Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
musculoskeletal system												
antiinflammatory and antirheumatic products	**131**	**(36.9)**	**229**	**(32.5)**	**248**	**(35.0)**	**477**	**(33.8)**	**79**	**(25.2)**	**731**	**(33.0)**
ketoprofen	5	(1.4)	3	(0.4)	6	(0.8)	9	(0.6)	2	(0.6)	16	(0.7)
ketoprofen lysine	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.0)
ketorolac tromethamine	4	(1.1)	5	(0.7)	9	(1.3)	14	(1.0)	2	(0.6)	20	(0.9)
lornoxicam	2	(0.6)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	5	(0.2)
loxoprofen	0	(0.0)	2	(0.3)	4	(0.6)	6	(0.4)	0	(0.0)	6	(0.3)
loxoprofen sodium	9	(2.5)	18	(2.6)	24	(3.4)	42	(3.0)	0	(0.0)	55	(2.5)
mefenamic acid	2	(0.6)	3	(0.4)	6	(0.8)	9	(0.6)	1	(0.3)	13	(0.6)
meloxicam	6	(1.7)	14	(2.0)	9	(1.3)	23	(1.6)	4	(1.3)	36	(1.6)
mucopolysaccharide polysulfate	16	(4.5)	22	(3.1)	28	(4.0)	50	(3.5)	0	(0.0)	66	(3.0)
nabumetone	0	(0.0)	2	(0.3)	2	(0.3)	4	(0.3)	1	(0.3)	5	(0.2)
naproxen	7	(2.0)	23	(3.3)	24	(3.4)	47	(3.3)	6	(1.9)	64	(2.9)
naproxen sodium	10	(2.8)	14	(2.0)	14	(2.0)	28	(2.0)	5	(1.6)	44	(2.0)
naproxen sodium (+) pseudoephedrine hydrochloride	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	2	(0.1)
nimesulide	0	(0.0)	1	(0.1)	2	(0.3)	3	(0.2)	1	(0.3)	4	(0.2)
piroxicam	0	(0.0)	2	(0.3)	1	(0.1)	3	(0.2)	0	(0.0)	3	(0.1)
piroxicam betadex	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
sulindac	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	2	(0.1)
tiaprofenic acid	2	(0.6)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	3	(0.1)
zaltoprofen	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
musculoskeletal system												
drugs for treatment of bone diseases	**3**	**(0.8)**	**3**	**(0.4)**	**3**	**(0.4)**	**6**	**(0.4)**	**1**	**(0.3)**	**12**	**(0.5)**
alendronate sodium	3	(0.8)	2	(0.3)	2	(0.3)	4	(0.3)	0	(0.0)	8	(0.4)
risedronate sodium	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)	1	(0.3)	3	(0.1)
strontium ranelate	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
muscle relaxants	**14**	**(3.9)**	**17**	**(2.4)**	**31**	**(4.4)**	**48**	**(3.4)**	**5**	**(1.6)**	**71**	**(3.2)**
acetaminophen (+) chlorzoxazone	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
acetaminophen (+) codeine phosphate (+) methocarbamol	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
acetaminophen (+) methocarbamol	0	(0.0)	3	(0.4)	3	(0.4)	6	(0.4)	0	(0.0)	6	(0.3)
acetaminophen (+) orphenadrine citrate	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.0)
aspirin (+) codeine phosphate (+) methocarbamol	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
baclofen	1	(0.3)	2	(0.3)	4	(0.6)	6	(0.4)	0	(0.0)	7	(0.3)
carisoprodol	1	(0.3)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	2	(0.1)
cyclobenzaprine hydrochloride	4	(1.1)	3	(0.4)	7	(1.0)	10	(0.7)	0	(0.0)	15	(0.7)
diclofenac sodium (+) orphenadrine citrate	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
eperisone hydrochloride	1	(0.3)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	2	(0.1)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
musculoskeletal system												
muscle relaxants	**14**	**(3.9)**	**17**	**(2.4)**	**31**	**(4.4)**	**48**	**(3.4)**	**5**	**(1.6)**	**71**	**(3.2)**
metaxalone	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
methocarbamol	3	(0.8)	2	(0.3)	4	(0.6)	6	(0.4)	0	(0.0)	9	(0.4)
onabotulinumtoxinA	1	(0.3)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	2	(0.1)
orphenadrine citrate	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
rocuronium bromide	0	(0.0)	0	(0.0)	3	(0.4)	3	(0.2)	1	(0.3)	4	(0.2)
succinylcholine chloride	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
tetrazepam	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	5	(0.2)
thiocolchicoside	2	(0.6)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	3	(0.1)
tizanidine hydrochloride	0	(0.0)	3	(0.4)	3	(0.4)	6	(0.4)	1	(0.3)	7	(0.3)
tolperisone	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
tolperisone hydrochloride	0	(0.0)	0	(0.0)	2	(0.3)	2	(0.1)	2	(0.6)	4	(0.2)
vecuronium bromide	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
other drugs for disorders of musculo-skeletal system	**4**	**(1.1)**	**6**	**(0.9)**	**6**	**(0.8)**	**12**	**(0.8)**	**1**	**(0.3)**	**17**	**(0.8)**
bromelains (+) rutin (+) trypsin	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
hyaluronate sodium	2	(0.6)	1	(0.1)	3	(0.4)	4	(0.3)	1	(0.3)	7	(0.3)
hyaluronic acid	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
pronase	2	(0.6)	3	(0.4)	3	(0.4)	6	(0.4)	0	(0.0)	8	(0.4)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
musculoskeletal system												
topical products for joint and muscular pain	**2**	**(0.6)**	**7**	**(1.0)**	**8**	**(1.1)**	**15**	**(1.1)**	**0**	**(0.0)**	**17**	**(0.8)**
allantoin (+) comfrey (+) panthenol (+) pine oil (+) rosemary oil (+) sage oil	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
arnica (+) glycol salicylate (+) glycyrrhizin (+) menthol	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
camphor (+) capsaicin (+) methyl salicylate	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
camphor (+) capsicum (+) glycol salicylate (+) menthol	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
camphor (+) enoxolone (+) menthol (+) methyl salicylate (+) vitamin E acetate	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
camphor (+) mate (+) menthol	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
camphor (+) mentha oil (+) menthol (+) methyl salicylate (+) nonivamide (+) vitamin E acetate	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
musculoskeletal system												
topical products for joint and muscular pain	**2**	**(0.6)**	**7**	**(1.0)**	**8**	**(1.1)**	**15**	**(1.1)**	**0**	**(0.0)**	**17**	**(0.8)**
camphor (+) menthol (+) methyl salicylate	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
camphor (+) menthol (+) methyl salicylate (+) thymol	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
diethylamine salicylate (+) heparin sodium (+) menthol	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
felbinac	0	(0.0)	1	(0.1)	3	(0.4)	4	(0.3)	0	(0.0)	4	(0.2)
felbinac (+) menthol	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
menthol (+) methyl salicylate	0	(0.0)	0	(0.0)	2	(0.3)	2	(0.1)	0	(0.0)	2	(0.1)
methyl salicylate	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
nervous system												
analgesics	**125**	**(35.2)**	**272**	**(38.6)**	**302**	**(42.7)**	**574**	**(40.6)**	**95**	**(30.4)**	**848**	**(38.3)**
acetaminophen	46	(13.0)	94	(13.3)	110	(15.5)	204	(14.4)	39	(12.5)	315	(14.2)
acetaminophen (+) apronalide (+) caffeine (+) propyphenazone	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
acetaminophen (+) ascorbic acid	0	(0.0)	1	(0.1)	2	(0.3)	3	(0.2)	0	(0.0)	3	(0.1)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
nervous system												
analgesics	**125**	**(35.2)**	**272**	**(38.6)**	**302**	**(42.7)**	**574**	**(40.6)**	**95**	**(30.4)**	**848**	**(38.3)**
acetaminophen (+) ascorbic acid (+) caffeine (+) chlorpheniramine maleate	1	(0.3)	4	(0.6)	6	(0.8)	10	(0.7)	1	(0.3)	13	(0.6)
acetaminophen (+) ascorbic acid (+) caffeine (+) phenylephrine hydrochloride (+) terpin hydrate	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
acetaminophen (+) ascorbic acid (+) pheniramine maleate (+) phenylephrine hydrochloride	1	(0.3)	3	(0.4)	0	(0.0)	3	(0.2)	0	(0.0)	4	(0.2)
acetaminophen (+) ascorbic acid (+) phenylephrine hydrochloride	0	(0.0)	2	(0.3)	1	(0.1)	3	(0.2)	0	(0.0)	3	(0.1)
acetaminophen (+) aspirin	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
acetaminophen (+) aspirin (+) caffeine	1	(0.3)	2	(0.3)	4	(0.6)	6	(0.4)	3	(1.0)	14	(0.6)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
nervous system												
analgesics	**125**	**(35.2)**	**272**	**(38.6)**	**302**	**(42.7)**	**574**	**(40.6)**	**95**	**(30.4)**	**848**	**(38.3)**
acetaminophen (+) benfotiamine (+) caffeine (+) clemastine fumarate (+) dihydrocodeine phosphate (+) lysozyme chloride (+) methy	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	2	(0.1)
acetaminophen (+) bromhexine hydrochloride (+) caffeine (+) carbinoxamine maleate (+) dihydrocodeine phosphate (+) lysozyme chlo	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.1)	0	(0.0)	2	(0.1)
acetaminophen (+) bromhexine hydrochloride (+) caffeine (+) chlorpheniramine maleate (+) dextromethorphan hydrobromide (+) methy	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
nervous system												
analgesics	**125**	**(35.2)**	**272**	**(38.6)**	**302**	**(42.7)**	**574**	**(40.6)**	**95**	**(30.4)**	**848**	**(38.3)**
