2.4)	11	(1.8)
Appendicitis	2	(0.3)	0	(0.0)	1	(0.2)	1	(0.2)	3	(0.5)	1	(0.2)
Arthritis infective	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Cellulitis	0	(0.0)	2	(0.3)	2	(0.3)	0	(0.0)	2	(0.3)	2	(0.3)
Cellulitis of male external genital organ	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Chronic sinusitis	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Cystitis	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Device related sepsis	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Diverticulitis	0	(0.0)	0	(0.0)	3	(0.5)	1	(0.2)	3	(0.5)	1	(0.2)
Gastroenteritis	2	(0.3)	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)	0	(0.0)
Gastroenteritis bacterial	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Hepatitis E	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Infectious colitis	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Otitis media acute	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)

Subjects With Serious Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Infections and infestations	6	(1.0)	7	(1.1)	9	(1.6)	8	(1.4)	15	(2.4)	11	(1.8)
Peritonitis	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Pneumonia	1	(0.2)	1	(0.2)	1	(0.2)	1	(0.2)	2	(0.3)	1	(0.2)
Pneumonia mycoplasmal	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Scrotal abscess	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Septic arthritis staphylococcal	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Staphylococcal infection	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Urinary tract infection	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Viral infection	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Injury, poisoning and procedural complications	6	(1.0)	3	(0.5)	5	(0.9)	4	(0.7)	9	(1.5)	7	(1.1)
Acetabulum fracture	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Bone contusion	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Brain contusion	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Facial bones fracture	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Foot fracture	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Incisional hernia	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Laceration	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Limb injury	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Lower limb fracture	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Procedural haemorrhage	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Procedural pain	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Skull fracture	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Tendon rupture	1	(0.2)	1	(0.2)	1	(0.2)	0	(0.0)	1	(0.2)	1	(0.2)

Subjects With Serious Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Injury, poisoning and procedural complications	6	(1.0)	3	(0.5)	5	(0.9)	4	(0.7)	9	(1.5)	7	(1.1)
Thoracic vertebral fracture	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Toxicity to various agents	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Wrist fracture	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Metabolism and nutrition disorders	0	(0.0)	1	(0.2)	2	(0.3)	0	(0.0)	2	(0.3)	1	(0.2)
Hypoglycaemia	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Obesity	0	(0.0)	1	(0.2)	1	(0.2)	0	(0.0)	1	(0.2)	1	(0.2)
Musculoskeletal and connective tissue disorders	8	(1.3)	3	(0.5)	7	(1.2)	5	(0.9)	10	(1.6)	7	(1.1)
Back pain	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Intervertebral disc degeneration	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Intervertebral disc protrusion	0	(0.0)	1	(0.2)	2	(0.3)	0	(0.0)	2	(0.3)	1	(0.2)
Jaw cyst	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Lumbar spinal stenosis	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Osteoarthritis	3	(0.5)	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)	0	(0.0)
Patellofemoral pain syndrome	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Psoriatic arthropathy	3	(0.5)	0	(0.0)	2	(0.3)	1	(0.2)	3	(0.5)	1	(0.2)
Rotator cuff syndrome	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Spinal column stenosis	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Spondylolisthesis	1	(0.2)	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)
Tenosynovitis	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)

Subjects With Serious Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	5	(0.8)	4	(0.6)	11	(1.9)	10	(1.7)	14	(2.3)	13	(2.1)
Basal cell carcinoma Benign	1	(0.2)	0	(0.0)	0	(0.0)	3	(0.5)	1	(0.2)	4	(0.6)
pancreatic neoplasm	0	(0.0)	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Bladder transitional cell carcinoma	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Breast cancer	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Breast cancer metastatic	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Cervix carcinoma	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Clear cell renal cell carcinoma	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Diffuse large B-cell lymphoma	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Intraductal proliferative breast lesion	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Invasive lobular breast carcinoma	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Leiomyosarcoma	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Lipoma	0	(0.0)	1	(0.2)	1	(0.2)	0	(0.0)	1	(0.2)	1	(0.2)
Lobular breast carcinoma in situ	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Malignant melanoma in situ	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Metastatic carcinoma of the bladder	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Non-Hodgkin's lymphoma	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Ovarian cancer	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Papillary thyroid cancer	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)	1	(0.2)
Prostate cancer	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Rectal adenocarcinoma	1	(0.2)	1	(0.2)	1	(0.2)	1	(0.2)	1	(0.2)	1	(0.2)
Nervous system disorders	6	(1.0)	2	(0.3)	8	(1.4)	8	(1.4)	11	(1.8)	8	(1.3)
Carotid artery stenosis	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.3)	0	(0.0)

Subjects With Serious Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Nervous system disorders	6	(1.0)	2	(0.3)	8	(1.4)	8	(1.4)	11	(1.8)	8	(1.3)
Carpal tunnel syndrome	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Cerebral haemorrhage	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Cerebral infarction	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Cerebrovascular accident	1	(0.2)	0	(0.0)	1	(0.2)	1	(0.2)	2	(0.3)	1	(0.2)
Epilepsy	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Haemorrhage intracranial	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Intensive care unit acquired weakness	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Intracranial aneurysm	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Ischaemic cerebral infarction	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Loss of consciousness	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Nerve root compression	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Sciatica	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Spinal cord compression	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Syncope	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Thrombotic cerebral infarction	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Transient ischaemic attack	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)	1	(0.2)
Psychiatric disorders	1	(0.2)	0	(0.0)	4	(0.7)	1	(0.2)	4	(0.6)	1	(0.2)
Completed suicide	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Delirium	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Depression	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.3)	0	(0.0)
Insomnia	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Renal and urinary disorders	1	(0.2)	0	(0.0)	3	(0.5)	2	(0.3)	3	(0.5)	2	(0.3)

Subjects With Serious Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Renal and urinary disorders	1	(0.2)	0	(0.0)	3	(0.5)	2	(0.3)	3	(0.5)	2	(0.3)
Calculus urinary	1	(0.2)	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.3)	0	(0.0)
Nephrolithiasis	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.2)	1	(0.2)	1	(0.2)
Ureteric obstruction	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Urinary retention	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Reproductive system and breast disorders	1	(0.2)	0	(0.0)	0	(0.0)	2	(0.3)	1	(0.2)	2	(0.3)
Adenomyosis	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)
Breast enlargement	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Uterovaginal prolapse	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Respiratory, thoracic and mediastinal disorders	1	(0.2)	1	(0.2)	4	(0.7)	6	(1.0)	4	(0.6)	8	(1.3)
Asphyxia	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)
Asthma	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Chronic obstructive pulmonary disease	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Laryngeal granuloma	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Nasal septum deviation	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Nasal turbinate hypertrophy	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Pulmonary embolism	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)
Pulmonary mass	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Respiratory failure	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Respiratory tract irritation	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Sleep apnoea syndrome	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.3)	0	(0.0)

Subjects With Serious Adverse Events (Incidence > 0% in Any Column)
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

	Application				SUR				Cumulative			
	MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg		MK-3222 100mg		MK-3222 200mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Surgical and medical procedures	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Gastrectomy	1	(0.2)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Vascular disorders	2	(0.3)	2	(0.3)	6	(1.0)	3	(0.5)	6	(1.0)	5	(0.8)
Aortic dissection	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)
Deep vein thrombosis	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)	2	(0.3)
Haematoma	0	(0.0)	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.2)	0	(0.0)
Hypertensive crisis	1	(0.2)	0	(0.0)	2	(0.3)	1	(0.2)	2	(0.3)	1	(0.2)
Peripheral arterial occlusive disease	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.3)	0	(0.0)
Varicose vein	1	(0.2)	1	(0.2)	1	(0.2)	0	(0.0)	1	(0.2)	1	(0.2)
NULL	1	(0.2)	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.3)
NULL	1	(0.2)	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.3)

Every subject is counted a single time for each applicable row and column.
A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.
[Source: 5.3.5.3-8]

付録 2.7.4-87
Listing of Subjects with Serious Adverse Events
Phase 3: Extension Safety Pool (SUR) All Subjects as Treated

Site Number	Subject ID	Onset Treatment	Rel Day of Onset†	Adverse Event	Intensity	Serious	Related	Action Taken	Outcome
Trial Number = 3222-010									
0104	[redacted]	MK-3222 200 mg	1144	Transient ischaemic attack	Moderate	Y	Not Related	Drug Withdrawn	Recovered/Resolved
0106	[redacted]	MK-3222 200 mg	824	Cellulitis	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
0106	[redacted]	MK-3222 200 mg	1150	Diverticulitis	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
0106	[redacted]	MK-3222 200 mg	1229	Diverticulitis	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
0111	[redacted]	MK-3222 100 mg	944	Osteoarthritis	Mild	Y	Not Related	Dose Not Changed	Recovered/Resolved
0113	[redacted]	MK-3222 200 mg	1088	Spinal cord compression	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
0113	[redacted]	MK-3222 200 mg	1089	Syncope	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
0113	[redacted]	MK-3222 200 mg	1089	Urinary retention	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
0113	[redacted]	MK-3222 200 mg	1089	Urinary tract infection	Moderate	Y	Not Related	Drug Interrupted	Recovered/Resolved
0113	[redacted]	MK-3222 200 mg	1091	Respiratory failure	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
0113	[redacted]	MK-3222 200 mg	1091	Uncoded	Severe	Y	Not Related	Drug Interrupted	Recovered/Resolved
0113	[redacted]	MK-3222 200 mg	933	Inappropriate antidiuretic hormone secretion	Severe	Y	Not Related	Drug Withdrawn	Recovered/Resolved
0114	[redacted]	MK-3222 100 mg	1291	Cervix carcinoma	Moderate	Y	Not Related	Drug Interrupted	Not Recovered/Not Resolved
0115	[redacted]	MK-3222 200 mg	1428	Lobular breast carcinoma in situ	Moderate	Y	Not Related	Drug Interrupted	Recovered/Resolved
0115	[redacted]	MK-3222 200 mg	884	Pulmonary embolism	Moderate	Y	Not Related	Drug Interrupted	Recovered/Resolved
0115	[redacted]	MK-3222 200 mg	899	Deep vein thrombosis	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved

Listing of Subjects with Serious Adverse Events
Phase 3: Extension Safety Pool (SUR) All Subjects as Treated

	Subject ID	Onset Treatment	Rel Day of Onset†	Advers e Event	Intensity	Serious	Related	Action Taken	Outcome
0115	[redacted]	MK-3222 200 mg	640	Deep vein thrombosis	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
0115	[redacted]	MK-3222 200 mg	641	Pulmonary embolism	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
0119	[redacted]	MK-3222 100 mg	919	Sleep apnoea syndrome	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
0119	[redacted]	MK-3222 100 mg	885	Obesity	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
0122	[redacted]	MK-3222 100 mg	1196	Pneumonia	Severe	Y	Related	Dose Not Changed	Recovered/Resolved
0123	[redacted]	MK-3222 200 mg	643	Lumbar spinal stenosis	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
0126	[redacted]	MK-3222 200 mg	469	Acute myocardial infarction	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
0127	[redacted]	MK-3222 200 mg	1242	Cerebrovascular accident	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
0127	[redacted]	MK-3222 100 mg	980	Hypertensive crisis	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
0127	[redacted]	MK-3222 100 mg	980	Transient ischaemic attack	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
0132	[redacted]	MK-3222 200 mg	763	Cellulitis	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
0132	[redacted]	MK-3222 200 mg	763	Cystitis	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
0134	[redacted]	MK-3222 100 mg	497	Gastroenteritis	Moderate	Y	Not Related	Not Applicable	Recovered/Resolved
0134	[redacted]	MK-3222 100 mg	1454	Pulmonary mass	Moderate	Y	Not Related	Dose Not Changed	Not Recovered/Not Resolved
0136	[redacted]	MK-3222 100 mg	1203	Ureteric obstruction	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
0137	[redacted]	MK-3222 100 mg	510	Diverticulum	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
0137	[redacted]	MK-3222 200 mg	1227	Completed suicide	Severe	Y	Not Related	Dose Not Changed	Fatal

Listing of Subjects with Serious Adverse Events
Phase 3: Extension Safety Pool (SUR) All Subjects as Treated

Site Number	Subject ID	Onset Treatment	Rel Day of Onset†	Adverse Event	Intensity	Serious	Related	Action Taken	Outcome
0137	[redacted]	MK-3222 100 mg	760	Rectal adenocarcinoma	Severe	Y	Not Related	Drug Withdrawn	Recovered/Resolved With Sequelae
0137	[redacted]	MK-3222 200 mg	511	Benign pancreatic neoplasm	Severe	Y	Not Related	Dose Not Changed	Not Recovered/Not Resolved
0137	[redacted]	MK-3222 200 mg	511	Bile duct obstruction	Severe	Y	Not Related	Dose Not Changed	Not Recovered/Not Resolved
0138	[redacted]	MK-3222 100 mg	1026	Cellulitis	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
0144	[redacted]	MK-3222 200 mg	987	Inguinal hernia	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
0144	[redacted]	MK-3222 100 mg	455	Osteoarthritis	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
0144	[redacted]	MK-3222 100 mg	645	Septic arthritis staphylococcal	Severe	Y	Related	Drug Withdrawn	Recovered/Resolved With Sequelae
0144	[redacted]	MK-3222 100 mg	799	Arthritis infective Acetabulum	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
0145	[redacted]	MK-3222 200 mg	698	fracture	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
0145	[redacted]	MK-3222 200 mg	705	Peptic ulcer	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
1101	[redacted]	MK-3222 200 mg	694	Papillary thyroid cancer	Severe	Y	Not Related	Drug Withdrawn	Not Recovered/Not Resolved
1101	[redacted]	MK-3222 100 mg	592	Congestive cardiomyopathy	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
1101	[redacted]	MK-3222 100 mg	592	Ventricular tachycardia	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
1101	[redacted]	MK-3222 200 mg	1266	Uncoded	Severe	Y	Not Related	Dose Not Changed	Recovering/Resolving
1102	[redacted]	MK-3222 100 mg	673	Papillary thyroid cancer	Moderate	Y	Not Related	Drug Interrupted	Recovered/Resolved
1104	[redacted]	MK-3222 100 mg	938	Invasive lobular breast carcinoma	Mild	Y	Not Related	Drug Withdrawn	Recovered/Resolved
1106	[redacted]	MK-3222 100 mg	1235	Metastatic carcinoma of the bladder	Moderate	Y	Related	Drug Withdrawn	Fatal

Listing of Subjects with Serious Adverse Events
Phase 3: Extension Safety Pool (SUR) All Subjects as Treated

Site Number	Subject ID	Onset Treatment	Rel Day of Onset†	Adverse Event	Intensity	Serious	Related	Action Taken	Outcome
1106	[redacted]	MK-3222 100 mg	1263	Delirium	Moderate	Y	Not Related	Not Applicable	Not Recovered/Not Resolved
1106	[redacted]	MK-3222 100 mg	1269	Haemorrhage intracranial	Moderate	Y	Not Related	Not Applicable	Fatal
1106	[redacted]	MK-3222 200 mg	959	Basal cell carcinoma	Mild	Y	Not Related	Dose Not Changed	Recovered/Resolved
1108	[redacted]	MK-3222 200 mg	920	Thoracic vertebral fracture	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
1115	[redacted]	MK-3222 100 mg	560	Cerebrovascular accident	Severe	Y	Related	Drug Withdrawn	Recovered/Resolved
1115	[redacted]	MK-3222 100 mg	1167	Atrial fibrillation	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
4402	[redacted]	MK-3222 100 mg	1014	Hypoglycaemia	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
6101	[redacted]	MK-3222 100 mg	785	Leiomyosarcoma	Moderate	Y	Not Related	Drug Withdrawn	Recovered/Resolved
6101	[redacted]	MK-3222 200 mg	1221	Psoriatic arthropathy	Severe	Y	Not Related	Dose Not Changed	Not Recovered/Not Resolved
6101	[redacted]	MK-3222 100 mg	1216	Portal hypertensive gastropathy	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
6101	[redacted]	MK-3222 100 mg	996	Cholelithiasis	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
6101	[redacted]	MK-3222 100 mg	544	Tenosynovitis	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
6101	[redacted]	MK-3222 200 mg	246	Sciatica	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
6101	[redacted]	MK-3222 200 mg	246	Sciatica	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
6101	[redacted]	MK-3222 200 mg	833	Breast enlargement	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
6102	[redacted]	MK-3222 100 mg	407	Cholelithiasis	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
6102	[redacted]	MK-3222 100 mg	1206	Clear cell renal cell carcinoma	Moderate	Y	Not Related	Drug Withdrawn	Recovered/Resolved

Listing of Subjects with Serious Adverse Events
Phase 3: Extension Safety Pool (SUR) All Subjects as Treated

	Subject ID	Onset Treatment	Rel Day of Onset†	Adverse Event	Intensity	Serious	Related	Action Taken	Outcome
6103	[redacted]	MK-3222 100 mg	1314	Diverticulitis	Severe	Y	Not Related	Drug Interrupted	Recovered/Resolved
6104	[redacted]	MK-3222 100 mg	729	Intraductal proliferative breast lesion	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
6106	[redacted]	MK-3222 200 mg	1044	Coronary artery stenosis	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
6107	[redacted]	MK-3222 100 mg	1007	Non-Hodgkin's lymphoma	Severe	Y	Related	Drug Withdrawn	Not Recovered/Not Resolved
8102	[redacted]	MK-3222 200 mg	930	Gastric polyps	Moderate	Y	Related	Drug Interrupted	Not Recovered/Not Resolved
8103	[redacted]	MK-3222 100 mg	852	Gastroenteritis	Severe	Y	Related	Dose Not Changed	Recovered/Resolved
8104	[redacted]	MK-3222 100 mg	772	Breast cancer	Severe	Y	Related	Drug Withdrawn	Not Recovered/Not Resolved
8105	[redacted]	MK-3222 100 mg	721	Diffuse large B-cell lymphoma	Severe	Y	Related	Drug Withdrawn	Not Recovered/Not Resolved
8105	[redacted]	MK-3222 200 mg	1237	Hepatitis E	Severe	Y	Not Related	Drug Withdrawn	Recovered/Resolved
8108	[redacted]	MK-3222 200 mg	1087	Large intestine polyp	Moderate	Y	Related	Dose Not Changed	Recovered/Resolved
8108	[redacted]	MK-3222 100 mg	648	Sleep apnoea syndrome	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
8109	[redacted]	MK-3222 100 mg	979	Anal fissure	Mild	Y	Not Related	Dose Not Changed	Recovered/Resolved
8110	[redacted]	MK-3222 200 mg	617	Cholelithiasis	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
8111	[redacted]	MK-3222 200 mg	1063	Colitis ischaemic	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
8119	[redacted]	MK-3222 100 mg	981	Thrombotic cerebral infarction	Moderate	Y	Not Related	Dose Not Changed	Recovering/Resolving
8122	[redacted]	MK-3222 200 mg	918	Large intestine polyp	Mild	Y	Not Related	Dose Not Changed	Recovered/Resolved
8124	[redacted]	MK-3222 100 mg	463	Brain contusion	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved

Listing of Subjects with Serious Adverse Events
Phase 3: Extension Safety Pool (SUR) All Subjects as Treated

Site Number	Subject ID	Onset Treatment	Rel Day of Onset†	Adverse Event	Intensity	Serious	Related	Action Taken	Outcome
8124	[redacted]	MK-3222 100 mg	463	Loss of consciousness	Severe	Y	Related	Dose Not Changed	Recovered/Resolved
8124	[redacted]	MK-3222 100 mg	463	Skull fracture	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
8124	[redacted]	MK-3222 100 mg	653	Large intestine polyp	Mild	Y	Not Related	Dose Not Changed	Recovered/Resolved
8125	[redacted]	MK-3222 100 mg	525	Intracranial aneurysm	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
8133	[redacted]	MK-3222 200 mg	1184	Aortic dissection	Severe	Y	Not Related	Dose Not Changed	Not Recovered/Not Resolved
8141	[redacted]	MK-3222 100 mg	741	Carotid artery stenosis	Severe	Y	Related	Dose Not Changed	Recovered/Resolved
8141	[redacted]	MK-3222 100 mg	741	Cerebral infarction	Severe	Y	Related	Dose Not Changed	Recovered/Resolved
8141	[redacted]	MK-3222 100 mg	901	Angina pectoris	Severe	Y	Related	Dose Not Changed	Recovered/Resolved
8142	[redacted]	MK-3222 100 mg	561	Cerebral haemorrhage	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
Trial Number = 3222-011									
0166	[redacted]	MK-3222 100 mg	640	Toxicity to various agents	Severe	Y	Not Related	Dose Not Changed	Fatal
0172	[redacted]	MK-3222 200 mg	1006	Breast cancer metastatic	Severe	Y	Not Related	Drug Withdrawn	Not Recovered/Not Resolved
0172	[redacted]	MK-3222 100 mg	510	Adenomyosis	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
0172	[redacted]	MK-3222 100 mg	557	Spondylolisthesis	Severe	Y	Not Related	Drug Interrupted	Recovered/Resolved
0172	[redacted]	MK-3222 100 mg	566	Intervertebral disc degeneration	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
0176	[redacted]	MK-3222 200 mg	986	Gastric ulcer	Severe	Y	Not Related	Dose Not Changed	Recovering/Resolving
0176	[redacted]	MK-3222 200 mg	986	Gastrointestinal haemorrhage	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved

Listing of Subjects with Serious Adverse Events
Phase 3: Extension Safety Pool (SUR) All Subjects as Treated

Site Number	Subject ID	Onset Treatment	Rel Day of Onset†	Adverse Event	Intensity	Serious	Related	Action Taken	Outcome
0176	[redacted]	MK-3222 200 mg	986	Haemorrhagic anaemia	Severe	Y	Not Related	Dose Not Changed	Recovering/Resolving
0178	[redacted]	MK-3222 100 mg	783	Appendicitis	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
0179	[redacted]	MK-3222 100 mg	1223	Appendicitis	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
0182	[redacted]	MK-3222 100 mg	1041	Cerebrovascular accident	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
0184	[redacted]	MK-3222 100 mg	623	Procedural haemorrhage	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
0187	[redacted]	MK-3222 100 mg	441	Pneumonia	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
0187	[redacted]	MK-3222 100 mg	978	Death	Severe	Y	Not Related	Not Applicable	Fatal
1162	[redacted]	MK-3222 100 mg	1048	Cellulitis	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
1162	[redacted]	MK-3222 200 mg	1031	Bone contusion	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
1162	[redacted]	MK-3222 200 mg	1219	Basal cell carcinoma	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
1163	[redacted]	MK-3222 200 mg	717	Bladder transitional cell carcinoma	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
1164	[redacted]	MK-3222 200 mg	768	Acute myocardial infarction	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
1164	[redacted]	MK-3222 100 mg	908	Viral infection	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
1171	[redacted]	MK-3222 100 mg	1017	Keratosis follicular	Severe	Y	Not Related	Drug Interrupted	Recovered/Resolved
1171	[redacted]	MK-3222 100 mg	1027	Cellulitis of male external genital organ	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
1171	[redacted]	MK-3222 100 mg	1027	Scrotal abscess	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
3101	[redacted]	MK-3222 200 mg	552	Obesity	Moderate	Y	Not Related	Drug Interrupted	Recovered/Resolved

Listing of Subjects with Serious Adverse Events
Phase 3: Extension Safety Pool (SUR) All Subjects as Treated

Site Number	Subject ID	Onset Treatment	Rel Day of Onset†	Adverse Event	Intensity	Serious	Related	Action Taken	Outcome
3204	[redacted]	MK-3222 100 mg	425	Calculus urinary	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
3204	[redacted]	MK-3222 100 mg	430	Procedural pain	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
3207	[redacted]	MK-3222 200 mg	1053	Coronary artery stenosis	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
3306	[redacted]	MK-3222 100 mg	1146	Wrist fracture	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
3307	[redacted]	MK-3222 200 mg	620	Laceration	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
3307	[redacted]	MK-3222 100 mg	489	Chest pain	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
3601	[redacted]	MK-3222 200 mg	573	Varicose vein	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
3602	[redacted]	MK-3222 200 mg	642	Epilepsy	Mild	Y	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
3602	[redacted]	MK-3222 200 mg	748	Spondylolisthesis	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
3603	[redacted]	MK-3222 100 mg	353	Cholelithiasis	Mild	Y	Not Related	Dose Not Changed	Recovered/Resolved
3906	[redacted]	MK-3222 200 mg	765	Rectal adenocarcinoma	Severe	Y	Not Related	Drug Withdrawn	Recovered/Resolved
3909	[redacted]	MK-3222 100 mg	493	Enterocolitis	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
4202	[redacted]	MK-3222 100 mg	856	Diverticulitis	Severe	Y	Not Related	Drug Withdrawn	Recovered/Resolved
4301	[redacted]	MK-3222 100 mg	754	Carotid artery stenosis	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
4801	[redacted]	MK-3222 200 mg	746	Asphyxia	Severe	Y	Not Related	Drug Withdrawn	Fatal
4801	[redacted]	MK-3222 100 mg	566	Psoriatic arthropathy	Moderate	Y	Not Related	Drug Withdrawn	Recovered/Resolved With Sequelae
4801	[redacted]	MK-3222 100 mg	742	Haematoma	Moderate	Y	Not Related	Dose Not Changed	Recovering/Resolving

Listing of Subjects with Serious Adverse Events
Phase 3: Extension Safety Pool (SUR) All Subjects as Treated