acetaminophen (+) bromisovalum (+) dihydrocodeine phosphate (+) diphenhydramine salicylate (+) dyphylline (+) methylephedrine hy	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
acetaminophen (+) butethamate citrate (+) chlorpheniramine maleate (+) etilefrine hydrochloride	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
acetaminophen (+) caffeine	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.1)	0	(0.0)	2	(0.1)
acetaminophen (+) caffeine (+) chlorpheniramine maleate (+) dihydrocodeine phosphate (+) hesperidin (+) isopropamide iodide (+)	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
nervous system												
analgesics	**125**	**(35.2)**	**272**	**(38.6)**	**302**	**(42.7)**	**574**	**(40.6)**	**95**	**(30.4)**	**848**	**(38.3)**
acetaminophen (+) caffeine (+) chlorpheniramine maleate (+) dihydrocodeine phosphate (+) licorice (+) methylephedrine hydrochlor	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
acetaminophen (+) caffeine (+) chlorpheniramine maleate (+) ethenzamide (+) methylephedrine hydrochloride (+) tipepidine hibenza	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
acetaminophen (+) caffeine (+) chlorpheniramine maleate (+) salicylamide	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
acetaminophen (+) caffeine (+) codeine	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
nervous system												
analgesics	**125**	**(35.2)**	**272**	**(38.6)**	**302**	**(42.7)**	**574**	**(40.6)**	**95**	**(30.4)**	**848**	**(38.3)**
acetaminophen (+) caffeine (+) codeine phosphate	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.0)
acetaminophen (+) caffeine (+) opium	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	2	(0.1)
acetaminophen (+) caffeine (+) promethazine methylenedisalicylate (+) salicylamide	5	(1.4)	12	(1.7)	7	(1.0)	19	(1.3)	0	(0.0)	26	(1.2)
acetaminophen (+) chlorpheniramine maleate	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
acetaminophen (+) chlorpheniramine maleate (+) dextromethorphan hydrobromide (+) phenylephrine bitartrate	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
nervous system												
analgesics	**125**	**(35.2)**	**272**	**(38.6)**	**302**	**(42.7)**	**574**	**(40.6)**	**95**	**(30.4)**	**848**	**(38.3)**
acetaminophen (+) chlorpheniramine maleate (+) dextromethorphan hydrobromide (+) phenylephrine hydrochloride	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
acetaminophen (+) chlorpheniramine maleate (+) dextromethorphan hydrobromide (+) pseudoephedrine hydrochloride	2	(0.6)	6	(0.9)	3	(0.4)	9	(0.6)	0	(0.0)	11	(0.5)
acetaminophen (+) chlorpheniramine maleate (+) phenylephrine hydrochloride	2	(0.6)	2	(0.3)	2	(0.3)	4	(0.3)	0	(0.0)	7	(0.3)
acetaminophen (+) chlorpheniramine maleate (+) pseudoephedrine hydrochloride	1	(0.3)	3	(0.4)	2	(0.3)	5	(0.4)	1	(0.3)	7	(0.3)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
nervous system												
analgesics	**125**	**(35.2)**	**272**	**(38.6)**	**302**	**(42.7)**	**574**	**(40.6)**	**95**	**(30.4)**	**848**	**(38.3)**
acetaminophen (+) codeine	1	(0.3)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	4	(0.2)
acetaminophen (+) codeine phosphate	4	(1.1)	10	(1.4)	14	(2.0)	24	(1.7)	1	(0.3)	31	(1.4)
acetaminophen (+) codeine phosphate (+) doxylamine succinate	2	(0.6)	0	(0.0)	2	(0.3)	2	(0.1)	0	(0.0)	4	(0.2)
acetaminophen (+) codeine phosphate (+) phenylephrine hydrochloride	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
acetaminophen (+) codeine phosphate (+) pseudoephedrine hydrochloride	1	(0.3)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	2	(0.1)
acetaminophen (+) codeine phosphate (+) pseudoephedrine hydrochloride (+) triprolidine hydrochloride	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
acetaminophen (+) dextromethorphan hydrobromide	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
nervous system												
analgesics	**125**	**(35.2)**	**272**	**(38.6)**	**302**	**(42.7)**	**574**	**(40.6)**	**95**	**(30.4)**	**848**	**(38.3)**
acetaminophen (+) dextromethorphan hydrobromide (+) doxylamine succinate	3	(0.8)	11	(1.6)	14	(2.0)	25	(1.8)	2	(0.6)	32	(1.4)
acetaminophen (+) dextromethorphan hydrobromide (+) doxylamine succinate (+) ephedrine sulfate	2	(0.6)	3	(0.4)	6	(0.8)	9	(0.6)	0	(0.0)	15	(0.7)
acetaminophen (+) dextromethorphan hydrobromide (+) doxylamine succinate (+) phenylephrine hydrochloride	0	(0.0)	2	(0.3)	2	(0.3)	4	(0.3)	0	(0.0)	4	(0.2)
acetaminophen (+) dextromethorphan hydrobromide (+) doxylamine succinate (+) pseudoephedrine hydrochloride	1	(0.3)	2	(0.3)	2	(0.3)	4	(0.3)	0	(0.0)	5	(0.2)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
nervous system												
analgesics	**125**	**(35.2)**	**272**	**(38.6)**	**302**	**(42.7)**	**574**	**(40.6)**	**95**	**(30.4)**	**848**	**(38.3)**
acetaminophen (+) dextromethorphan hydrobromide (+) guaifenesin (+) phenylephrine hydrochloride	0	(0.0)	1	(0.1)	2	(0.3)	3	(0.2)	2	(0.6)	5	(0.2)
acetaminophen (+) dextromethorphan hydrobromide (+) guaifenesin (+) pseudoephedrine hydrochloride	0	(0.0)	0	(0.0)	2	(0.3)	2	(0.1)	1	(0.3)	4	(0.2)
acetaminophen (+) dextromethorphan hydrobromide (+) phenylephrine hydrochloride	4	(1.1)	5	(0.7)	6	(0.8)	11	(0.8)	0	(0.0)	18	(0.8)
acetaminophen (+) dextromethorphan hydrobromide (+) phenylpropanolamine hydrochloride	1	(0.3)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	3	(0.1)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
nervous system												
analgesics	**125**	**(35.2)**	**272**	**(38.6)**	**302**	**(42.7)**	**574**	**(40.6)**	**95**	**(30.4)**	**848**	**(38.3)**
acetaminophen (+) dextromethorphan hydrobromide (+) pseudoephedrine hydrochloride	2	(0.6)	0	(0.0)	4	(0.6)	4	(0.3)	0	(0.0)	6	(0.3)
acetaminophen (+) diclofenac	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
acetaminophen (+) diclofenac sodium	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
acetaminophen (+) diphenhydramine citrate	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
acetaminophen (+) diphenhydramine hydrochloride	0	(0.0)	2	(0.3)	1	(0.1)	3	(0.2)	3	(1.0)	7	(0.3)
acetaminophen (+) diphenhydramine hydrochloride (+) phenylephrine hydrochloride	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.0)
acetaminophen (+) diphenhydramine hydrochloride (+) pseudoephedrine hydrochloride	0	(0.0)	2	(0.3)	1	(0.1)	3	(0.2)	0	(0.0)	4	(0.2)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
nervous system												
analgesics	**125**	**(35.2)**	**272**	**(38.6)**	**302**	**(42.7)**	**574**	**(40.6)**	**95**	**(30.4)**	**848**	**(38.3)**
acetaminophen (+) doxylamine succinate (+) phenylephrine hydrochloride	0	(0.0)	1	(0.1)	3	(0.4)	4	(0.3)	0	(0.0)	4	(0.2)
acetaminophen (+) guaifenesin (+) phenylephrine hydrochloride	0	(0.0)	1	(0.1)	2	(0.3)	3	(0.2)	0	(0.0)	3	(0.1)
acetaminophen (+) hydrocodone bitartrate	9	(2.5)	14	(2.0)	17	(2.4)	31	(2.2)	4	(1.3)	45	(2.0)
acetaminophen (+) menthol	0	(0.0)	3	(0.4)	1	(0.1)	4	(0.3)	0	(0.0)	4	(0.2)
acetaminophen (+) metoclopramide	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
acetaminophen (+) oxycodone hydrochloride	3	(0.8)	5	(0.7)	4	(0.6)	9	(0.6)	3	(1.0)	16	(0.7)
acetaminophen (+) pheniramine maleate (+) phenylephrine hydrochloride	1	(0.3)	2	(0.3)	0	(0.0)	2	(0.1)	1	(0.3)	4	(0.2)
acetaminophen (+) phenylephrine hydrochloride	1	(0.3)	4	(0.6)	4	(0.6)	8	(0.6)	0	(0.0)	10	(0.5)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
nervous system												
analgesics	**125**	**(35.2)**	**272**	**(38.6)**	**302**	**(42.7)**	**574**	**(40.6)**	**95**	**(30.4)**	**848**	**(38.3)**
acetaminophen (+) pseudoephedrine hydrochloride	0	(0.0)	8	(1.1)	11	(1.6)	19	(1.3)	0	(0.0)	19	(0.9)
acetaminophen (+) tramadol hydrochloride	0	(0.0)	1	(0.1)	3	(0.4)	4	(0.3)	2	(0.6)	6	(0.3)
analgesic (unspecified)	0	(0.0)	1	(0.1)	2	(0.3)	3	(0.2)	0	(0.0)	3	(0.1)
ascorbic acid (+) aspirin	1	(0.3)	1	(0.1)	0	(0.0)	1	(0.1)	2	(0.6)	6	(0.3)
ascorbic acid (+) rutin (+) salicylamide	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
aspirin	47	(13.2)	94	(13.3)	88	(12.4)	182	(12.9)	32	(10.2)	272	(12.3)
aspirin (+) caffeine	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
aspirin (+) calcium carbonate	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
aspirin (+) chlorpheniramine maleate (+) dextromethorphan hydrobromide (+) phenylephrine hydrochloride	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	2	(0.1)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
nervous system												