Site Number	Subject ID	Onset Treatment	Rel Day of Onset†	Adverse Event	Intensity	Serious	Related	Action Taken	Outcome
4802	[redacted]	MK-3222 100 mg	603	Psoriatic arthropathy	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
4802	[redacted]	MK-3222 100 mg	939	Hiatus hernia	Moderate	Y	Not Related	Dose Not Changed	Recovering/Resolving
4802	[redacted]	MK-3222 200 mg	842	Limb injury	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
4804	[redacted]	MK-3222 200 mg	1043	Jaw cyst	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
4804	[redacted]	MK-3222 200 mg	529	Chronic sinusitis	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
4804	[redacted]	MK-3222 200 mg	942	Nasal septum deviation	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
4804	[redacted]	MK-3222 200 mg	942	Nasal turbinate hypertrophy	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
4804	[redacted]	MK-3222 200 mg	1134	Ischaemic cerebral infarction	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
4804	[redacted]	MK-3222 200 mg	1190	Patellofemoral pain syndrome	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
4804	[redacted]	MK-3222 200 mg	1070	Carpal tunnel syndrome	Moderate	Y	Not Related	Dose Not Changed	Not Recovered/Not Resolved
4804	[redacted]	MK-3222 200 mg	1138	Coronary artery disease	Moderate	Y	Not Related	Drug Withdrawn	Not Recovered/Not Resolved
4804	[redacted]	MK-3222 200 mg	874	Acute myocardial infarction	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
4804	[redacted]	MK-3222 200 mg	874	Coronary artery disease	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
4805	[redacted]	MK-3222 200 mg	867	Appendicitis	Severe	Y	Related	Dose Not Changed	Recovered/Resolved
4805	[redacted]	MK-3222 200 mg	867	Peritonitis	Moderate	Y	Related	Dose Not Changed	Recovered/Resolved
4807	[redacted]	MK-3222 100 mg	797	Varicose vein	Mild	Y	Not Related	Dose Not Changed	Recovered/Resolved
4807	[redacted]	MK-3222 200 mg	514	Cataract	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae

Listing of Subjects with Serious Adverse Events
Phase 3: Extension Safety Pool (SUR) All Subjects as Treated

Site	Subject	Onset	Rel Day of Onset	Adverse Event	Intensity	Serious	Related	Action Taken	Outcome
4901	[redacted]	MK-3222 200 mg	1144	Facial bones fracture	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
4902	[redacted]	MK-3222 200 mg	589	Gastroenteritis bacterial	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
4902	[redacted]	MK-3222 100 mg	1004	Intervertebral disc protrusion	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
4904	[redacted]	MK-3222 100 mg	935	Peripheral arterial occlusive disease	Mild	Y	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
4905	[redacted]	MK-3222 100 mg	449	Basal cell carcinoma	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
4908	[redacted]	MK-3222 200 mg	968	Coronary artery stenosis	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
4908	[redacted]	MK-3222 200 mg	583	Intervertebral disc protrusion	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
4911	[redacted]	MK-3222 200 mg	225	Tendon rupture	Severe	Y	Not Related	Dose Not Changed	Recovering/Resolving
4911	[redacted]	MK-3222 200 mg	833	Basal cell carcinoma	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
4911	[redacted]	MK-3222 100 mg	942	Intervertebral disc protrusion	Severe	Y	Not Related	Dose Not Changed	Not Recovered/Not Resolved
4911	[redacted]	MK-3222 100 mg	893	Diverticulitis	Severe	Y	Related	Dose Not Changed	Recovered/Resolved
4912	[redacted]	MK-3222 100 mg	783	Cholelithiasis	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
4913	[redacted]	MK-3222 100 mg	533	Foot fracture	Severe	Y	Not Related	Dose Not Changed	Not Recovered/Not Resolved
4913	[redacted]	MK-3222 100 mg	1031	Incisional hernia	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
4913	[redacted]	MK-3222 100 mg	688	Appendicitis	Severe	Y	Related	Dose Not Changed	Recovered/Resolved
4913	[redacted]	MK-3222 200 mg	764	Prostate cancer	Severe	Y	Not Related	Drug Withdrawn	Not Recovered/Not Resolved
4915	[redacted]	MK-3222 100 mg	575	Depression	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae

Listing of Subjects with Serious Adverse Events
Phase 3: Extension Safety Pool (SUR) All Subjects as Treated

Site Number	Subject ID	Onset Treatment	Rel Day of Onset†	Adverse Event	Intensity	Serious	Related	Action Taken	Outcome
4915	[redacted]	MK-3222 200 mg	1075	Chronic obstructive pulmonary disease	Severe	Y	Related	Drug Withdrawn	Recovered/Resolved
4915	[redacted]	MK-3222 100 mg	1221	Coronary artery disease	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
4916	[redacted]	MK-3222 100 mg	706	Non-cardiac chest pain	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
4917	[redacted]	MK-3222 100 mg	729	Psoriatic arthropathy	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
4918	[redacted]	MK-3222 200 mg	610	Lipoma	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
4918	[redacted]	MK-3222 100 mg	629	Thyrotoxic crisis	Severe	Y	Related	Drug Withdrawn	Recovered/Resolved
4918	[redacted]	MK-3222 100 mg	922	Depression	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
4919	[redacted]	MK-3222 200 mg	404	Atrial fibrillation	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
4921	[redacted]	MK-3222 100 mg	594	Peripheral arterial occlusive disease	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
4921	[redacted]	MK-3222 100 mg	450	Hypertensive crisis	Moderate	Y	Related	Dose Not Changed	Recovered/Resolved
4921	[redacted]	MK-3222 200 mg	922	Spinal column stenosis	Severe	Y	Not Related	Drug Interrupted	Recovered/Resolved With Sequelae
4922	[redacted]	MK-3222 100 mg	685	Rotator cuff syndrome	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
4922	[redacted]	MK-3222 100 mg	756	Calculus urinary	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
4922	[redacted]	MK-3222 100 mg	756	Nephrolithiasis	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
4923	[redacted]	MK-3222 100 mg	1102	Atrioventricular block second degree	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
4923	[redacted]	MK-3222 100 mg	580	Tendon rupture	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
4923	[redacted]	MK-3222 100 mg	648	Atrial fibrillation	Mild	Y	Not Related	Dose Not Changed	Recovered/Resolved

Listing of Subjects with Serious Adverse Events
Phase 3: Extension Safety Pool (SUR) All Subjects as Treated

Site Number	Subject ID	Onset Treatment	Rel Day of Onset†	Adverse Event	Intensity	Serious	Related	Action Taken	Outcome
4923	[redacted]	MK-3222 100 mg	754	Nerve root compression	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
4923	[redacted]	MK-3222 200 mg	996	Large intestine polyp	Mild	Y	Not Related	Dose Not Changed	Recovered/Resolved
4924	[redacted]	MK-3222 200 mg	1249	Hypertensive crisis	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
4924	[redacted]	MK-3222 200 mg	919	Nephrolithiasis	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
4924	[redacted]	MK-3222 200 mg	481	Infectious colitis	Severe	Y	Related	Drug Interrupted	Recovered/Resolved
4924	[redacted]	MK-3222 200 mg	638	Basal cell carcinoma	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
4924	[redacted]	MK-3222 200 mg	785	Basal cell carcinoma	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
4924	[redacted]	MK-3222 200 mg	1010	Myocardial infarction	Severe	Y	Not Related	Drug Interrupted	Recovered/Resolved With Sequelae
4925	[redacted]	MK-3222 100 mg	894	Umbilical hernia	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
4925	[redacted]	MK-3222 100 mg	969	Ovarian cancer	Severe	Y	Not Related	Drug Withdrawn	Not Recovered/Not Resolved
4926	[redacted]	MK-3222 200 mg	386	Umbilical hernia	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
4926	[redacted]	MK-3222 200 mg	1077	Pneumonia	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
4926	[redacted]	MK-3222 200 mg	758	Pneumonia mycoplasmal	Severe	Y	Related	Drug Interrupted	Recovered/Resolved
4926	[redacted]	MK-3222 200 mg	800	Device related sepsis	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
4926	[redacted]	MK-3222 200 mg	805	Pneumonia	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
4926	[redacted]	MK-3222 200 mg	808	Intensive care unit acquired weakness	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
4927	[redacted]	MK-3222 100 mg	884	Lower limb fracture	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae

Listing of Subjects with Serious Adverse Events
Phase 3: Extension Safety Pool (SUR) All Subjects as Treated

Site Number	Subject ID	Onset Treatment	Rel Day of Onset†	Adverse Event	Intensity	Serious	Related	Action Taken	Outcome
4928	[redacted]	MK-3222 200 mg	948	Non-cardiac chest pain	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
4928	[redacted]	MK-3222 100 mg	977	Lipoma	Mild	Y	Not Related	Dose Not Changed	Recovered/Resolved
4933	[redacted]	MK-3222 200 mg	860	Asthma	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
4934	[redacted]	MK-3222 200 mg	709	Malocclusion	Mild	Y	Not Related	Dose Not Changed	Recovered/Resolved
4934	[redacted]	MK-3222 200 mg	1125	Malignant melanoma in situ	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
4934	[redacted]	MK-3222 200 mg	1077	Duodenal polyp	Moderate	Y	Not Related	Dose Not Changed	Not Recovered/Not Resolved
4934	[redacted]	MK-3222 200 mg	679	Uterovaginal prolapse	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
4934	[redacted]	MK-3222 200 mg	904	Diverticulum intestinal	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
4938	[redacted]	MK-3222 100 mg	1273	Supraventricular tachycardia	Severe	Y		Dose Not Changed	Not Recovered/Not Resolved
4939	[redacted]	MK-3222 100 mg	247	Insomnia	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
4939	[redacted]	MK-3222 200 mg	512	Inguinal hernia	Mild	Y	Not Related	Dose Not Changed	Recovered/Resolved

Listing of Subjects with Serious Adverse Events
Phase 3: Extension Safety Pool (SUR) All Subjects as Treated

Site Number	Subject ID	Onset Treatment	Rel Day of Onset†	Adverse Event	Intensity	Serious	Related	Action Taken	Outcome
4939	[redacted]	MK-3222 200 mg	829	Respiratory tract irritation	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
4939	[redacted]	MK-3222 200 mg	660	Otitis media acute	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
4939	[redacted]	MK-3222 100 mg	467	Gastritis erosive	Moderate	Y	Related	Dose Not Changed	Recovered/Resolved
4939	[redacted]	MK-3222 100 mg	470	Mesenteric artery thrombosis	Moderate	Y	Related	Dose Not Changed	Recovered/Resolved With Sequelae
4939	[redacted]	MK-3222 100 mg	474	Laryngeal granuloma	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved

Action Taken: None = DOSE NOT CHANGED, Reduced = DOSE REDUCED, Interrupted = DRUG INTERRUPTED, Discontinued = DRUG WITHDRAWN, Increased = DOSE INCREASED, N/A = NOT APPLICABLE.

Outcome: Resolved = RECOVERED/RESOLVED, Resolving = RECOVERING/RESOLVING, Sequelae = RECOVERED/RESOLVED WITH SEQUELAE, Not resolved = NOT RECOVERED/NOT RESOLVED.

Related: Investigator-assessed relationship of the adverse event to study medication.

† Relative to start of Base Period

Note: For the Phase 2 study (P003), the adverse event field of "action/outcome" reported as "None" in the legacy data base was mapped to "Not Applicable" and "Additional Medication, Hospitalization, Disability, Death or Therapeutic Procedure" was mapped to a "blank" field. For the Phase 3 trials (P010 and P011), the "action/outcome" of "Not Applicable" was used for AEs where no study medication was administered or for AEs occurring before the first dose of study medication. The "action /outcome" of "None" applies to AEs occurring in the follow-up period, overdoses in absence of an AE, or where no change was made to study medication.

[Source: 5.3.5.3-8]

付録 2.7.4-88
Listing of Subjects with Adverse Events resulting in Discontinuation
Phase 3: Extension Safety Pool (SUR) All Subjects as Treated

Site Number	Subject ID	Onset Treatment	Rel Day of Onset†	Adverse Event	Intensity	Serious	Related	Action Taken	Outcome
Trial Number = 3222-010									
0104	[redacted]	MK-3222 200 mg	1144	Transient ischaemic attack	Moderate	Y	Not Related	Drug Withdrawn	Recovered/Resolved
0107	[redacted]	MK-3222 100 mg	802	Arthritis	Moderate	N	Related	Drug Withdrawn	Recovered/Resolved
0112	[redacted]	MK-3222 200 mg	998	Hyperglycaemia	Moderate	N	Not Related	Drug Withdrawn	Not Recovered/Not Resolved
0112	[redacted]	MK-3222 200 mg	998	Tachycardia	Moderate	N	Not Related	Drug Withdrawn	Not Recovered/Not Resolved
0113	[redacted]	MK-3222 200 mg	933	Inappropriate antidiuretic hormone secretion	Severe	Y	Not Related	Drug Withdrawn	Recovered/Resolved
0137	[redacted]	MK-3222 100 mg	760	Rectal adenocarcinoma	Severe	Y	Not Related	Drug Withdrawn	Recovered/Resolved With Sequelae
0144	[redacted]	MK-3222 100 mg	645	Septic arthritis staphylococcal	Severe	Y	Related	Drug Withdrawn	Recovered/Resolved With Sequelae
1101	[redacted]	MK-3222 200 mg	694	Papillary thyroid cancer	Severe	Y	Not Related	Drug Withdrawn	Not Recovered/Not Resolved
1104	[redacted]	MK-3222 100 mg	938	Invasive lobular breast carcinoma	Mild	Y	Not Related	Drug Withdrawn	Recovered/Resolved
1106	[redacted]	MK-3222 100 mg	1235	Metastatic carcinoma of the bladder	Moderate	Y	Related	Drug Withdrawn	Fatal
1115	[redacted]	MK-3222 100 mg	560	Cerebrovascular accident	Severe	Y	Related	Drug Withdrawn	Recovered/Resolved
6101	[redacted]	MK-3222 100 mg	785	Leiomyosarcoma	Moderate	Y	Not Related	Drug Withdrawn	Recovered/Resolved
6102	[redacted]	MK-3222 100 mg	1206	Clear cell renal cell carcinoma	Moderate	Y	Not Related	Drug Withdrawn	Recovered/Resolved
6107	[redacted]	MK-3222 100 mg	1007	Non-Hodgkin's lymphoma	Severe	Y	Related	Drug Withdrawn	Not Recovered/Not Resolved
8104	[redacted]	MK-3222 100 mg	772	Breast cancer	Severe	Y	Related	Drug Withdrawn	Not Recovered/Not Resolved
8105	[redacted]	MK-3222 100 mg	721	Diffuse large B-cell lymphoma	Severe	Y	Related	Drug Withdrawn	Not Recovered/Not Resolved
8105	[redacted]	MK-3222 200 mg	1237	Hepatitis E	Severe	Y	Not Related	Drug Withdrawn	Recovered/Resolved

Listing of Subjects with Adverse Events resulting in Discontinuation
Phase 3: Extension Safety Pool (SUR) All Subjects as Treated

Site Number	Subject ID	Onset Treatment	Rel Day of Onset†	Adverse Event	Intensity	Serious	Related	Action Taken	Outcome
Trial Number = 3222-011									
0163	[redacted]	MK-3222 200 mg	700	Psoriasis	Moderate	N	Not Related	Drug Withdrawn	Recovered/Resolved
0172	[redacted]	MK-3222 200 mg	1006	Breast cancer metastatic	Severe	Y	Not Related	Drug Withdrawn	Not Recovered/Not Resolved
0172	[redacted]	MK-3222 100 mg	1092	Psoriatic arthropathy	Severe	N	Not Related	Drug Withdrawn	Not Recovered/Not Resolved
1162	[redacted]	MK-3222 100 mg	554	Eczema	Severe	N	Not Related	Drug Withdrawn	Not Recovered/Not Resolved
3204	[redacted]	MK-3222 100 mg	682	Arthritis	Severe	N	Not Related	Drug Withdrawn	Recovering/Resolving
3902	[redacted]	MK-3222 100 mg	869	Aspartate aminotransferase increased	Mild	N	Not Related	Drug Withdrawn	Not Recovered/Not Resolved
3906	[redacted]	MK-3222 200 mg	765	Rectal adenocarcinoma	Severe	Y	Not Related	Drug Withdrawn	Recovered/Resolved
4202	[redacted]	MK-3222 100 mg	856	Diverticulitis	Severe	Y	Not Related	Drug Withdrawn	Recovered/Resolved
4501	[redacted]	MK-3222 100 mg	450	Psoriatic arthropathy	Moderate	N	Not Related	Drug Withdrawn	Recovering/Resolving
4801	[redacted]	MK-3222 200 mg	746	Asphyxia	Severe	Y	Not Related	Drug Withdrawn	Fatal
4801	[redacted]	MK-3222 100 mg	566	Psoriatic arthropathy	Moderate	Y	Not Related	Drug Withdrawn	Recovered/Resolved With Sequelae
4804	[redacted]	MK-3222 200 mg	1138	Coronary artery disease	Moderate	Y	Not Related	Drug Withdrawn	Not Recovered/Not Resolved
4913	[redacted]	MK-3222 200 mg	764	Prostate cancer	Severe	Y	Not Related	Drug Withdrawn	Not Recovered/Not Resolved
4915	[redacted]	MK-3222 100 mg	417	Dysphagia	Moderate	N	Related	Drug Withdrawn	Recovered/Resolved
4915	[redacted]	MK-3222 200 mg	1075	Chronic obstructive pulmonary disease	Severe	Y	Related	Drug Withdrawn	Recovered/Resolved
4915	[redacted]	MK-3222 200 mg	1082	Bronchitis	Moderate	N	Related	Drug Withdrawn	Recovering/Resolving
4918	[redacted]	MK-3222 100 mg	629	Hyperthyroidism	Moderate	N	Related	Drug Withdrawn	Not Recovered/Not Resolved

Listing of Subjects with Adverse Events resulting in Discontinuation
Phase 3: Extension Safety Pool (SUR) All Subjects as Treated

Site Number	Subject ID	Onset Treatment	Rel Day of Onset†	Adverse Event	Intensity	Serious	Related	Action Taken	Outcome
4918	[redacted]	MK-3222 100 mg	629	Thyrotoxic crisis	Severe	Y	Related	Drug Withdrawn	Recovered/Resolved
4921	[redacted]	MK-3222 100 mg	532	Psoriatic arthropathy	Severe	N	Related	Drug Withdrawn	Not Recovered/Not Resolved
4925	[redacted]	MK-3222 100 mg	969	Ovarian cancer	Severe	Y	Not Related	Drug Withdrawn	Not Recovered/Not Resolved
4928	[redacted]	MK-3222 200 mg	660	Psoriasis	Moderate	N	Related	Drug Withdrawn	Recovered/Resolved

Action Taken: None = DOSE NOT CHANGED, Reduced = DOSE REDUCED, Interrupted = DRUG INTERRUPTED, Discontinued = DRUG WITHDRAWN, Increased = DOSE INCREASED, N/A = NOT APPLICABLE.

Outcome: Resolved = RECOVERED/RESOLVED, Resolving = RECOVERING/RESOLVING, Sequelae = RECOVERED/RESOLVED WITH SEQUELAE, Not resolved = NOT RECOVERED/NOT RESOLVED.

Related: Investigator-assessed relationship of the adverse event to study medication.

† Relative to start of Base Period

Note: For the Phase 2 study (P003), the adverse event field of "action/outcome" reported as "None" in the legacy data base was mapped to "Not Applicable" and "Additional Medication, Hospitalization, Disability, Death or Therapeutic Procedure" was mapped to a "blank" field. For the Phase 3 trials (P010 and P011), the "action/outcome" of "Not Applicable" was used for AEs where no study medication was administered or for AEs occurring before the first dose of study medication. The "action /outcome" of "None" applies to AEs occurring in the follow-up period, overdoses in absence of an AE, or where no change was made to study medication.

[Source: 5.3.5.3-8]

付録 2.7.4-89
Narratives for Subjects with Hypersensitivity Events
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

Subject [redacted], a 6[redacted]-year-old Asian female with a medical history of psoriasis, back pain, angina pectoris, Prinzmetal angina, cataract, chronic gastritis, breast cyst, large intestine polyp, drug hypersensitivity, dyslipidemia, osteoporosis, hypertension, and arthralgia. The subject experienced 2 occurrences of hypersensitivity events (drug eruption) during the follow-up period of the study. On Day 1, the subject was randomized and received placebo for Part 1, rerandomized to tildrakizumab 100 mg for Part 2 (Day 85) and Part 3 (Day 281) in the base study and continued on this treatment into the extension study (Day 533 through Day 701). Relevant concomitant medications included acetaminophen, amino acids (unspecified) (+) electrolytes (unspecified) (+) vitamins (unspecified), *Clostridium butyricum*, cyclophosphamide, dextrose, dextrose (+) sodium chloride (+) sodium lactate, epinastine hydrochloride, ethacridine lactate, filgrastim, fosaprepitant dimeglumine, furosemide, granisetron, heparin sodium, insulin human, lansoprazole, lenograstimmagnesium oxide, meperidine hydrochloride, mucopolysaccharide polysulfate, pirarubicin, potassium chloride, prednisolone, rituximab, sodium gualenate, sodium picosulfate, and vincristine sulfate. The subject's last dose of tildrakizumab 100 mg was taken on Day 701. On Day 721, an SAE of diffuse large B-cell lymphoma (severe intensity, not resolved) was reported. The subject was discontinued from the study on Day 729 in response to the event of diffuse large B-cell lymphoma. On Day 761 (during the follow- up/wash-out period), the subject experienced the event of drug eruption (first occurrence). Treatment included epinastine, and hydrochloride diphenhydramine hydrochloride (+) enoxolone (+) zinc oxide. The drug eruption (first occurrence) was considered resolved on Day 769. On Day 782 (81 days after the last dose of study medication, during the follow- up/wash-out period), the subject experienced a second occurrence of drug eruption which was considered resolved on Day 800. Action taken with regard to study medication was not applicable. Both events of drug eruptions were considered to be mild in intensity and were assessed by the investigator to be not related to the study medication but were considered related to concomitant medications (filgrastim and lansoprazole). Last contact with the subject occurred at the end of the follow-up period on Day 841.

Subject [redacted], a 3[redacted]-year-old Asian male with no other medical history except psoriasis, experienced a hypersensitivity event of urticaria on Day 1026. On Day 1, the subject was randomized to and received tildrakizumab 100 mg for Part 1 in the base study and continued on this treatment for Parts 2 and 3, and into the extension study (start Day 533). Relevant concomitant medication included loxoprofen sodium. On Day 1026, the subject experienced a nonserious event of urticaria which resolved after 10 minutes. No additional information and no treatment were reported for this event. No action was taken with regard to study medication. The subject's last dose of tildrakizumab 100 mg administered prior to the event was on Day 953 with subsequent administration of study medication through Day 1205. The event of urticaria was considered to be m ld in intensity and was assessed by the investigator to be not related to the study medication.

Subject [redacted], a 6[redacted]-year-old Asian male with a medical history of psoriasis, seborrheic keratosis, and former tobacco user (31 pack years), experienced a hypersensitivity event of urticaria on Day 1030. On Day 1, the subject was randomized to and received placebo for Part 1 in the base study,

was rerandomized to tildrakizumab 200 mg for Part 2 (Day 82) and continued on this treatment for Part 3 (Day 278) and into the extension study (start Day 530). On Day 1030, the subject experienced an event of urticaria and was treated with azelastine hydrochloride (on Day 1031), white petrolatum, diphenhydramine hydrochloride (+) enoxolone (+) zinc oxide (Day 1032 to ongoing), and bepotastine besylate (Day 1032 to Day 1085). The event of urticaria was considered resolved on Day 1085. No additional information was reported for this event. No action was taken with regard to study medication and the subject continued in the extension study. The subject's last dose of tildrakizumab 200 mg prior to the event was on Day 782. The event of urticaria was considered to be mild in intensity and was assessed by the investigator to be not related to the study medication.

Subject [redacted], a 5[redacted]-year-old white male with a medical history of inguinal hernia, drug hypersensitivity, iodine allergy, meningitis, type 2 diabetes mellitus, psoriasis, hypertension, and former tobacco user (3 pack years), had 2 hypersensitivity events of urticaria on Day 45 and Day 1192. On Day 1, the subject was randomized to placebo for Part 1, then rerandomized to tildrakizumab 100 mg for Part 2 (Day 85) and Part 3 in the base study, and continued receiving this treatment in the extension study (start Day 533). Relevant concomitant medications included amlodipine, atenolol, glyburide, metformin, hydrochlorothiazide, irbesartan, insulin, insulin glargine, aspirin, atorvastatin, collagen, and acetaminophen. On Day 45, the subject experienced the first event of urticaria, with swelling of the tongue and left side of the throat. The subject's last dose of study medication before this event was on Day 29. No rash, itching or red eyes were reported. The subject was referred to the ER. No blood tests or any other tests were performed. The subject was treated only with diphenhydramine 50 mg PO BID until Day 47. The event of urticaria was considered resolved on Day 47 and diagnosed as food allergic reaction. On Day 88, cetirizine hydrochloride was started for the treatment of urticaria (stop date was not reported). On Day 533, the subject enrolled in the extension study. On Day 1192, the subject experienced the second event of urticaria which had worsened on Day 1193. The subject's last dose of tildrakizumab 100 mg prior to this report of urticaria was on Day 1121. The subject was treated with diphenhydramine hydrochloride (Day 1193 to Day 1196) and prednisone (Day 1193 to Day 1203). On Day 1200, the second event of urticaria was considered resolved. No action was taken with regard to study medication in response to both events of urticaria. The subject continued in the study. Both events of urticaria were considered to be moderate in intensity and were assessed by the investigator to be not related to the study medication.