analgesics	**125**	**(35.2)**	**272**	**(38.6)**	**302**	**(42.7)**	**574**	**(40.6)**	**95**	**(30.4)**	**848**	**(38.3)**
aspirin (+) chlorpheniramine maleate (+) dextromethorphan hydrobromide (+) phenylpropanolamine bitartrate	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
aspirin (+) chlorpheniramine maleate (+) phenylpropanolamine hydrochloride	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
aspirin (+) citric acid (+) sodium bicarbonate	2	(0.6)	2	(0.3)	1	(0.1)	3	(0.2)	0	(0.0)	5	(0.2)
aspirin (+) codeine phosphate (+) diphenhydramine hydrochloride (+) meprobamate (+) niacin	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.0)
aspirin (+) codeine phosphate (+) pseudoephedrine hydrochloride	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
nervous system												
analgesics	**125**	**(35.2)**	**272**	**(38.6)**	**302**	**(42.7)**	**574**	**(40.6)**	**95**	**(30.4)**	**848**	**(38.3)**
aspirin (+) pseudoephedrine hydrochloride	1	(0.3)	4	(0.6)	4	(0.6)	8	(0.6)	2	(0.6)	12	(0.5)
aspirin lysine	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.1)	0	(0.0)	2	(0.1)
calcium bromide (+) dibucaine hydrochloride (+) sodium salicylate	1	(0.3)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	2	(0.1)
choline salicylate	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.0)
codeine phosphate (+) ibuprofen	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
dihydrocodeine	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
dihydrocodeine bitartrate	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	1	(0.3)	2	(0.1)
dihydrocodeine phosphate	2	(0.6)	3	(0.4)	1	(0.1)	4	(0.3)	0	(0.0)	8	(0.4)
dihydrocodeine thiocyanate	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
dipyrone	6	(1.7)	16	(2.3)	13	(1.8)	29	(2.1)	11	(3.5)	49	(2.2)
eletriptan hydrobromide	0	(0.0)	1	(0.1)	2	(0.3)	3	(0.2)	0	(0.0)	3	(0.1)
fentanyl	2	(0.6)	3	(0.4)	7	(1.0)	10	(0.7)	2	(0.6)	15	(0.7)
flupirtine maleate	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	2	(0.1)
frovatriptan succinate	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
hydromorphone	2	(0.6)	5	(0.7)	4	(0.6)	9	(0.6)	1	(0.3)	12	(0.5)
hydromorphone hydrochloride	1	(0.3)	4	(0.6)	5	(0.7)	9	(0.6)	0	(0.0)	10	(0.5)
lomerizine hydrochloride	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
nervous system												
analgesics	**125**	**(35.2)**	**272**	**(38.6)**	**302**	**(42.7)**	**574**	**(40.6)**	**95**	**(30.4)**	**848**	**(38.3)**
meperidine hydrochloride	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)	1	(0.3)	4	(0.2)
morphine	2	(0.6)	6	(0.9)	7	(1.0)	13	(0.9)	1	(0.3)	16	(0.7)
morphine hydrochloride	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
morphine sulfate	1	(0.3)	4	(0.6)	7	(1.0)	11	(0.8)	0	(0.0)	12	(0.5)
naloxone hydrochloride (+) oxycodone hydrochloride	1	(0.3)	0	(0.0)	1	(0.1)	1	(0.1)	1	(0.3)	3	(0.1)
naloxone hydrochloride (+) tilidine hydrochloride	0	(0.0)	2	(0.3)	4	(0.6)	6	(0.4)	0	(0.0)	6	(0.3)
naratriptan hydrochloride	0	(0.0)	1	(0.1)	2	(0.3)	3	(0.2)	0	(0.0)	3	(0.1)
oxycodone	2	(0.6)	3	(0.4)	4	(0.6)	7	(0.5)	0	(0.0)	9	(0.4)
oxycodone hydrochloride	2	(0.6)	4	(0.6)	2	(0.3)	6	(0.4)	1	(0.3)	10	(0.5)
piritramide	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)	2	(0.6)	4	(0.2)
pizotyline malate	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
rizatriptan benzoate	1	(0.3)	0	(0.0)	2	(0.3)	2	(0.1)	0	(0.0)	3	(0.1)
sodium salicylate	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
sumatriptan	2	(0.6)	2	(0.3)	4	(0.6)	6	(0.4)	1	(0.3)	9	(0.4)
tramadol hydrochloride	7	(2.0)	13	(1.8)	21	(3.0)	34	(2.4)	7	(2.2)	54	(2.4)
anesthetics	**24**	**(6.8)**	**35**	**(5.0)**	**54**	**(7.6)**	**89**	**(6.3)**	**16**	**(5.1)**	**142**	**(6.4)**
anesthetic (unspecified)	0	(0.0)	4	(0.6)	3	(0.4)	7	(0.5)	1	(0.3)	8	(0.4)
articaine	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
articaine hydrochloride	1	(0.3)	1	(0.1)	2	(0.3)	3	(0.2)	2	(0.6)	6	(0.3)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
nervous system												
anesthetics	**24**	**(6.8)**	**35**	**(5.0)**	**54**	**(7.6)**	**89**	**(6.3)**	**16**	**(5.1)**	**142**	**(6.4)**
articaine hydrochloride (+) epinephrine bitartrate	1	(0.3)	2	(0.3)	1	(0.1)	3	(0.2)	1	(0.3)	5	(0.2)
articaine hydrochloride (+) racepinephrine hydrochloride	0	(0.0)	1	(0.1)	2	(0.3)	3	(0.2)	0	(0.0)	3	(0.1)
benzocaine (+) resorcinol	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
bupivacaine	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
bupivacaine hydrochloride	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	2	(0.1)
epinephrine (+) lidocaine (+) sodium bicarbonate	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	1	(0.3)	2	(0.1)
epinephrine (+) lidocaine hydrochloride	6	(1.7)	14	(2.0)	7	(1.0)	21	(1.5)	0	(0.0)	34	(1.5)
epinephrine (+) mepivacaine hydrochloride (+) sodium chloride	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
epinephrine (+) prilocaine hydrochloride	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
general anesthesia (unspecified)	2	(0.6)	4	(0.6)	1	(0.1)	5	(0.4)	0	(0.0)	8	(0.4)
isopropyl palmitate (+) ketamine hydrochloride (+) lecithin (+) poloxamer 407	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
nervous system												
anesthetics	**24**	**(6.8)**	**35**	**(5.0)**	**54**	**(7.6)**	**89**	**(6.3)**	**16**	**(5.1)**	**142**	**(6.4)**
ketamine hydrochloride	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
lidocaine	9	(2.5)	9	(1.3)	15	(2.1)	24	(1.7)	5	(1.6)	40	(1.8)
lidocaine (+) propofol	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.0)
lidocaine hydrochloride	4	(1.1)	4	(0.6)	5	(0.7)	9	(0.6)	1	(0.3)	14	(0.6)
mepivacaine hydrochloride	1	(0.3)	2	(0.3)	5	(0.7)	7	(0.5)	2	(0.6)	11	(0.5)
nitrous oxide	0	(0.0)	0	(0.0)	2	(0.3)	2	(0.1)	0	(0.0)	2	(0.1)
prilocaine hydrochloride	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.1)
procaine hydrochloride	0	(0.0)	0	(0.0)	2	(0.3)	2	(0.1)	1	(0.3)	3	(0.1)
propipocaine	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
propofol	2	(0.6)	3	(0.4)	9	(1.3)	12	(0.8)	3	(1.0)	17	(0.8)
remifentanil hydrochloride	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	2	(0.1)
ropivacaine	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	2	(0.1)
ropivacaine hydrochloride	1	(0.3)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	2	(0.1)
sevoflurane	0	(0.0)	0	(0.0)	2	(0.3)	2	(0.1)	0	(0.0)	2	(0.1)
sufentanil citrate	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
anti-Parkinson drugs	**0**	**(0.0)**	**2**	**(0.3)**	**3**	**(0.4)**	**5**	**(0.4)**	**2**	**(0.6)**	**7**	**(0.3)**
biperiden hydrochloride	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
biperiden lactate	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
orphenadrine	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	1	(0.3)	2	(0.1)
pramipexole	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.0)
ropinirole hydrochloride	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.1)	0	(0.0)	2	(0.1)
trihexyphenidyl hydrochloride	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
nervous system												
antiepileptics	**14**	**(3.9)**	**19**	**(2.7)**	**33**	**(4.7)**	**52**	**(3.7)**	**10**	**(3.2)**	**82**	**(3.7)**
carbamazepine	0	(0.0)	0	(0.0)	2	(0.3)	2	(0.1)	1	(0.3)	3	(0.1)
clonazepam	4	(1.1)	5	(0.7)	4	(0.6)	9	(0.6)	2	(0.6)	17	(0.8)
divalproex sodium	0	(0.0)	2	(0.3)	1	(0.1)	3	(0.2)	0	(0.0)	4	(0.2)
gabapentin	4	(1.1)	8	(1.1)	12	(1.7)	20	(1.4)	2	(0.6)	27	(1.2)
gamma-aminobutyric acid	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
lamotrigine	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)	1	(0.3)	3	(0.1)
levetiracetam	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.6)	2	(0.1)
oxcarbazepine	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
phenytoin	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
pregabalin	2	(0.6)	1	(0.1)	10	(1.4)	11	(0.8)	2	(0.6)	17	(0.8)
primidone	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.0)
topiramate	3	(0.8)	2	(0.3)	1	(0.1)	3	(0.2)	0	(0.0)	7	(0.3)
valproate sodium	0	(0.0)	2	(0.3)	1	(0.1)	3	(0.2)	1	(0.3)	5	(0.2)
valproate sodium (+) valproic acid	1	(0.3)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	3	(0.1)
other nervous system drugs	**4**	**(1.1)**	**16**	**(2.3)**	**11**	**(1.6)**	**27**	**(1.9)**	**4**	**(1.3)**	**36**	**(1.6)**
acamprosate calcium	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.0)
betahistine	1	(0.3)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	2	(0.1)
betahistine hydrochloride	1	(0.3)	3	(0.4)	1	(0.1)	4	(0.3)	0	(0.0)	6	(0.3)
betahistine mesylate	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