Subject [redacted], a 6[redacted]-year-old Asian male with a medical history of psoriasis, seborrheic keratosis, and former tobacco user (31 pack years), experienced a hypersensitivity event of urticaria on Day 1030. On Day 1, the subject was randomized to and received placebo for Part 1 in the base study, was rerandomized to tildrakizumab 200 mg for Part 2 (Day 82) and continued on this treatment for Part 3 (Day 278) and into the extension study (start Day 530). On Day 1030, the subject experienced an event of urticaria and was treated with azelastine hydrochloride (on Day 1031), white petrolatum, diphenhydramine hydrochloride (+) enoxolone (+) zinc oxide (Day 1032 to ongoing), and bepotastine besylate (Day 1032 to Day 1085). The event of urticaria was considered resolved on Day 1085. No additional information was reported for this event. No action was taken with regard to study medication and the subject continued in the extension study. The subject's last dose of tildrakizumab 200 mg prior to the event was on Day 782. The event of urticaria was considered to be mild in intensity and was assessed by the investigator to be not related to the study medication.

Subject [redacted], a 5[redacted]-year-old white male with a medical history of inguinal hernia, drug

hypersensitivity, iodine allergy, meningitis, type 2 diabetes mellitus, psoriasis, hypertension, and former tobacco user (3 pack years), had 2 hypersensitivity events of urticaria on Day 45 and Day 1192. On Day 1, the subject was randomized to placebo for Part 1, then rerandomized to tildrakizumab 100 mg for Part 2 (Day 85) and Part 3 in the base study, and continued receiving this treatment in the extension study (start Day 533). Relevant concomitant medications included amlodipine, atenolol, glyburide, metformin, hydrochlorothiazide, irbesartan, insulin, insulin glargine, aspirin, atorvastatin, collagen, and acetaminophen. On Day 45, the subject experienced the first event of urticaria, with swelling of the tongue and left side of the throat. The subject's last dose of study medication before this event was on Day 29. No rash, itching or red eyes were reported. The subject was referred to the ER. No blood tests or any other tests were performed. The subject was treated only with diphenhydramine 50 mg PO BID until Day 47. The event of urticaria was considered resolved on Day 47 and diagnosed as food allergic reaction. On Day 88, cetirizine hydrochloride was started for the treatment of urticaria (stop date was not reported). On Day 533, the subject enrolled in the extension study. On Day 1192, the subject experienced the second event of urticaria which had worsened on Day 1193. The subject's last dose of tildrakizumab 100 mg prior to this report of urticaria was on Day 1121. The subject was treated with diphenhydramine hydrochloride (Day 1193 to Day 1196) and prednisone (Day 1193 to Day 1203). On Day 1200, the second event of urticaria was considered resolved. No action was taken with regard to study medication in response to both events of urticaria. The subject continued in the study. Both events of urticaria were considered to be moderate in intensity and were assessed by the investigator to be not related to the study medication.
[Source: 5.3.5.3-8]

付録 2.7.4-90
Narratives for Subjects with Confirmed MACE/Extended MACE Events
Phase 3: Extension Safety Pool (SUR)
All Subjects as Treated

Subject [redacted], a 5[redacted]-year-old Asian male with a medical history of psoriasis, seasonal allergy, and tobacco use (18 pack years) was reported to have had a confirmed MACE event due to thrombotic cerebral infarction on Day 981. On Day 1, the subject was randomized to and received tildrakizumab 100 mg for Part 1 in the base study and continued on this treatment for Parts 2 and 3, and into the extension study (start Day 526). On Day 981, the subject experienced an SAE of thrombotic cerebral infarction. The subject also experienced hypoesthesia (numbness of extremities) and was hospitalized. A brain magnetic resonance imaging (MRI) and head magnetic resonance angiography (MRA) were performed on Day 981, and showed suspected observation as cerebral infarction from the left thalamus to crus posterius capsulae internae; no acute infarction and left posterior cerebral artery stenosis. A head (brain) computed CT showed no obvious abnormal findings on Day 981. Treatment for the event included clopidogrel bisulfate 75 mg, argatroban, cilostazol, dextrose (+) electrolytes (unspecified) (+) sodium lactate, edaravone, electrolytes (unspecified) (+) sodium acetate, and lansoprazole 15 mg tablet, QD. On Day 984, a follow-up brain MRI reported acute infarction on left outside of thalamus, left posterior cerebral artery stenosis; right internal carotid artery stenosis and the subject was diagnosed with atherothrombotic brain infarction. A neurological exam on Day 984 showed altered sensation at right upper and lower extremities and mild motor paralysis. Results from a diffusion weighted imaging, head fluid-attenuated inversion-recovery and MRA were consistent with results from the brain MRI. The subject received sodium chloride (normal saline) and started rehabilitation on Day 984. Other nonserious AEs reported as ongoing at the time of thrombotic cerebral infarction were osteoarthritis (knee; Day 221) and tension headache (Day 963).
Musculoskeletal stiffness (shoulder) started on Day 989 and treatment included acetaminophen, pregabalin 25 mg capsules, eperisone hydrochloride, and loxoprofen. On Day 995, the event of thrombotic cerebral infarction was considered resolving, and the subject was discharged from the hospital with a diagnosis of atherothrombotic brain infarction. No action was taken with regard to study medication and the subject continued in the study. The event of thrombotic brain infarction was considered to be moderate in intensity and was assessed by the investigator to be not related to the study medication. The SAE of thrombotic brain infarction was reviewed by the blinded adjudication committee and determined to be an event of ischemic stroke, nonfatal from a small artery occlusion (lacune) (confirmed MACE, extended MACE and confirmed thrombotic, embolic, or ischemic cardiovascular event.

Subject [redacted], a 5[redacted]-year-old white male non-smoker with a medical history of obesity (BMI = 34.6 kg/m^2), type 2 diabetes mellitus, hyperlipidemia, hypertension, psoriasis, erectile dysfunction, psoriatic arthropathy, and positive family history for cerebrovascular accident, experienced a confirmed MACE event due to cerebrovascular accident (CVA) on Day 1242. On Day 1, the subject was randomized to tildrakizumab 200 mg for Part 1 in the base study and continued on the same treatment for Parts 2 and 3 and into the extension study (start Day 538). Relevant concomitant medications included insulin human, glipizide, metformin, enalapril, At baseline, the subject's blood pressure was 138/70 mmHg, and laboratory results showed cholesterol within NR and fasting glucose 139 mg/dL

(NR = 60- 115 mg/dL). On Day 1186, the following nonserious AEs were reported: type 2 diabetes mellitus, diabetic neuropathy, hyperlipidemia, and hypertension (aggravated). Treatment for diabetic neuropathy was pregabalin. Treatment for worsening of type 2 diabetes mellitus included glimepride, insulin lispro, and insulin human (+) insulin human isophane. Treatment for worsening of hyperlipidemia included fenofibrate, niacin, and atorvastatin calcium. Treatment for worsening of hypertension included in doxazosin mesylate and metoprolol. On Day 1242, the subject experienced the event of CVA. The subject reported having left sided tingling and numbness, and tingling over the whole face on that day, however, it resolved later in the day and no medical attention was requested. Subsequently, on Day 1245, the subject collapsed while walking in a store and was transported to the hospital. Blood pressure (BP) on admission was 160/87 (units not provided). In the ER, the subject presented with new onset of weakness and moderate numbness in the left arm and left leg, as well as moderate numbness of the right face, right arm, and right leg, with left numbness more notable than on the right. The subject could not speak, move the left arm, or walk. The subject was admitted to the hospital and diagnosed with cerebrovascular event involving the left side of the body. The subject's chief complaint at admission was bilateral weakness and paresthesia with altered consciousness-near syncope. The finger to nose test was abnormal (slow). Persistent weakness of the right arm (mild), right leg (mild), left face (moderate), left arm and left leg (both mild), normal strength and coordination on right side were also reported. The subject's last dose of tildrakizumab 200 mg prior to the event was on Day 1037. On Day 1245, a computed tomography (CT) of the brain without contrast showed no acute intracranial abnormality, normal carotid ultrasound, normal chest X-ray, and electrocardiogram (ECG) showed normal sinus rhythm (NSR), abnormal QRS complex, and right bundle branch block (RBBB) (incomplete). Complete blood count, coagulation profile, cardiac profile and chemistry were also performed (units not provided) and all were within normal limits except hemoglobin was 13.7 (low), glucose 19 (high), A1C 10.2 (high), blood urea nitrogen 20 (high), triglycerides 497 (high) and cholesterol 220 (high) (units and normal ranges were not provided). The subject's cardiac profile was reported within normal limits. Speech and physical therapy was recommended for the subject. Since Day 1245, the subject received treatment with clopidogrel 75 mg QD for CVA prophylaxis, enoxaparin sodium 30 mg SQ QD for deep vein thrombosis prophylaxis, atorvastatin calcium 40 mg (also reported as 80 mg) QD for hyperlipidemia, aspirin 325 mg QD for coronary artery disease and CVA prophylaxis, and continued home medications for hypertension and type 2 diabetes mellitus. On Day 1246, a neurology consultation revealed physical exam within normal limits except decreased alertness (mild-sleepy), cranial nerves exam revealed left upper motor neuron facial asymmetry, and motor exam revealed dense left hemiplegia (normal); ECGs showed NSR, abnormal QRS complex, and RBBB (incomplete); and a 2D echocardiogram was normal. On Day 1247, a brain MRI without contrast showed focal acute infarct within the right basal ganglia. The subject could not remember all of the medications given in the hospital. On Day 1250, the event of CVA was considered resolved with sequelae and the subject was discharged with a diagnosis of cerebrovascular accident of right basal ganglia and secondary diagnoses of uncontrolled diabetes, uncontrolled hypertension and uncontrolled hyperlipidemia. The subject could speak clearly, but deliberately and more slowly than before the event, and was able to walk with a cane. The subject's right side of body had fully recovered strength and movement, but the left side was still weak. The subject denied difficulty swallowing and presented without any facial drooping. No action was taken with regard to study medication. The subject continued in the study. The event of CVA was considered to be severe in intensity and was assessed by the investigator to be not related to the study medication. The SAE of cerebrovascular accident was reviewed by the blinded adjudication committee and determined to be an event of ischemic stroke, nonfatal (confirmed MACE, extended MACE and confirmed thrombotic, embolic, or ischemic cardiovascular event).

Subject [redacted], a 6[redacted]-year-old white male with a medical history of psoriasis, cellulitis of the leg, diabetes, hypercholesterolemia, coronary artery bypass, hypertension, family history of coronary artery disease (CAD) (subject's father died of CAD), and former tobacco user (pack years not reported), had 2 confirmed MACE events of ischemic stroke on Day 449 and Day 1144. On Day 1, the subject was randomized to placebo for Part 1 in the base study, then rerandomized to tildrakizumab 200 mg for Part 2 (Day 85), and continued on this treatment for Part 3 and into the extension study (Day 534 through Day 1122). Relevant concomitant medications included metformin, atorvastatin, lisinopril, glyburide, metoprolol, metoprolol tartrate, and vitamins (unspecified). At baseline, the subject's blood pressure was 141/74 mmHg, and laboratory results for lipids were: LDL-C 63 mg/dL (NR=50-160 mg/dL), HDL- C 36 mg/dL (NR=40-60 mg/dL), and total cholesterol 121 mg/dL (NR=125-200 mg/dL). On Day 449, the subject experienced an SAE of transient ischemic attack (TIA). On the same day, the subject had acute onset of right upper extremity weakness, heaviness of the right arm, and slurred speech. The subject went to the ER upon onset of the TIA symptoms. Treatment for the event included aspirin, clopidogrel bisulfate, acetaminophen, enoxaparin sodium, and sodium chloride. Symptoms associated with the TIA resolved in less than 24 hours. On Day 449, a CT scan of the head showed no intracranial hemorrhage or large vascular territory infarct, low attenuation white matter foci were nonspecific however may represent chronic small vessel ischemic disease; a computed tomography angiogram (CTA) of the head with and without contrast was unremarkable; a CTA of the neck with contrast and post processing was unremarkable; an ECG was normal; a chest x-ray showed no significant cardiopulmonary abnormality; MRA of the neck and head was negative. On the same day, a MRI of the brain, without contrast, showed findings consistent with multifocal punctate areas of ischemia within both hemispheres, predominately posteriorly; the distribution suggested multifocal embolic disease. The subject's National Institute of Neurological Disorders and Stroke score was very low in the ER; no deficits were found. On Day 450, the subject was admitted to the hospital from the ER for further evaluation of the complaint. Laboratory results on that day showed elevated glucose results of 259 mg/dL, 294 mg/dl and 360 mg/dL (NR = 70-99 mg/dL). On the same day, a carotid evaluation showed plaque disease involving the carotid bifurcations, which was slightly more prominent than on the prior examination but still associated with flow parameters consistent with stenosis of less than 50% by North American Symptomatic Carotid Endarterectomy Trial criteria. On the same day, a transthoracic echocardiogram showed normal sized LV cavity, wall thickness mildly increased, estimated EF was 50%, and possible hypokinesis of the anteroseptal myocardium, consistent with postoperative changes; an electroencephalogram (EEG) was normal A Doppler echocardiogram showed parameters consistent with abnormal LV relaxation (grade 1 diastolic dysfunction), moderately dilated left atrium; an atrial septum showed no shunt, the mitral valve annulus was moderately calcified, the trileaflet aortic valve was mildly thickened, with leaflets mildly calcified, the aortic root was trivially dilated, in the extracardiac pericardium a trivial pericardial effusion was identified, there was no evidence of hemodynamic compromise, inferior vena cava had normal size. A CT scan of the head was negative. On Day 451, the transient ischemic attack was considered resolved and, after a complete normal stroke work up, the subject was discharged from the hospital with a diagnosis of TIA. Post-hospitalization, follow-up with subject's cardiologist was scheduled for further evaluation. After discharge, the subject denied presence of any TIA symptoms.This case was adjudicated by the external CAC as an event of ischemic stroke, nonfatal with inadequate documentation (confirmed MACE and confirmed thrombotic, embolic, or ischemic cardiovascular event). No action was taken with regard to study medication. The event of transient ischemic attack was considered to be mild in intensity and was assessed by the investigator to be not related to study medication. On Day 1144 (22 days after the last dose of study medication), the subject