carpronium chloride	1	(0.3)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	2	(0.1)
cinnarizine (+) dimenhydrinate	0	(0.0)	0	(0.0)	2	(0.3)	2	(0.1)	0	(0.0)	2	(0.1)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
nervous system												
other nervous system drugs	**4**	**(1.1)**	**16**	**(2.3)**	**11**	**(1.6)**	**27**	**(1.9)**	**4**	**(1.3)**	**36**	**(1.6)**
disulfiram	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
edaravone	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
methadone hydrochloride	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	2	(0.1)
naltrexone	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.0)
neostigmine methylsulfate	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)	1	(0.3)	3	(0.1)
nicotine	0	(0.0)	5	(0.7)	2	(0.3)	7	(0.5)	2	(0.6)	9	(0.4)
nicotine polacrilex	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.0)
riluzole	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
varenicline tartrate	0	(0.0)	4	(0.6)	2	(0.3)	6	(0.4)	0	(0.0)	6	(0.3)
psychoanaleptics	**41**	**(11.5)**	**87**	**(12.3)**	**95**	**(13.4)**	**182**	**(12.9)**	**33**	**(10.5)**	**275**	**(12.4)**
acetylcarnitine	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
acetylcarnitine hydrochloride	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
agomelatine	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	1	(0.3)	2	(0.1)
amitriptyline hydrochloride	2	(0.6)	6	(0.9)	10	(1.4)	16	(1.1)	2	(0.6)	24	(1.1)
amoxapine	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
amphetamine aspartate (+) amphetamine sulfate (+) dextroamphetamine saccharate (+) dextroamphetamine sulfate	3	(0.8)	4	(0.6)	1	(0.1)	5	(0.4)	0	(0.0)	9	(0.4)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
nervous system												
psychoanaleptics	**41**	**(11.5)**	**87**	**(12.3)**	**95**	**(13.4)**	**182**	**(12.9)**	**33**	**(10.5)**	**275**	**(12.4)**
armodafinil	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.0)
bupropion hydrochloride	6	(1.7)	5	(0.7)	5	(0.7)	10	(0.7)	3	(1.0)	20	(0.9)
caffeine	2	(0.6)	4	(0.6)	2	(0.3)	6	(0.4)	0	(0.0)	10	(0.5)
citalopram	3	(0.8)	9	(1.3)	7	(1.0)	16	(1.1)	5	(1.6)	25	(1.1)
citalopram hydrobromide	1	(0.3)	8	(1.1)	2	(0.3)	10	(0.7)	3	(1.0)	15	(0.7)
clomipramine hydrochloride	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.1)	0	(0.0)	2	(0.1)
desvenlafaxine	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
desvenlafaxine succinate	0	(0.0)	3	(0.4)	1	(0.1)	4	(0.3)	0	(0.0)	4	(0.2)
dextroamphetamine	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
diazepam (+) dothiepin hydrochloride	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.0)
dothiepin hydrochloride	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
doxepin hydrochloride	0	(0.0)	2	(0.3)	1	(0.1)	3	(0.2)	1	(0.3)	4	(0.2)
duloxetine hydrochloride	7	(2.0)	6	(0.9)	7	(1.0)	13	(0.9)	0	(0.0)	21	(0.9)
escitalopram	3	(0.8)	1	(0.1)	3	(0.4)	4	(0.3)	0	(0.0)	8	(0.4)
escitalopram oxalate	5	(1.4)	9	(1.3)	10	(1.4)	19	(1.3)	5	(1.6)	31	(1.4)
fluoxetine	2	(0.6)	5	(0.7)	9	(1.3)	14	(1.0)	0	(0.0)	16	(0.7)
fluoxetine hydrochloride	1	(0.3)	2	(0.3)	5	(0.7)	7	(0.5)	1	(0.3)	9	(0.4)
flupentixol hydrochloride (+) melitracen hydrochloride	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
imipramine pamoate	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
nervous system												
psychoanaleptics	**41**	**(11.5)**	**87**	**(12.3)**	**95**	**(13.4)**	**182**	**(12.9)**	**33**	**(10.5)**	**275**	**(12.4)**
lisdexamfetamine dimesylate	0	(0.0)	0	(0.0)	4	(0.6)	4	(0.3)	1	(0.3)	5	(0.2)
methylphenidate	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
methylphenidate hydrochloride	0	(0.0)	3	(0.4)	4	(0.6)	7	(0.5)	0	(0.0)	7	(0.3)
mianserin hydrochloride	1	(0.3)	0	(0.0)	1	(0.1)	1	(0.1)	1	(0.3)	3	(0.1)
mirtazapine	2	(0.6)	6	(0.9)	0	(0.0)	6	(0.4)	1	(0.3)	11	(0.5)
moclobemide	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	2	(0.1)
modafinil	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
nortriptyline	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
opipramol hydrochloride	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	2	(0.1)
paroxetine	2	(0.6)	3	(0.4)	4	(0.6)	7	(0.5)	1	(0.3)	11	(0.5)
paroxetine hydrochloride	2	(0.6)	1	(0.1)	3	(0.4)	4	(0.3)	2	(0.6)	9	(0.4)
piracetam	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	2	(0.1)
sertraline hydrochloride	4	(1.1)	6	(0.9)	13	(1.8)	19	(1.3)	5	(1.6)	30	(1.4)
tianeptine sodium	1	(0.3)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	2	(0.1)
trazodone hydrochloride	3	(0.8)	7	(1.0)	7	(1.0)	14	(1.0)	4	(1.3)	22	(1.0)
venlafaxine hydrochloride	3	(0.8)	11	(1.6)	15	(2.1)	26	(1.8)	4	(1.3)	34	(1.5)
vilazodone	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
vinpocetine	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.0)
vortioxetine hydrobromide	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
psycholeptics	**38**	**(10.7)**	**66**	**(9.4)**	**76**	**(10.7)**	**142**	**(10.0)**	**26**	**(8.3)**	**220**	**(9.9)**
acetaminophen (+) butalbital (+) caffeine	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)	1	(0.3)	3	(0.1)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
nervous system												
psycholeptics	**38**	**(10.7)**	**66**	**(9.4)**	**76**	**(10.7)**	**142**	**(10.0)**	**26**	**(8.3)**	**220**	**(9.9)**
alprazolam	5	(1.4)	6	(0.9)	18	(2.5)	24	(1.7)	7	(2.2)	38	(1.7)
amisulpride	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.0)
aripiprazole	1	(0.3)	3	(0.4)	1	(0.1)	4	(0.3)	0	(0.0)	5	(0.2)
asenapine maleate	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	2	(0.1)
bromazepam	0	(0.0)	2	(0.3)	2	(0.3)	4	(0.3)	1	(0.3)	5	(0.2)
bromisovalum	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
brotizolam	1	(0.3)	1	(0.1)	2	(0.3)	3	(0.2)	0	(0.0)	5	(0.2)
buspirone hydrochloride	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)	1	(0.3)	3	(0.1)
chlordiazepoxide hydrochloride	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	1	(0.3)	2	(0.1)
clorazepate dipotassium	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.0)
cloxazolam	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
clozapine	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
diazepam	2	(0.6)	3	(0.4)	4	(0.6)	7	(0.5)	0	(0.0)	12	(0.5)
estazolam	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
etizolam	0	(0.0)	1	(0.1)	2	(0.3)	3	(0.2)	0	(0.0)	3	(0.1)
flunitrazepam	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	2	(0.1)
flupentixol hydrochloride	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
flurazepam	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
haloperidol	0	(0.0)	0	(0.0)	2	(0.3)	2	(0.1)	0	(0.0)	2	(0.1)
hydroxyzine	9	(2.5)	7	(1.0)	5	(0.7)	12	(0.8)	3	(1.0)	26	(1.2)
hydroxyzine hydrochloride	5	(1.4)	4	(0.6)	3	(0.4)	7	(0.5)	3	(1.0)	16	(0.7)
hydroxyzine pamoate	0	(0.0)	3	(0.4)	1	(0.1)	4	(0.3)	0	(0.0)	4	(0.2)
levomepromazine	2	(0.6)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	4	(0.2)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
nervous system												
psycholeptics	**38**	**(10.7)**	**66**	**(9.4)**	**76**	**(10.7)**	**142**	**(10.0)**	**26**	**(8.3)**	**220**	**(9.9)**
levosulpiride	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
lithium	1	(0.3)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	2	(0.1)
lithium carbonate	0	(0.0)	1	(0.1)	2	(0.3)	3	(0.2)	1	(0.3)	4	(0.2)
lithium gluconate	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
lorazepam	8	(2.3)	13	(1.8)	12	(1.7)	25	(1.8)	0	(0.0)	35	(1.6)
lormetazepam	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	2	(0.1)
melatonin	2	(0.6)	2	(0.3)	2	(0.3)	4	(0.3)	1	(0.3)	7	(0.3)
midazolam	0	(0.0)	5	(0.7)	5	(0.7)	10	(0.7)	1	(0.3)	11	(0.5)
midazolam hydrochloride	2	(0.6)	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.6)	5	(0.2)
nitrazepam	1	(0.3)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	3	(0.1)
olanzapine	0	(0.0)	1	(0.1)	3	(0.4)	4	(0.3)	1	(0.3)	6	(0.3)
oxazepam	0	(0.0)	1	(0.1)	3	(0.4)	4	(0.3)	0	(0.0)	4	(0.2)
pipamperone	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.0)
prazepam	0	(0.0)	0	(0.0)	2	(0.3)	2	(0.1)	0	(0.0)	2	(0.1)
prochlorperazine	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.1)	1	(0.3)	3	(0.1)
prochlorperazine maleate	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
prothipendyl hydrochloride	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
quetiapine fumarate	1	(0.3)	5	(0.7)	6	(0.8)	11	(0.8)	0	(0.0)	13	(0.6)
rilmazafone hydrochloride	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
risperidone	1	(0.3)	1	(0.1)	3	(0.4)	4	(0.3)	0	(0.0)	5	(0.2)