experienced a second SAE of TIA. The subject was transported to the ER due to headaches, sudden onset of speech disturbance, slurred speech and tingling sensation in both hands, associated with confusion and stumbling around the house. In the ER, glucose was 248 mg/dL; an ECG revealed sinus tachycardia and a chest X-ray had no infiltrates. On Day 1145, the subject was admitted to the hospital for further evaluation and treatment. An ECG showed sinus rhythm with premature atrial complexes (normal), however, sinus tachycardia was assessed by the ER physician. Normal results were reported for a chest X-ray and electroencephalogram. A CT scan of the head without contrast showed no bleed or mass effect, and small vessel disease; CTA of the head and neck with and without contrast revealed atherosclerotic carotid calcifications; no evidence of patent aneurysm or occlusion in visualized portions of circle Willis; Doppler ultrasound of bilateral carotids showed 1 to 49% stenosis, cardiology picture archiving and communication system echocardiogram was extremely technically limited due to poor acoustic windows, with normal left ventricular size and systolic function; estimated ejection fraction was 60% to 65%; bubble study was grossly negative for the right to left shunt; and no significant structural or valvular pathology. A brain MRI with and without contrast showed multiple foci of diffusion restriction which suggested embolic areas of ischemia without abnormal enhancement. Transesophageal echocardiogram showed normal left ventricular size and systolic function, estimated ejection fraction of 60% to 65%, presence of fossa atrioseptal defect/patent foramen ovale, degenerative changes of the mitral valve with trace to mild regurgitation, and no other significant valvular abnormalities were noted. On Day 1147, the event of TIA was considered resolved and the subject was discharged from the hospital with a diagnosis of TIA, coronary artery disease of native artery, hyperlipidemia, essential hypertension, and diabetes mellitus with hemoglobin A1C of 7.9 (poorly controlled) treated with oral medication. On Day 1156, a cardiologist diagnosed an atrial septal defect which was reported to be a causative factor of subject's recurrent TIA episodes. On Day 1182, the subject had a right heart catheterization, intracardiac echography (ICE) imaging and percutaneous closure of the fossa/atrial septal defect with a 35 mm Amplatzer cribriform occlusion device. The conclusions of this procedure were: elevated right heart filling pressures, mild pulmonary hypertension, presence of fossa type atrial septal defect (ASD) with significant right-to-left shunting, and successful percutaneous closure of fossa type atrial septal defect with a 35 mm Amplatzer cribriform device. On Day 1192, the subject's status post percutaneous closure was that no new symptoms were revealed, atherosclerosis of native coronary artery without angina pectoris, multi vessel CAD, and essential hypertension, adequately controlled and mixed hyperlipidemia. No medication changes were reported. As per subject's cardiologist records, an atrial septal defect appeared to be the causative factor of subject's recurrent TIA episodes. Action taken with the study medication with regard to this event was reported as drug withdrawn. This second event of TIA was considered to be moderate in intensity and was assessed by the investigator to be not related to study medication. The subject was discontinued from the study on Day 1206 due to this event. Last contact with the subject occurred during follow-up on Day 1282. The SAE of transient ischemic attack was reviewed by the blinded adjudication committee and determined to be an event of ischemic stroke, nonfatal due to a cardioembolism (confirmed MACE and confirmed thrombotic, embolic, or ischemic cardiovascular event).

Subject [redacted], a 3[redacted]-year-old white male with a medical history of drug hypersensitivity (codeine), seasonal allergy, blood pressure increased, and psoriasis, was reported to have had a confirmed MACE event (sudden death) on Day 978. On Day 1, the subject was randomized to and received tildrakizumab 100 mg in the base study (Parts 1, 2, and 3) then continued on this treatment into the extension study (Day 421 to Day 932). Concomitant medications included ascorbic acid (+)

beet (+) grape seeds (+) magnesium oxide (+) quercetin (+) potassium nitrate (+) spinach, omega-3 marine triglycerides, loratadine, acetaminophen (+) hydrocodone bitartrate, ondansetron, and tamsulosin hydrochloride. During the study, the nonserious AEs of blood pressure increased (Day 155; ongoing) and nephrolithiasis (Day 918; ongoing) were reported. On Day 978 (47 days after the last dose of study medication), the subject died. A family contact reported that the subject fell and could not be resuscitated. The cause of death was not provided. The source of notification of the subject's death was reported as family. An autopsy was performed however the autopsy report could not be obtained by the study site after several unsuccessful attempts. Last contact with subject's family contact occurred on Day 1103. The subject's last dose of tildrakizumab 100 mg was on Day 932. The subject was discontinued from the study due to this event. The investigator considered the event of death to be not related to the study medication and action taken with the study medication was reported as not applicable. This SAE of death was reviewed by the blinded adjudication committee and determined to be an event of sudden death (confirmed MACE and extended MACE).

Subject [redacted], a 5[redacted]-year-old white male with a medical history of cardiac murmur, drug hypersensitivity (penicillin), complex regional pain syndrome, psoriasis, rosacea, finger amputation, and former tobacco user (unknown number of pack years) was reported to have had a confirmed MACE event of cerebrovascular accident on Day 1041. On Day 1, the subject was randomized to the placebo treatment group for Part 1 of the base study and was rerandomized to tildrakizumab 100 mg (Day 84) for Parts 2 and 3. The subject continued receiving tildrakizumab 100 mg in the extension study (start Day 422). Relevant concomitant medications included anesthetic (unspecified), acetaminophen (+) hydrocodone bitartrate, ibuprofen, influenza virus vaccine (unspecified), and vitamin D (unspecified). On Day 252, the subject presented to the clinic with 7 mm crusted papule on left hand diagnosed as Bowen's disease (SAE). The lesion was biopsied and showed malignant squamous cell carcinoma in situ on the left hand, and subsequently an excision was performed. The subject had no family history of skin cancer and no prior history of skin cancer. No prior light therapy or tanning bed usage or excessive sun exposure was reported by the subject. A subsequent biopsy from the excision showed margins of the excision were free of tumor. Pathology from the surgical excision revealed clear margins and the area healed without incidence. The subject received lidocaine for the biopsy and epinephrine (+) lidocaine hydrochloride for anesthesia during excision; and acetaminophen (+) hydrocodone bitartrate and promethazine hydrochloride were received post excision. On Day 270, the event of Bowens's disease was considered resolved. No action was taken with regard to study medication. The event of Bowen's disease was assessed by the investigator to be not related to the study medication. On Day 1041, the subject experienced an SAE of cerebrovascular accident. On Day 1062, the subject visited the emergency room (ER) after developing left- sided weakness 3 weeks prior, slurred speech for 1 week, and continued pain in the left upper extremity and left lower extremity with difficulty "controlling" the left arm. The subject also reported going to another ER 1 week prior with complaint on left lower extremity but was sent home. On Day 1062, a computerized tomogram (CT) of the head showed evolving right posterior parietal infarct. This progressed since the prior study, however the previous study results were not provided. There was no acute intracranial hemorrhage reported. On the same day, an ECG was not clinically significant; and a nonserious AE of carotid artery stenosis of moderate intensity was reported. A physical exam revealed slight facial droop, bilateral carotid bruits, no jugular vein distention or thyroid mass palpable; regular rate and rhythm with a very slight systolic murmur, no

rub or gallop; left-sided weakness, 3/5 to the left upper extremity, and 4/5 left lower extremity. Laboratory test results revealed: albumin 2.9 g/dL (abnormal); calcium 8.5 mg/dL (abnormal), cholesterol 208 mg/dL (abnormal), LDL 36 mg/dL (abnormal), HDL 172 mg/dL (abnormal), hematocrit 40.4 (abnormal; units not reported), mean corpuscular volume of 81.3 (abnormal; units not reported), and troponin negative. Urinalysis was unremarkable. A thyroid function panel was within normal limits. The subject received treatment with heparin, 0.9 % sodium chloride and dextran for the event. On Day 1073, a right carotid endarterectomy due to right carotid stenosis and posterior right hemispheric stroke was performed under general anesthesia and continuous electroencephalography monitoring and bovine pericardial patch angioplasty and Doppler ultrasound interrogation. Also on Day 1073, the nonserious AE of carotid artery stenosis was considered resolved. Following the right carotid endarterectomy, the subject was stable and cleared for discharge. On Day 1074, the SAE of cerebrovascular accident was considered resolved with sequelae and the subject was discharged with the diagnoses of right cerebrovascular accident, right carotid stenosis, hypertension, chronic pain, psoriasis, and left knee pain. The subject's treatment included the following medications: aspirin, clopidogrel bisulfate, atorvastatin calcium, and potassium. The subject would return in 4 weeks to follow up with cardiothoracic surgery, and would be scheduled for left carotid endarterectomy. The PI felt that chronic pain and left knee pain was related to reflex sympathetic dystrophy syndrome (complex regional pain syndrome), which was reported in the subject's medical history. Additionally, the left knee pain was considered a combination of the reflex sympathetic dystrophy syndrome and the numbness of the left leg (hypoesthesia) which had been reported as an NSAE of mild intensity on Day 1008. No action was taken with regard to study medication. The subject continued in the study. The event of cerebrovascular accident was considered to be moderate in intensity and was assessed by the investigator to be not related to the study medication. Also, the investigator considered the event of posterior right hemispheric stroke to be medically significant. This SAE of cerebrovascular accident was reviewed by the blinded adjudication committee and determined to be an event of ischemic stroke (nonfatal) due to a large-artery atherosclerosis (confirmed MACE, extended MACE and confirmed thrombotic, embolic, or ischemic cardiovascular event).

Subject [redacted], a 5[redacted]-year-old white male with a medical history of cellulitis, debridement, diabetes mellitus, psoriasis, hypertension, and former tobacco user (20 pack years) had a confirmed MACE event due to coronary artery stenosis on Day 1150. On Day 1, the subject was randomized to and received tildrakizumab 200 mg in the base study and continued receiving this treatment in the extension study (start Day 420). Relevant concomitant medications included ramipril, metformin, aspirin, metoprolol, simvastatin, and ticagrelor. At baseline, the subject's blood pressure was 140/69 mmHg and laboratory results showed cholesterol 184 mg/dL (NR = 125-200 mg/dL) and fasting glucose 140 mg/dL (NR=60-115 mg/dL). The subject reported periodic left sided chest pain since Day 802 and was diagnosed with angina pectoris (mild intensity, NSAE) on Day 802. Subsequently, the subject presented to the ER after being referred by the general practitioner. At that time, the subject reported no symptoms. On Day 1150, the subject was admitted to the hospital due to the SAE of coronary artery stenosis (with onset reported on Day 968). On the same day, an electrocardiogram and a chest X-ray were assessed as normal. Subsequently, on Day 1151, a transthoracic echocardiography was also normal, and the subject underwent a cardiac catheter examination, which confirmed the coronary stenosis one vessel disease. No laboratory data related to the event was provided. On Day

1152, the events of angina pectoris and coronary artery stenosis were considered resolved and the subject was discharged from the hospital with a diagnosis of coronary one vessel disease. At discharge, the subject's treatment included aspirin, metoprolol, ramipril, simvastatin and ticagrelor for the event. The event of angina pectoris was considered to be severe in intensity and was assessed by the investigator to be not related to study medication. No action was taken with regard to study medication. The subject continued in the extension study. This SAE of coronary artery stenosis was reviewed by the blinded adjudication committee and determined to be an event of acute myocardial infarction, nonfatal (confirmed MACE, extended MACE and confirmed thrombotic, embolic, or ischemic cardiovascular event).