suriclone	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
temazepam	0	(0.0)	3	(0.4)	3	(0.4)	6	(0.4)	0	(0.0)	6	(0.3)
triazolam	0	(0.0)	1	(0.1)	2	(0.3)	3	(0.2)	0	(0.0)	3	(0.1)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
nervous system												
psycholeptics	**38**	**(10.7)**	**66**	**(9.4)**	**76**	**(10.7)**	**142**	**(10.0)**	**26**	**(8.3)**	**220**	**(9.9)**
valerian	0	(0.0)	2	(0.3)	1	(0.1)	3	(0.2)	0	(0.0)	3	(0.1)
zolpidem	0	(0.0)	3	(0.4)	6	(0.8)	9	(0.6)	1	(0.3)	11	(0.5)
zolpidem tartrate	2	(0.6)	6	(0.9)	9	(1.3)	15	(1.1)	2	(0.6)	19	(0.9)
zopiclone	2	(0.6)	2	(0.3)	8	(1.1)	10	(0.7)	3	(1.0)	17	(0.8)
respiratory system												
antihistamines for systemic use	**69**	**(19.4)**	**115**	**(16.3)**	**109**	**(15.4)**	**224**	**(15.9)**	**31**	**(9.9)**	**347**	**(15.7)**
azelastine hydrochloride	1	(0.3)	1	(0.1)	0	(0.0)	1	(0.1)	1	(0.3)	3	(0.1)
bepotastine besylate	3	(0.8)	7	(1.0)	6	(0.8)	13	(0.9)	0	(0.0)	19	(0.9)
bepotastine besylate (+) menthol	1	(0.3)	2	(0.3)	4	(0.6)	6	(0.4)	0	(0.0)	7	(0.3)
bromelains (+) isopropamide iodide (+) chlorpheniramine maleate	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
carbinoxamine maleate	1	(0.3)	2	(0.3)	0	(0.0)	2	(0.1)	0	(0.0)	4	(0.2)
cetirizine hydrochloride	21	(5.9)	23	(3.3)	18	(2.5)	41	(2.9)	8	(2.6)	77	(3.5)
chlorpheniramine	0	(0.0)	0	(0.0)	2	(0.3)	2	(0.1)	0	(0.0)	2	(0.1)
chlorpheniramine maleate	0	(0.0)	4	(0.6)	1	(0.1)	5	(0.4)	0	(0.0)	5	(0.2)
clemastine fumarate	3	(0.8)	1	(0.1)	3	(0.4)	4	(0.3)	0	(0.0)	8	(0.4)
desloratadine	5	(1.4)	4	(0.6)	10	(1.4)	14	(1.0)	4	(1.3)	24	(1.1)
dexchlorpheniramine maleate	2	(0.6)	3	(0.4)	3	(0.4)	6	(0.4)	0	(0.0)	8	(0.4)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
respiratory system												
antihistamines for systemic use	**69**	**(19.4)**	**115**	**(16.3)**	**109**	**(15.4)**	**224**	**(15.9)**	**31**	**(9.9)**	**347**	**(15.7)**
dimenhydrinate	1	(0.3)	6	(0.9)	6	(0.8)	12	(0.8)	0	(0.0)	14	(0.6)
dimethindene maleate	2	(0.6)	1	(0.1)	3	(0.4)	4	(0.3)	2	(0.6)	9	(0.4)
diphenhydramine	5	(1.4)	6	(0.9)	4	(0.6)	10	(0.7)	4	(1.3)	19	(0.9)
diphenhydramine hydrochloride	7	(2.0)	22	(3.1)	18	(2.5)	40	(2.8)	4	(1.3)	53	(2.4)
diphenhydramine lauryl sulfate	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
doxylamine succinate	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
ebastine	0	(0.0)	2	(0.3)	2	(0.3)	4	(0.3)	1	(0.3)	5	(0.2)
epinastine	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
epinastine hydrochloride	4	(1.1)	10	(1.4)	5	(0.7)	15	(1.1)	0	(0.0)	21	(0.9)
fexofenadine hydrochloride	17	(4.8)	15	(2.1)	21	(3.0)	36	(2.5)	2	(0.6)	57	(2.6)
ketotifen fumarate	0	(0.0)	3	(0.4)	0	(0.0)	3	(0.2)	0	(0.0)	3	(0.1)
levocetirizine	0	(0.0)	0	(0.0)	2	(0.3)	2	(0.1)	0	(0.0)	2	(0.1)
levocetirizine dihydrochloride	2	(0.6)	9	(1.3)	6	(0.8)	15	(1.1)	3	(1.0)	20	(0.9)
loratadine	12	(3.4)	19	(2.7)	10	(1.4)	29	(2.1)	7	(2.2)	51	(2.3)
meclizine	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	3	(0.1)
mequitazine	2	(0.6)	3	(0.4)	2	(0.3)	5	(0.4)	0	(0.0)	8	(0.4)
mizolastine	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
oxatomide	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.1)	0	(0.0)	2	(0.1)
pheniramine maleate	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
respiratory system												
antihistamines for systemic use	**69**	**(19.4)**	**115**	**(16.3)**	**109**	**(15.4)**	**224**	**(15.9)**	**31**	**(9.9)**	**347**	**(15.7)**
promethazine	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.6)	3	(0.1)
promethazine hydrochloride	3	(0.8)	3	(0.4)	2	(0.3)	5	(0.4)	1	(0.3)	10	(0.5)
rupatadine fumarate	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	2	(0.1)
trimethobenzamide hydrochloride	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
cough and cold preparations	**37**	**(10.4)**	**64**	**(9.1)**	**82**	**(11.6)**	**146**	**(10.3)**	**15**	**(4.8)**	**213**	**(9.6)**
acetylcysteine	3	(0.8)	5	(0.7)	9	(1.3)	14	(1.0)	7	(2.2)	25	(1.1)
acetylcysteine (+) ascorbic acid	0	(0.0)	3	(0.4)	1	(0.1)	4	(0.3)	1	(0.3)	5	(0.2)
ambroxol	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
ambroxol hydrochloride	4	(1.1)	4	(0.6)	6	(0.8)	10	(0.7)	0	(0.0)	15	(0.7)
ammonium carbonate (+) balsam fir (+) camphor (+) capsicum (+) Irish moss (+) menthol (+) potassium bicarbonate	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
ammonium carbonate (+) camphor (+) menthol (+) potassium bicarbonate	0	(0.0)	0	(0.0)	3	(0.4)	3	(0.2)	0	(0.0)	3	(0.1)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
respiratory system												
cough and cold preparations	**37**	**(10.4)**	**64**	**(9.1)**	**82**	**(11.6)**	**146**	**(10.3)**	**15**	**(4.8)**	**213**	**(9.6)**
ammonium chloride (+) dihydrocodeine phosphate (+) ephedrine hydrochloride	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
benproperine phosphate	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	2	(0.1)
benzonatate	0	(0.0)	2	(0.3)	3	(0.4)	5	(0.4)	0	(0.0)	5	(0.2)
benzyl cinnamate (+) citral (+) guaiacol (+) pine oil (+) terpin hydrate (+) thyme oil	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
bromhexine hydrochloride	1	(0.3)	2	(0.3)	1	(0.1)	3	(0.2)	0	(0.0)	5	(0.2)
brompheniramine maleate (+) dextromethorphan hydrobromide (+) pseudoephedrine hydrochloride	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
butamirate citrate	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
carbetapentane	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	2	(0.1)
carbocysteine	5	(1.4)	10	(1.4)	11	(1.6)	21	(1.5)	0	(0.0)	27	(1.2)
cherry bark extract (+) codeine phosphate	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
chlophedianol hydrochloride	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	2	(0.1)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
respiratory system												
cough and cold preparations	**37**	**(10.4)**	**64**	**(9.1)**	**82**	**(11.6)**	**146**	**(10.3)**	**15**	**(4.8)**	**213**	**(9.6)**
chlophedianol hydrochloride (+) guaifenesin (+) pseudoephedrine hydrochloride	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
chlorpheniramine maleate (+) dextromethorphan hydrobromide	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	2	(0.1)
chlorpheniramine maleate (+) dextromethorphan hydrobromide (+) guaifenesin (+) phenylephrine hydrochloride	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
chlorpheniramine maleate (+) dextromethorphan hydrobromide (+) phenylephrine hydrochloride	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
respiratory system												
cough and cold preparations	**37**	**(10.4)**	**64**	**(9.1)**	**82**	**(11.6)**	**146**	**(10.3)**	**15**	**(4.8)**	**213**	**(9.6)**
chlorpheniramine maleate (+) dihydrocodeine phosphate (+) methylephedrine hydrochloride	1	(0.3)	2	(0.3)	2	(0.3)	4	(0.3)	0	(0.0)	6	(0.3)
chlorpheniramine polistirex (+) hydrocodone polistirex	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	2	(0.1)
clobutinol hydrochloride	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
cloperastine fendizoate	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	2	(0.1)
codeine	1	(0.3)	4	(0.6)	3	(0.4)	7	(0.5)	0	(0.0)	8	(0.4)
codeine (+) guaifenesin	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	2	(0.1)
codeine phosphate	1	(0.3)	1	(0.1)	2	(0.3)	3	(0.2)	0	(0.0)	5	(0.2)
codeine phosphate (+) guaifenesin	1	(0.3)	0	(0.0)	2	(0.3)	2	(0.1)	0	(0.0)	3	(0.1)
codeine phosphate (+) potassium guaiacolsulfonate	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
codeine phosphate (+) promethazine hydrochloride	1	(0.3)	0	(0.0)	3	(0.4)	3	(0.2)	0	(0.0)	4	(0.2)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
respiratory system												
cough and cold preparations	**37**	**(10.4)**	**64**	**(9.1)**	**82**	**(11.6)**	**146**	**(10.3)**	**15**	**(4.8)**	**213**	**(9.6)**
codeine phosphate (+) pseudoephedrine hydrochloride (+) triprolidine hydrochloride	1	(0.3)	0	(0.0)	2	(0.3)	2	(0.1)	0	(0.0)	4	(0.2)
cough, cold, and flu therapies (unspecified)	2	(0.6)	2	(0.3)	7	(1.0)	9	(0.6)	0	(0.0)	13	(0.6)
dextromethorphan	1	(0.3)	3	(0.4)	1	(0.1)	4	(0.3)	1	(0.3)	9	(0.4)
dextromethorphan hydrobromide	5	(1.4)	6	(0.9)	6	(0.8)	12	(0.8)	1	(0.3)	19	(0.9)
dextromethorphan hydrobromide (+) doxylamine succinate	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
dextromethorphan hydrobromide (+) fennel (+) pine oil	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.0)
dextromethorphan hydrobromide (+) guaifenesin	2	(0.6)	2	(0.3)	4	(0.6)	6	(0.4)	1	(0.3)	11	(0.5)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