Subject [redacted], a 5[redacted]-year-old white female with a medical history of psoriasis, arthralgia, psoriatic arthropathy, hypercholesterolaemia, gastrooesophageal reflux disease, and tobacco user (1.5 pack years) was reported to have had a confirmed MACE event of ischemic cerebral infarction. On Day 1, the subject was randomized to the placebo treatment group for Part 1 of the base study and was rerandomized to tildrakizumab 200 mg for Part 2 (Day 85) and Part 3. The subject continued receiving tildrakizumab 200 mg in the extension study (start Day 421). Relevant concomitant medications included atorvastatin calcium, aspirin, and itopride hydrochloride. On Day 1134, the subject experienced an SAE of ischemic cerebral infarction. The subject reported pain in the left arm and scotomas in her right eye. Subsequently, the subject was consulted by a neurologist who assessed subject as conscious, with normal speech, ambulatory without help, and with negative Romberg test. On that day, the subject was admitted to the hospital for observation. The nonserious adverse events (NSAEs) of arteriosclerosis (moderate intensity, ongoing), cerebral arteriosclerosis (moderate intensity, ongoing), and hyperlipidemia (moderate intensity, ongoing) were also reported with an onset of Day 1134. A computerized tomography revealed no bleeding in the central nervous system; in the white matter of the brain there were singular hypodense spots (from different times, of vascular origin); and calcifications in the subcortical nuclei, with middle structures unmoved. A chest X-ray showed lungs without inflammation and with normal heart shade; and a left arm and shoulder X-ray were assessed as normal. In addition, a 12 lead ECG showed sinus rhythm, heart rate of 60/minute, left axis deviation, flat T (wave) in III (lead), high in point J in V2-V6 (leads). Abdominal ultrasonography was also performed and only normal gallbladder with few singular hyperechogenic spots (up to 0.4 cm in size) was revealed. On Day 1135, the NSAEs of cholelithiasis (moderate, ongoing) and renal cyst (moderate) were reported. On the same day, laboratory tests results showed: cholesterol 261 mg/dL (NR=0-190 mg/dL), creatinine 1.13 mg/dL (NR=0.51-0.95 mg/dL), sodium 147 mmol/L (NR=135-145 mmol/L), triglycerides 209 mg/dL (NR=0-150 mg/dL) and low density lipoprotein 165 mg/dL (NR= 0-115 mg/dL). Treatment for the SAE included heparin, sodium chloride (0.9 %), pantoprazole and acetaminophen (+) tramadol hydrochloride, and rivaroxaban. On Day 1136, a NSAE of atrial fibrillation (moderate, ongoing) was reported and treated with aspirin and metoprolol tartrate. On Day 1137, the SAE of ischemic cerebral infarction was considered resolved and the subject was discharged from the hospital in good condition, with the diagnoses of atherosclerosis, atherosclerotic brain damage, hyperlipidemia, paroxysmal atrial fibrillation, cerebral infarction, and psoriasis. On Day 1190, the subject experienced right knee pain (meniscus injury) and the SAE of patellofemoral pain syndrome and synovial disorder were reported. On the same day, the subject was admitted to the hospital and an arthroscopy of the right knee was successfully performed, where part of cracked meniscus was removed, middle synovial folds were cut and microfractures were performed. Post-arthroscopy, the subject was treated with dalteparin sodium. On Day 1191, the subject received post-surgery treatment with clindamycin and meloxicam. The events patellofemoral pain syndrome,

meniscus injury, and synovial disorder were considered resolved and the subject was discharged with crutches from the hospital with the diagnoses of chondromalacia patellae, cracked middle meniscus in back corner, and overgrown middle synovial folds of the right knee. No action was taken with regard to study medication. The subject continued in the study. The events of ischemic cerebral infarction and patellofemoral pain syndrome were considered to be moderate in intensity and were assessed by the investigator to be not related to study medication. This SAE of ischemic cerebral infarction was reviewed by the blinded adjudication committee and determined to be an event of nonfatal ischemic stroke as a result of a cardioembolism (confirmed MACE, extended MACE and confirmed thrombotic, embolic, or ischemic cardiovascular event).

Subject [redacted], a 5[redacted]-year-old white male with a medical history of coronary artery disease, hypercholesterolemia, psoriasis, hypertension, myocardial infarction, appendicectomy, cholecystectomy, hypertension, coronary angioplasty (in 2010), and former-tobacco user (30 pack years) had a confirmed MACE event of acute myocardial infarction . On Day 1, the subject was randomized to and received tildrakizumab 100 mg for Part 1 and Part 2 in the base study and was rerandomized to tildrakizumab 200 mg for Part 3. The subject continued on tildrakizumab 200 mg treatment in the extension study (Day 421 through Day 1121). Concomitant medications included ascorbic acid (+) rutin, aspirin, atorvastatin calcium, bisoprolol fumarate, candesartan cilexetil, clindamycin, clopidogrel bisulfate, codeine phosphate (+) potassium guaiacolsulfonate, diazepam, eplerenone, ezetimibe (+) rosuvastatin zinc, nebivolol hydrochloride, omeprazole, pantoprazole sodium, perindopril arginine, potassium chloride, simvastatin, sodium chloride, telmisartan, torsemide, tramadol hydrochloride, and trimetazidine hydrochloride. On Day 1138 (18 days after the last dose of tildrakizumab 200 mg), the subject experienced a recurrence of coronary artery disease. The subject had prior confirmed extended MACE events of acute myocardial infarction and coronary revascularization both with onset on Day 874. On Day 1145, the subject was admitted to the hospital due to pain in the chest area present for about a week prior to admission. He was also diagnosed with chronic kidney disease (mild intensity, ongoing). On Day 1146, laboratory test results showed: ALT, AST, CK-MB, total cholesterol, LDL, HDL, triglycerides, and TSH within normal range; and troponin T 15.53 pg/mL (abnormal; NR = 0-13 pg/mL). On the same day, a coronarography was performed and revealed left main (LM) coronary artery with no changes; left anterior descending (LAD) artery: totally amputated before stent, circuit imperceptible, diagonal branch barely perceptible; circumflex (Cx) OM tightened 40%, at Cx tightened 30-40%; and right coronary artery (RCA): amputated proximally. On Day 1146, the subject was diagnosed with mitral valve incompetence (mitral regurgitation; mild intensity, ongoing). A heart ultrasonography (USG) showed ejection fraction (EF) 30%. On the same day, a heart Doppler USG showed the following results: mitral flow E/A more than 1, E/e' equal 18; feedback wave second degree; "PISA(r)" 4-5 mm; effective regurgitant orifice area (EROA): 0.23 cm^2; MR dP/dt 780 mmHg/s; aortal flow Vmax 1.2 m/s with pleural flow left (L) "AcT" 110 ms; triple flow with feedback wave I/II degree. On Day 1148, laboratory test results were normal for TSH and slightly abnormal for glomerular filtration rate (GFR) according to Modification of Diet in Renal Disease (MDRD) 65 mL/min/1.73m^2 (normal lower limit = 60 mL/min/1.73m^2), CK-MB 12.5 U/L, creatinine 1.21 mg/dL (NR = 0.7-1.2 mg/dL), and troponin T 23.3 pg/mL. On Day 1149, a 12 lead ECG showed heart rate (HR) of 96/minute, “sinistrogram” (left axis deviation); left atrial hypertrophy (LAH), left atrium enlarged, left heart chamber enlarged, QS and ST-T elevation in V1-V2 leads, ST-T elevation in V3-V4 leads. On the same day, a Holter ECG showed the following results: average HR 74 /minute, max HR 111 /minute,

min HR 60 /minute, pauses longer than 2 seconds to zero; overall 1093 ventricular stimulations (1% of all) with longest ventricular sequence of 2 stimulations. On Day 1149, the subject was treated with ivabradine hydrochloride for ischemic heart disease and discharged from the hospital with the diagnoses of chronic heart disease, hypertension, mitral regurgitation, dyslipidemia, psoriasis, chronic renal disease, angiotensin-converting enzyme inhibitor (ACE-I) intolerance and unstable angina. The subject was readmitted to the hospital on Day 1175 for a contrast magnetic resonance imaging (MRI) and released the same day. Results of the MRI were: left chamber EF 28%, stroke volume (SV) 53.6 mL; cardiac output (CO) 2.6 mL/min; left ventricle (LV) enlarged; and global thinning walls of the heart. Additionally, on the same day, laboratory test results reported were within normal range for creatinine, potassium, and sodium. Abnormal laboratory results were reported for chloride 111 mmol/L (NR = 98-107 mmol/L), and GFR according to MDRD 68 mL/min/1.73m^2. On Day 1199, the subject received bisoprolol fumarate for ischemic heart disease. The subject was scheduled for a cardioverter defibrillator implantation on Day 1219 as a precautionary measure due to potential risk for arrhythmia, sudden cardiac arrest, or cardiac death. The subject was discontinued from the study on Day 1205 by the investigator (decision). As of Day 1227, the subject did not report any symptoms of arrhythmia. The outcome of the event of coronary artery disease (aggravated) was reported as not resolved. Action taken with regard to study medication was reported as drug withdrawn. The eve t of aggravated coronary artery disease was considered to be moderate in intensity and was assessed by the investigator to be not related to the study medication. This SAE of aggravated coronary artery disease was reviewed by the blinded adjudication committee and determined to be an event of acute myocardial infarction, nonfatal (confirmed MACE, extended MACE and confirmed thrombotic, embolic, or ischemic cardiovascular event).

Subject [redacted], a 6[redacted]-year-old male (race not reported) with a medical history of psoriasis, aortic valve incompetence, aortic aneurysm, glucose tolerance impaired, osteoarthritis, osteoporosis, obesity (BMI = 37.8 kg/m2), thalassemia, hypertension, and former tobacco user (15 pack years) had a confirmed MACE event due to coronary artery stenosis on Day 1053. The subject had no past medical history of angina. On Day 1, the subject was randomized to the placebo treatment group for Part 1 of the base study and was rerandomized to tildrakizumab 200 mg (Day 85) for Parts 2 and 3. The subject continued receiving tildrakizumab 200 mg in the extension study (start Day 422). Concomitant medications included diltiazem hydrochloride, alendronate sodium, glycerin (+) mineral oil (+) petrolatum white, calcium carbonate, cholecalciferol, metformin hydrochloride, and alprazolam. On Day 1024, the subject experienced high blood pressure (hypertension; nonserious, mild, ongoing) was reported. On Day 1053, the subject reported substernal chest pain radiating down both arms. The event coronary artery stenosis was reported. The subject went to the ER on Day 1055 where an ECG was performed and showed suspicion of fissuring aneurysm of abdominal aorta. Subsequently, the subject was admitted to the hospital and a trans-esophageal ultrasound was performed showing no fissuring aneurysm of abdominal aorta. A computerized tomography (CT) angiogram of the aorta revealed no fissuring, and thoracic aorta dilatation of -/+ 50mm. On Day 1055, bronchitis (moderate) was reported. Laboratory test results reporting values outside the normal range included: troponin I 4.140 ng/L (NR = 0.0- 0.045 ng/L), AST 62 U/L (NR = 15-37 U/L), CK 422 U/L NR = 39-308 U/L), CK-MB 45.9 ng/mL (NR -= 0-0.045 ng/mL), LDH 302 U/L (NR = 85 - 245 U/L) and hemoglobin 12.4 g/dL (NR = 12.6-17.3 g/dL). On Day 1055, a chest CT scan showed no pulmonary, pleural or pericardium lesion. On Day 1056 a coronary angiography showed a significant stenosis of anterior descending coronary artery and significant stenosis of right coronary artery (70-90%), and aortic insufficiency. A Doppler of the neck showed atheromatous thickening of the 2 carotids <50%, and

vertebral arteries were "ok". On Day 1057, the subject's hemoglobin decreased to 2.4 g/dL and anemia (moderate, resolving) was reported. On Day 1058, a chest X-ray showed no pleural effusion and no source of infection. An additional coronary angiography with angioplasty was performed on Day 1059 to clear up stenosis of the right coronary artery but was unsuccessful. On Day 1062, an ultrasound of the right femoral artery showed a hematoma, and aneurysm post angioplasty of 3 cm. On Day 1064, the subject's hemoglobin was 9.5 g/dL and the subject was discharged from the hospital with a diagnosis of heart attack. On Day 1071, a Doppler ultrasound of the aorta and iliac axes revealed no aneurysm dilation of distal abdominal aorta, and thrombosis of pseudoaneurysm of the right femoral artery. On Day 1104, the bronchitis resolved. On Day 1127, the subject received 9 units of blood during transfusion. On the same day, CK and troponin I were normal. On Day 1128, the subject underwent surgery for Bentall procedure (cardiac bioprosthesis) and bypass right coronary artery (results reported as "ok"). Post- surgery anemia occurred due to severe bleeding and was treated with blood transfusions until Day 1150. On Day 1129, the event of coronary artery stenosis was considered resolved with sequelae. On the same day, laboratory results showed hemoglobin 8.9 g/dL, CK 6747 U/L and troponin I 54.4 ng/mL. It was reported that on Day 1154 the subject was discharged home and was very tired. The subject's treatment was reported as: rest, kinesiotherapy, aspirin for heart attack (also reported for platelets) and "osler" prevention if necessary. No action was taken with regard to study medication in response to this event. The event of coronary artery stenosis was considered to be severe in intensity and was assessed by the investigator to be not related to study medication. This SAE of coronary artery stenosis was reviewed by the blinded adjudication committee and determined to be an event of acute myocardial infarction, nonfatal (confirmed MACE, extended MACE and confirmed thrombotic, embolic, or ischemic cardiovascular event).