respiratory system												
cough and cold preparations	**37**	**(10.4)**	**64**	**(9.1)**	**82**	**(11.6)**	**146**	**(10.3)**	**15**	**(4.8)**	**213**	**(9.6)**
dextromethorphan hydrobromide (+) guaifenesin (+) menthol (+) pseudoephedrine hydrochloride	0	(0.0)	0	(0.0)	2	(0.3)	2	(0.1)	0	(0.0)	2	(0.1)
dextromethorphan hydrobromide (+) guaifenesin (+) phenylephrine hydrochloride	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
dextromethorphan polistirex	1	(0.3)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	2	(0.1)
dimemorfan phosphate	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.1)	0	(0.0)	2	(0.1)
eprazinone hydrochloride	1	(0.3)	0	(0.0)	2	(0.3)	2	(0.1)	0	(0.0)	3	(0.1)
erdosteine	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.0)
eucalyptol	1	(0.3)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	3	(0.1)
guaifenesin	4	(1.1)	12	(1.7)	10	(1.4)	22	(1.6)	2	(0.6)	30	(1.4)
guaifenesin (+) pseudoephedrine hydrochloride	2	(0.6)	0	(0.0)	1	(0.1)	1	(0.1)	1	(0.3)	4	(0.2)
hydrocodone	3	(0.8)	5	(0.7)	3	(0.4)	8	(0.6)	0	(0.0)	11	(0.5)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
respiratory system												
cough and cold preparations	**37**	**(10.4)**	**64**	**(9.1)**	**82**	**(11.6)**	**146**	**(10.3)**	**15**	**(4.8)**	**213**	**(9.6)**
ipratropium bromide (+) xylometazoline hydrochloride	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
licorice (+) menthol (+) squill	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
noscapine	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	3	(0.1)
noscapine (+) promethazine	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
noscapine polistirex	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
potassium guaiacolsulfonate	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
thebacon hydrochloride	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
tipepidine hibenzate	1	(0.3)	1	(0.1)	2	(0.3)	3	(0.2)	0	(0.0)	4	(0.2)
drugs for obstructive airway diseases	**28**	**(7.9)**	**59**	**(8.4)**	**68**	**(9.6)**	**127**	**(9.0)**	**18**	**(5.8)**	**186**	**(8.4)**
aclidinium bromide	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
albuterol	7	(2.0)	17	(2.4)	18	(2.5)	35	(2.5)	7	(2.2)	54	(2.4)
albuterol (+) ipratropium bromide	0	(0.0)	0	(0.0)	2	(0.3)	2	(0.1)	0	(0.0)	2	(0.1)
albuterol sulfate	3	(0.8)	8	(1.1)	7	(1.0)	15	(1.1)	4	(1.3)	23	(1.0)
albuterol sulfate (+) ipratropium bromide	0	(0.0)	1	(0.1)	2	(0.3)	3	(0.2)	0	(0.0)	3	(0.1)
arformoterol tartrate	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.0)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
respiratory system												
drugs for obstructive airway diseases	**28**	**(7.9)**	**59**	**(8.4)**	**68**	**(9.6)**	**127**	**(9.0)**	**18**	**(5.8)**	**186**	**(8.4)**
beclomethasone dipropionate	2	(0.6)	3	(0.4)	2	(0.3)	5	(0.4)	1	(0.3)	8	(0.4)
budesonide	1	(0.3)	1	(0.1)	1	(0.1)	2	(0.1)	1	(0.3)	5	(0.2)
budesonide (+) formoterol fumarate	2	(0.6)	9	(1.3)	4	(0.6)	13	(0.9)	3	(1.0)	20	(0.9)
ciclesonide	1	(0.3)	3	(0.4)	1	(0.1)	4	(0.3)	0	(0.0)	5	(0.2)
cromolyn sodium	1	(0.3)	1	(0.1)	0	(0.0)	1	(0.1)	1	(0.3)	4	(0.2)
dexchlorpheniramine maleate (+) dyphylline (+) methylephedrine hydrochloride (+) nandina (+) schisandra	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
ephedrine	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	2	(0.1)
epinephrine	3	(0.8)	3	(0.4)	3	(0.4)	6	(0.4)	0	(0.0)	9	(0.4)
epinephrine hydrochloride	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
fenoterol hydrobromide	1	(0.3)	0	(0.0)	1	(0.1)	1	(0.1)	1	(0.3)	4	(0.2)
fenoterol hydrobromide (+) ipratropium bromide	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
fenspiride hydrochloride	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
fluticasone	2	(0.6)	1	(0.1)	2	(0.3)	3	(0.2)	1	(0.3)	6	(0.3)
fluticasone furoate	2	(0.6)	1	(0.1)	5	(0.7)	6	(0.4)	1	(0.3)	10	(0.5)
fluticasone furoate (+) vilanterol trifenatate	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
respiratory system												
drugs for obstructive airway diseases	**28**	**(7.9)**	**59**	**(8.4)**	**68**	**(9.6)**	**127**	**(9.0)**	**18**	**(5.8)**	**186**	**(8.4)**
fluticasone propionate	5	(1.4)	8	(1.1)	6	(0.8)	14	(1.0)	3	(1.0)	23	(1.0)
fluticasone propionate (+) formoterol fumarate	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
fluticasone propionate (+) salmeterol xinafoate	3	(0.8)	9	(1.3)	9	(1.3)	18	(1.3)	1	(0.3)	24	(1.1)
formoterol fumarate	2	(0.6)	1	(0.1)	2	(0.3)	3	(0.2)	2	(0.6)	9	(0.4)
formoterol fumarate (+) mometasone furoate	1	(0.3)	3	(0.4)	5	(0.7)	8	(0.6)	1	(0.3)	10	(0.5)
ibudilast	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
indacaterol maleate	0	(0.0)	0	(0.0)	2	(0.3)	2	(0.1)	0	(0.0)	2	(0.1)
ipratropium bromide	0	(0.0)	0	(0.0)	5	(0.7)	5	(0.4)	1	(0.3)	6	(0.3)
levalbuterol hydrochloride	0	(0.0)	0	(0.0)	2	(0.3)	2	(0.1)	0	(0.0)	2	(0.1)
methylephedrine hydrochloride	2	(0.6)	4	(0.6)	1	(0.1)	5	(0.4)	0	(0.0)	9	(0.4)
montelukast	0	(0.0)	2	(0.3)	2	(0.3)	4	(0.3)	0	(0.0)	4	(0.2)
montelukast sodium	3	(0.8)	4	(0.6)	6	(0.8)	10	(0.7)	0	(0.0)	14	(0.6)
pranlukast	0	(0.0)	3	(0.4)	0	(0.0)	3	(0.2)	0	(0.0)	3	(0.1)
procaterol hydrochloride	1	(0.3)	1	(0.1)	2	(0.3)	3	(0.2)	0	(0.0)	4	(0.2)
salmeterol xinafoate	1	(0.3)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	2	(0.1)
suplatast tosylate	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
terbutaline sulfate	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	2	(0.1)
theophylline	1	(0.3)	3	(0.4)	2	(0.3)	5	(0.4)	0	(0.0)	7	(0.3)
tiotropium bromide	2	(0.6)	2	(0.3)	4	(0.6)	6	(0.4)	2	(0.6)	10	(0.5)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
respiratory system												
drugs for obstructive airway diseases	**28**	**(7.9)**	**59**	**(8.4)**	**68**	**(9.6)**	**127**	**(9.0)**	**18**	**(5.8)**	**186**	**(8.4)**
tranilast	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
tulobuterol	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.1)	0	(0.0)	2	(0.1)
tulobuterol hydrochloride	1	(0.3)	2	(0.3)	2	(0.3)	4	(0.3)	0	(0.0)	5	(0.2)
nasal preparations	**13**	**(3.7)**	**32**	**(4.5)**	**34**	**(4.8)**	**66**	**(4.7)**	**5**	**(1.6)**	**88**	**(4.0)**
acetylcysteine (+) benzalkonium chloride (+) tuaminoheptane sulfate	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
acrivastine (+) pseudoephedrine hydrochloride	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
azelastine hydrochloride (+) fluticasone propionate	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
belladonna alkaloids (+) caffeine (+) Chinese wild ginger (+) dexchlorpheniramine maleate (+) pseudoephedrine hydrochloride	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
respiratory system												
nasal preparations	**13**	**(3.7)**	**32**	**(4.5)**	**34**	**(4.8)**	**66**	**(4.7)**	**5**	**(1.6)**	**88**	**(4.0)**
belladonna alkaloids (+) caffeine (+) dexchlorpheniramine maleate (+) dipotassium glycyrrhizate (+) pseudoephedrine hydrochlorid	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
belladonna alkaloids (+) chlorpheniramine maleate (+) phenylpropanolamine hydrochloride	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
benzalkonium chloride (+) benzyl alcohol (+) sodium chloride (+) sodium phosphate, dibasic (+) sodium phosphate, monobasic	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
benzalkonium chloride (+) chlorpheniramine maleate (+) lidocaine (+) naphazoline hydrochloride	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
respiratory system												
nasal preparations	**13**	**(3.7)**	**32**	**(4.5)**	**34**	**(4.8)**	**66**	**(4.7)**	**5**	**(1.6)**	**88**	**(4.0)**
calcium lactate (+) dextrose (+) potassium chloride (+) sodium bicarbonate (+) sodium chloride	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
cathine	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
cetirizine hydrochloride (+) pseudoephedrine hydrochloride	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
cetrimide (+) naphazoline nitrate (+) phenylephrine hydrochloride (+) prednisolone	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
chlorpheniramine maleate (+) lidocaine (+) naphazoline hydrochloride	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
chlorpheniramine maleate (+) phenylephrine hydrochloride	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
chlorpheniramine maleate (+) pseudoephedrine hydrochloride	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
respiratory system												
nasal preparations	**13**	**(3.7)**	**32**	**(4.5)**	**34**	**(4.8)**	**66**	**(4.7)**	**5**	**(1.6)**	**88**	**(4.0)**
dexamethasone isonicotinate (+) neomycin sulfate (+) tramazoline hydrochloride	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
dexpanthenol (+) xylometazoline hydrochloride	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
fexofenadine hydrochloride (+) pseudoephedrine hydrochloride	0	(0.0)	1	(0.1)	2	(0.3)	3	(0.2)	0	(0.0)	3	(0.1)
framycetin sulfate (+) naphazoline nitrate (+) prednisolone acetate	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
levocabastine hydrochloride	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	2	(0.1)
lidocaine hydrochloride (+) oxymetazoline hydrochloride	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
loratadine (+) pseudoephedrine sulfate	1	(0.3)	3	(0.4)	1	(0.1)	4	(0.3)	0	(0.0)	5	(0.2)
naphazoline hydrochloride	0	(0.0)	0	(0.0)	2	(0.3)	2	(0.1)	0	(0.0)	2	(0.1)
naphazoline nitrate	1	(0.3)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	2	(0.1)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
respiratory system												
nasal preparations	**13**	**(3.7)**	**32**	**(4.5)**	**34**	**(4.8)**	**66**	**(4.7)**	**5**	**(1.6)**	**88**	**(4.0)**
naphazoline nitrate (+) prednisolone	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
oxymetazoline hydrochloride	0	(0.0)	3	(0.4)	5	(0.7)	8	(0.6)	0	(0.0)	8	(0.4)
pemirolast potassium	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
phenylephrine	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
phenylephrine hydrochloride	1	(0.3)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	3	(0.1)
propylhexedrine	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
pseudoephedrine	1	(0.3)	1	(0.1)	2	(0.3)	3	(0.2)	1	(0.3)	5	(0.2)
pseudoephedrine hydrochloride	3	(0.8)	5	(0.7)	5	(0.7)	10	(0.7)	1	(0.3)	14	(0.6)
pseudoephedrine sulfate	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
sea water	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
tetrahydrozoline hydrochloride	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
tixocortol pivalate	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
tramazoline hydrochloride	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
xylometazoline hydrochloride	3	(0.8)	9	(1.3)	8	(1.1)	17	(1.2)	3	(1.0)	24	(1.1)
other respiratory system products	**2**	**(0.6)**	**4**	**(0.6)**	**5**	**(0.7)**	**9**	**(0.6)**	**1**	**(0.3)**	**12**	**(0.5)**
Emser salt	1	(0.3)	1	(0.1)	0	(0.0)	1	(0.1)	1	(0.3)	3	(0.1)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
respiratory system												
other respiratory system products	**2**	**(0.6)**	**4**	**(0.6)**	**5**	**(0.7)**	**9**	**(0.6)**	**1**	**(0.3)**	**12**	**(0.5)**
camphor (+) eucalyptus oil (+) menthol	1	(0.3)	0	(0.0)	3	(0.4)	3	(0.2)	0	(0.0)	4	(0.2)
camphor (+) eucalyptus oil (+) menthol (+) nutmeg oil (+) thuja oil (+) thymol (+) turpentine	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	2	(0.1)
eucalyptus oil (+) menthol	1	(0.3)	2	(0.3)	0	(0.0)	2	(0.1)	0	(0.0)	3	(0.1)
menthol (+) pine tar	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
throat preparations	**5**	**(1.4)**	**1**	**(0.1)**	**12**	**(1.7)**	**13**	**(0.9)**	**3**	**(1.0)**	**23**	**(1.0)**
aluminum chloride (+) potassium chlorate	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
amylmetacresol (+) dichlorobenzyl alcohol	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
amylmetacresol (+) dichlorobenzyl alcohol (+) menthol	0	(0.0)	0	(0.0)	2	(0.3)	2	(0.1)	1	(0.3)	4	(0.2)
ascorbic acid (+) dequalinium chloride	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
benzalkonium chloride (+) benzocaine (+) tyrothricin	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
respiratory system												
throat preparations	**5**	**(1.4)**	**1**	**(0.1)**	**12**	**(1.7)**	**13**	**(0.9)**	**3**	**(1.0)**	**23**	**(1.0)**
benzalkonium chloride (+) eucalyptus oil (+) menthol (+) peppermint oil (+) thymol	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.0)
benzethonium chloride	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
benzethonium chloride (+) chlorhexidine gluconate	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
benzocaine (+) cetylpyridinium chloride	2	(0.6)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	3	(0.1)
benzocaine (+) menthol	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.0)
benzocaine (+) tyrothricin	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
bismuth valproate	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
camphor (+) menthol	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
cetylpyridinium chloride	0	(0.0)	0	(0.0)	2	(0.3)	2	(0.1)	0	(0.0)	2	(0.1)
cetylpyridinium chloride (+) lysozyme chloride	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
chlorhexidine gluconate (+) chlorobutanol	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
fusafungine	0	(0.0)	0	(0.0)	2	(0.3)	2	(0.1)	0	(0.0)	2	(0.1)
sensory organs												
ophthalmological and otological preparations	**0**	**(0.0)**	**3**	**(0.4)**	**1**	**(0.1)**	**4**	**(0.3)**	**0**	**(0.0)**	**4**	**(0.2)**

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
sensory organs												
ophthalmological and otological preparations	**0**	**(0.0)**	**3**	**(0.4)**	**1**	**(0.1)**	**4**	**(0.3)**	**0**	**(0.0)**	**4**	**(0.2)**
betamethasone sodium phosphate (+) gentamicin sulfate	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
dexamethasone (+) framycetin sulfate (+) gramicidin	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
dexamethasone (+) gentamicin sulfate	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
hydrocortisone (+) neomycin sulfate (+) polymyxin B sulfate	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
ophthalmologicals	**18**	**(5.1)**	**34**	**(4.8)**	**26**	**(3.7)**	**60**	**(4.2)**	**4**	**(1.3)**	**86**	**(3.9)**
acetazolamide	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	1	(0.3)	2	(0.1)
bimatoprost	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
boric acid (+) potassium chloride (+) sodium carbonate (+) sodium chloride (+) sodium phosphate, dibasic	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
sensory organs												
ophthalmologicals	**18**	**(5.1)**	**34**	**(4.8)**	**26**	**(3.7)**	**60**	**(4.2)**	**4**	**(1.3)**	**86**	**(3.9)**
borneol (+) camphor (+) chlorpheniramine maleate (+) dipotassium glycyrrhizate (+) menthol (+) pyridoxine hydrochloride (+) tetr	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
brimonidine tartrate	0	(0.0)	1	(0.1)	3	(0.4)	4	(0.3)	1	(0.3)	5	(0.2)
brimonidine tartrate (+) brinzolamide	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
brimonidine tartrate (+) timolol maleate	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.0)
brinzolamide	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
brinzolamide (+) timolol maleate	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
bromfenac sodium	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	2	(0.1)
carbomer	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
carboxymethylcellulose sodium (+) hypromellose	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
ciprofloxacin hydrochloride (+) dexamethasone	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.1)	0	(0.0)	2	(0.1)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
sensory organs												
ophthalmologicals	**18**	**(5.1)**	**34**	**(4.8)**	**26**	**(3.7)**	**60**	**(4.2)**	**4**	**(1.3)**	**86**	**(3.9)**
dexamethasone (+) neomycin sulfate (+) polymyxin B sulfate	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
dexamethasone (+) tobramycin	0	(0.0)	2	(0.3)	2	(0.3)	4	(0.3)	0	(0.0)	4	(0.2)
dexamethasone (+) tobramycin sulfate	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
dexamethasone isonicotinate (+) oxytetracycline hydrochloride	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.0)
dexamethasone sodium phosphate (+) gentamicin sulfate	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	2	(0.1)
dextran (+) riboflavin phosphate	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
dextrose (+) hypromellose (+) menthol (+) potassium chloride (+) sodium chloride	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
diquafosol tetrasodium	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
dorzolamide hydrochloride	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
dorzolamide hydrochloride (+) timolol maleate	2	(0.6)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	4	(0.2)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
sensory organs												