Subject [redacted], a 4[redacted]-year-old white female with a medical history of cataract, gastrooesophageal reflux disease, allergy to animal, drug hypersensitivity, hidradenitis, psoriasis, cholecystectomy, hysterectomy, family history of heart attack (mother and father) and tobacco user (15 pack years) was reported to have a confirmed MACE of myocardial infarction on Day 1010. On Day 1, the subject was randomized to and received tildrakizumab 100 mg for Part 1 and Part 2 and rerandomized to tildrakizumab 200 mg for Part 3 (Day 195) in the base study, and continuing on tildrakizumab 200 mg in the extension study (start Day 420). Relevant concomitant medications included rifampin, brinzolamide, nitroxoline, enoxacin, ibuprofen, clindamycin phosphate, noscapine polistirex, ibuprofen lysine, levofloxacin, ofloxacin, furosemide, dipyrone, and pantoprazole. On Day 1010, the subject experienced an SAE of myocardial infarction. On that day an echocardiography showed limited left ventricular ejection fraction (45%); a chest X-ray was performed (result not provided); and coronary angiography revealed thrombotic occlusion of first coronary diagonal branch. Subsequently, the subject underwent percutaneous transluminal coronary angioplasty with implantation of a drug eluting stent. Hypokalemia, of moderate intensity, was also reported. During that night, the subject developed angina pectoris symptoms due to coronary artery disease (nonserious AE of moderate intensity, ongoing), and went to the ER. No laboratory results were provided. An ECG showed ST (segment) elevation in I and aVL (leads). The subject was diagnosed with myocardial infarction and treated with furosemide, aspirin, ticagrelor, metoprolol, simvastatin, potassium bicarbonate (+) potassium citrate, and ramipril. The subject was hospitalized on Day 1011. Multiple stents were implanted and additional treatment with torsemide was initiated. On Day 1015, the subject was discharged from the hospital with the diagnoses of myocardial infarction, coronary heart disease (1 vessel), and hypertension. On Day 1078, an

echocardiography revealed heart cavities of normal size, atrial fibrillation, normal systolic left ventricular function, no signs of changes in movements of right ventricular heart wall, normal heart valve activity and left ventricular ejection fraction 55%. On Day 1079, hypokalemia was considered resolved. On Day 1098, the SAE of myocardial infarction was considered resolved with sequelae and the subject was discharged from rehabilitation with uneventful course of disease. It was also reported that coronary heart disease was considered sequelae to the SAE of myocardial infarction. Study medication was interrupted due to this event (on Day 1011) and was resumed on Day 1114. The event of myocardial infarction was considered to be severe in intensity and was assessed by the investigator to be not related to the study medication and considered to be immediately life threatening by the investigator. This SAE of myocardial infarction was reviewed by the blinded adjudication committee and determined to be an event of acute myocardial infarction (nonfatal) with coronary revascularization (confirmed MACE, extended MACE and confirmed thrombotic, embolic, or ischemic cardiovascular event). The coronary revascularization was confirmed by the adjudication committee as an extended MACE.

[Source: 5.3.5.3-8]

イルミア皮下注 100mg シリンジ

2.7.5　参考文献

サンファーマ株式会社

目次

目次 2
2.7.5.1 2.7.1 で使用した参考文献 3
2.7.5.2 2.7.2 で使用した参考文献 3
2.7.5.3 2.7.3 で使用した参考文献 3
2.7.5.4 2.7.4 で使用した参考文献 4

2.7.5.1　2.7.1 で使用した参考文献

（FDA Guidance, 2009）	FDA Guidance, Assay Development for Immunogenicity Testing of Therapeutic Proteins. 2009.

2.7.5.2　2.7.2 で使用した参考文献

（Dallas, 2013）	Dallas S, Chattopadhyay S, Sensenhauser C, Batheja A, Singer M, Silva J. Interleukins-12 and -23 do not alter expression or activity of multiple cytochrome P450 enzymes in cryopreserved human hepatocytes. Drug Metab Dispos. 2013; 41(4): 689-93.
（Dirks, 2010）	Dirks NL, Meibohm B. Population pharmacokinetics of therapeutic monoclonal antibodies. Clin Pharmacokinet. 2010; 49(10): 633-59.
（Dostalek, 2013）	Dostalek M, Gardner I, Gurbaxani BM, Rose RH, Chetty M. Pharmacokinetics, pharmacodynamics and physiologically-based pharmacokinetic modelling of monoclonal antibodies. Clin Pharmacokinet. 2013; 52: 83-124.
（Fasanmade, 2010）	Fasanmade AA, Adedokun OJ, Olson A, Strauss R, Davis HM. Serum albumin concentration: a predictive factor of infliximab pharmacokinetics and clinical response in patients with ulcerative colitis. Int J Clin Pharmacol Ther. 2010; 48(5): 297-308.
（Keizer, 2010）	Keizer RJ, Huitema ADR, Schellens JHM, Beijnen JH. Clinical pharmacokinetics of therapeutic monoclonal antibodies. Clin Pharmacokinet 2010; 49(8): 493-507.
（Kopp, 2015）	Kopp T, Riedl E, Bangert C, Bowman EP, Greisenegger E, Horowitz A, et al. Clinical improvement in psoriasis with specific targeting of interleukin-23. Nature. 2015; 521(7551): 222-6.
（Nguyen, 2015）	Nguyen TV, Ukairo O, Khetani SR, McVay M, Kanchagar C, Seghezzi W, et al. Establishment of a hepatocyte-kupffer cell coculture model for assessment of proinflammatory cytokine effects on metabolizing enzymes and drug transporters. Drug Metab Dispos. 2015; 43(5): 774-85.

2.7.5.3　2.7.3 で使用した参考文献

（CHMP/EWP/2454/02-corr）	GUIDELINE ON CLINICAL INVESTIGATION OF MEDICINAL PRODUCTS INDICATED FOR THE TREATMENT OF PSORIASIS; EMEA; 18 November 2004.
（EMEA/H/SA/2165/1/FU/1/2012/III）	Follow-up Scientific Advice.M3222(SCH 900222); EUROPEAN MEDICINES AGENCY; EMEA/H/SA/2165/1/FU/1/2012/III.
（Griffiths, 2010）	Griffiths CE, Strober BE, van de Kerkhof P, Ho V, Fidelus-Gort R, Yeilding N, Guzzo C, Xia Y, Zhou B, Li S, Dooley LT, Goldstein NH, Menter A; ACCEPT Study Group. Comparison of ustekinumab and etanercept for moderate-to-severe psoriasis. N Engl J Med. 2010 Jan 14; 362(2): 118-28.
（Kopp, 2015）	Kopp T, Riedl E, Bangert C, Bowman EP, Greisenegger E, Horowitz A, et al. Clinical improvement in psoriasis with specific targeting of interleukin-23. Nature. 2015; 521(7551): 222-6.

（Leonardi, 2003）	Leonardi CL, Powers JL, Matheson RT, Goffe BS, Zitnik R, Wang A, Gottlieb AB; Etanercept Psoriasis Study Group. Etanercept as monotherapy in patients with psoriasis. N Engl J Med. 2003; 349(21): 2014-22.
（Papp, 2005）	Papp KA, Tyring S, Lahfa M, Prinz J, Griffiths CE, Nakanishi AM, Zitnik R, van de Kerkhof PC, Melvin L; Etanercept Psoriasis Study Group. A global phase III randomized controlled trial of etanercept in psoriasis: safety, efficacy, and effect of dose reduction. Br J Dermatol. 2005; 152(6): 1304-12.
（Zhou, 2010）	Zhou H, Hu C, Zhu Y, Lu M, Liao S, Yeilding N, et al. Population-based exposure-efficacy modeling of ustekinumab in patients with moderate to severe plaque psoriasis. J Clin Pharmacol. 2010; 50(3): 257-67.

2.7.5.4　2.7.4 で使用した参考文献

（Armstrong, 2013a）	Armstrong EJ, Harskamp CT, Armstrong AW. Psoriasis and major adverse cardiovascular events: a systematic review and meta-analysis of observational studies. J Am Heart Assoc. 2013; 2(2): e000062.
（Bachmeyer, 2007）	Bachmeyer C, Thiolière B, Khosrotehrani K, Cattan E. Acute myelogenous leukemia in a patient receiving etanercept for psoriasis. J Am Acad Dermatol. 2007; 56(1): 169-70.
（Bachmeyer 2008）	Bachmeyer C. Etanercept therapy and acute myeloid leukemia. Am J Hematol. 2008; 83(4): 345; author reply 345. doi: 10.1002/ajh.21140.
（Bakland, 2003）	Bakland G, Nossent H. Acute myelogenous leukaemia following etanercept therapy. Rheumatology 2003; 42: 900–1.
（Colamesta, 2016）	Colamesta V, D'Aguanno S, Breccia M, Bruffa S, Cartoni C, La Torre G. Do the smoking intensity and duration, the years since quitting, the methodological quality and the year of publication of the studies affect the results of the meta-analysis on cigarette smoking and Acute Myeloid Leukemia (AML) in adults? Critical Reviews in Oncology/Hematology. 2016; 99: 376-88.
（FDA Alert, 2009）	Food and Drug Administration ALERT [8/4/2009]: "Information for Healthcare Professionals: Tumor Necrosis Factor (TNF) Blockers (marketed as Remicade, Enbrel, Humira, Cimzia, and Simponi); Available from: http://www.fda.gov/Drugs/DrugSafety/PostmarketDrugSafetyInformationforPatientsandProviders/DrugSafetyInformationforHeathcareProfessionals/ucm174474.htm.
（Fircanis, 2014）	Fircanis S, Merrian P, Khan N, Castillo JJ. The relation between cigarette smoking and risk of acute myeloid leukemia: an updated meta-analysis of epidemiological studies.Am J Hematol. 2014 Aug; 89(8): E125-E132.
（Gratton, 2011）	Gratton et al. Reversible Posterior Leukoencephalopathy Syndrome in a Patient Treated With Ustekinumab. 2011; 147(10): 1197-1202
（Lee, 2008）	Lee et al., 2008. Clinical Spectrum of Reversible Posterior Leukoencephalopathy Syndrome. Arch Neurol. 2008; 65(2): 205-10.
（Löbermann, 2012）	Micha Löbermann et al., Immunization in the adult immunocompromised host. Autoimmunity Reviews 11. 2012; 212–8
（Mehta, 2011）	Mehta NN, Yu Y, Pinnelas R, Krishnamoorthy P, Shin DB, Troxel AB, Gelfand JM. Attributable Risk Estimate of Severe Psoriasis on Major Cardiovascular Events. The Am J Medicine. 2011; 124, 775.e1-6

（Mehta, 2012）	Mehta NN, Krishnamoorthy P, Yu Y, Khan O, Raper A, Van Voorhees A, et al. The impact of psoriasis on 10-year Framingham risk. J Am Acad Dermatol. 2012; 67(4): 796-8.
（Nair 2007）	Nair B, Raval G, Mehta P. TNF-α inhibitor etanercept and hematologic malignancies: Report of a case and review of the literature. Am J Hematol 2007; 82: 1022–4.
（Posner, 2007）	Columbia Classification Algorithm of Suicide Assessment (C-CASA): Classification of Suicidal Events in the FDA's Pediatric Suicidal Risk Analysis of Antidepressants Am J Psychiatry. 2007; 164: 1035–43
（Prey, 2010）	Prey S, Paul C, Bronsard V, Puzenat E, Gourraud PA, Aractingi S, et al. Cardiovascular risk factors in patients with plaque psoriasis: a systematic review of epidemiological studies. J Eur Acad Dermatol Venereol. 2010; 24 Suppl 2: 23-30.
（Qureshi , 2009）	Qureshi AA, Choi HK, Setty AR, Curhan GC. Psoriasis and the risk of diabetes and hypertension: a prospective study of US female nurses. Arch Dermatol. 2009; 145(4): 379-82.
（USPI COSENTYX®, 2018）	U.S. Prescribing Information：COSENTYX® (secukinumab) injection：2018
（USPI TALTZ®, 2018）	U.S. Prescribing Information：TALTZ® (ixekizumab) injection：2018
（トルツ®添付文書, 2018）	トルツ®添付文書 2018 年