ophthalmologicals	**18**	**(5.1)**	**34**	**(4.8)**	**26**	**(3.7)**	**60**	**(4.2)**	**4**	**(1.3)**	**86**	**(3.9)**
emedastine	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
emedastine difumarate	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
glycerin (+) hypromellose (+) povidone	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
glycerin (+) naphazoline hydrochloride	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
hypromellose	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
isosorbide	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.0)
latanoprost	2	(0.6)	1	(0.1)	3	(0.4)	4	(0.3)	1	(0.3)	7	(0.3)
latanoprost (+) timolol maleate	1	(0.3)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	2	(0.1)
levobunolol hydrochloride	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
loteprednol etabonate	0	(0.0)	2	(0.3)	1	(0.1)	3	(0.2)	0	(0.0)	3	(0.1)
methazolamide	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
mineral oil (+) petrolatum, white	1	(0.3)	2	(0.3)	1	(0.1)	3	(0.2)	0	(0.0)	5	(0.2)
olopatadine hydrochloride	11	(3.1)	12	(1.7)	10	(1.4)	22	(1.6)	0	(0.0)	36	(1.6)
oxytetracycline hydrochloride (+) prednisolone	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
polyethylene glycol (+) propylene glycol	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
pranoprofen	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	2	(0.1)
ranibizumab	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
sensory organs												
ophthalmologicals	**18**	**(5.1)**	**34**	**(4.8)**	**26**	**(3.7)**	**60**	**(4.2)**	**4**	**(1.3)**	**86**	**(3.9)**
timolol maleate (+) travoprost	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)	1	(0.3)	3	(0.1)
travoprost	1	(0.3)	2	(0.3)	1	(0.1)	3	(0.2)	0	(0.0)	4	(0.2)
otologicals	**1**	**(0.3)**	**0**	**(0.0)**	**1**	**(0.1)**	**1**	**(0.1)**	**0**	**(0.0)**	**3**	**(0.1)**
alcohol (+) boric acid	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
antipyrine (+) lidocaine hydrochloride	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
antipyrine (+) procaine hydrochloride	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
systemic hormonal preparations, excl. sex hormones and insulins												
calcium homeostasis	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.0)**
salcatonin	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
corticosteroids for systemic use	**24**	**(6.8)**	**54**	**(7.7)**	**53**	**(7.5)**	**107**	**(7.6)**	**19**	**(6.1)**	**164**	**(7.4)**
betamethasone	1	(0.3)	1	(0.1)	1	(0.1)	2	(0.1)	2	(0.6)	6	(0.3)
betamethasone (+) dexchlorpheniramine maleate	0	(0.0)	1	(0.1)	2	(0.3)	3	(0.2)	0	(0.0)	3	(0.1)
betamethasone butyrate propionate	2	(0.6)	12	(1.7)	5	(0.7)	17	(1.2)	0	(0.0)	20	(0.9)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
systemic hormonal preparations, excl. sex hormones and insulins												
corticosteroids for systemic use	**24**	**(6.8)**	**54**	**(7.7)**	**53**	**(7.5)**	**107**	**(7.6)**	**19**	**(6.1)**	**164**	**(7.4)**
betamethasone dipropionate (+) betamethasone sodium phosphate	0	(0.0)	0	(0.0)	2	(0.3)	2	(0.1)	0	(0.0)	2	(0.1)
betamethasone sodium phosphate	0	(0.0)	0	(0.0)	2	(0.3)	2	(0.1)	0	(0.0)	2	(0.1)
corticosteroids (unspecified)	2	(0.6)	1	(0.1)	3	(0.4)	4	(0.3)	0	(0.0)	6	(0.3)
cortisone	0	(0.0)	3	(0.4)	4	(0.6)	7	(0.5)	0	(0.0)	8	(0.4)
dexamethasone	2	(0.6)	3	(0.4)	4	(0.6)	7	(0.5)	5	(1.6)	14	(0.6)
dexamethasone dipropionate	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
dexamethasone palmitate	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
dexamethasone sodium metasulfobenzoate	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
dexamethasone sodium phosphate	1	(0.3)	4	(0.6)	1	(0.1)	5	(0.4)	0	(0.0)	6	(0.3)
halobetasol propionate	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
hydrocortisone	5	(1.4)	2	(0.3)	5	(0.7)	7	(0.5)	0	(0.0)	17	(0.8)
hydrocortisone sodium succinate	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
methylprednisolone	3	(0.8)	1	(0.1)	2	(0.3)	3	(0.2)	0	(0.0)	6	(0.3)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
systemic hormonal preparations, excl. sex hormones and insulins												
corticosteroids for systemic use	**24**	**(6.8)**	**54**	**(7.7)**	**53**	**(7.5)**	**107**	**(7.6)**	**19**	**(6.1)**	**164**	**(7.4)**
methylprednisolone acetate	0	(0.0)	2	(0.3)	7	(1.0)	9	(0.6)	0	(0.0)	9	(0.4)
methylprednisolone sodium succinate	0	(0.0)	0	(0.0)	2	(0.3)	2	(0.1)	0	(0.0)	3	(0.1)
prednisolone	2	(0.6)	8	(1.1)	4	(0.6)	12	(0.8)	5	(1.6)	20	(0.9)
prednisolone acetate	0	(0.0)	3	(0.4)	2	(0.3)	5	(0.4)	0	(0.0)	5	(0.2)
prednisolone sodium succinate	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
prednisolone valerate acetate	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	3	(0.1)
prednisone	2	(0.6)	7	(1.0)	9	(1.3)	16	(1.1)	2	(0.6)	20	(0.9)
rimexolone	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
triamcinolone	1	(0.3)	6	(0.9)	5	(0.7)	11	(0.8)	4	(1.3)	18	(0.8)
triamcinolone acetonide	3	(0.8)	4	(0.6)	2	(0.3)	6	(0.4)	3	(1.0)	14	(0.6)
pancreatic hormones	**0**	**(0.0)**	**1**	**(0.1)**	**0**	**(0.0)**	**1**	**(0.1)**	**0**	**(0.0)**	**1**	**(0.0)**
glucagon	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
pituitary and hypothalamic hormones and analogues	**0**	**(0.0)**	**3**	**(0.4)**	**1**	**(0.1)**	**4**	**(0.3)**	**0**	**(0.0)**	**4**	**(0.2)**
desmopressin	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	2	(0.1)
vasopressin	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.1)	0	(0.0)	2	(0.1)
thyroid therapy	**21**	**(5.9)**	**29**	**(4.1)**	**41**	**(5.8)**	**70**	**(5.0)**	**23**	**(7.3)**	**120**	**(5.4)**
carbimazole	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
systemic hormonal preparations, excl. sex hormones and insulins												
thyroid therapy	**21**	**(5.9)**	**29**	**(4.1)**	**41**	**(5.8)**	**70**	**(5.0)**	**23**	**(7.3)**	**120**	**(5.4)**
levothyroxine sodium	20	(5.6)	25	(3.5)	36	(5.1)	61	(4.3)	22	(7.0)	109	(4.9)
levothyroxine sodium (+) potassium iodide	1	(0.3)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	3	(0.1)
methimazole	0	(0.0)	2	(0.3)	2	(0.3)	4	(0.3)	0	(0.0)	4	(0.2)
thyroid	0	(0.0)	1	(0.1)	2	(0.3)	3	(0.2)	1	(0.3)	4	(0.2)
various												
all other non-therapeutic products	**3**	**(0.8)**	**4**	**(0.6)**	**2**	**(0.3)**	**6**	**(0.4)**	**0**	**(0.0)**	**10**	**(0.5)**
Dead Sea salt	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
allantoin (+) arginine (+) glycerin (+) niacinamide (+) shea butter (+) sodium lauroamphoacetate (+) sodium pidolate (+) sodium	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
cetostearyl alcohol (+) sodium lauryl sulfate (+) decyl oleate (+) soybean oil	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
creatinine	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
dressing (unspecified)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
various												
all other non-therapeutic products	**3**	**(0.8)**	**4**	**(0.6)**	**2**	**(0.3)**	**6**	**(0.4)**	**0**	**(0.0)**	**10**	**(0.5)**
petrolatum (+) sodium cocoyl isethionate (+) stearic acid	2	(0.6)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	4	(0.2)
polyethylene	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
all other therapeutic products	**35**	**(9.9)**	**70**	**(9.9)**	**77**	**(10.9)**	**147**	**(10.4)**	**24**	**(7.7)**	**225**	**(10.2)**
American ginseng	2	(0.6)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.1)
American ginseng (+) Asian ginseng (+) caffeine (+) niacinamide (+) pyridoxine hydrochloride	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.0)
Apis mellifera (+) belladonna (+) Spongia officinalis (+) white bryony	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
Asian ginseng (+) Chinese licorice (+) jujube (+) ophiopogon (+) pinellia (+) rice sprout	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
various												
all other therapeutic products	**35**	**(9.9)**	**70**	**(9.9)**	**77**	**(10.9)**	**147**	**(10.4)**	**24**	**(7.7)**	**225**	**(10.2)**
Asian ginseng (+) bupleurum (+) calcium (unspecified) (+) cassia (+) Chinese skullcap (+) dragon bone (+) ginger (+) jujube (+)	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
Asian water plantain (+) Asiatic dogwood (+) cassia (+) Chinese yam (+) poria (+) rehmannia (+) Sichuan aconite (+) tree peony	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
Asian water plantain (+) cang zhu atractylodes (+) cassia (+) poria (+) zhu ling (sclerotium)	1	(0.3)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	2	(0.1)
Chinese licorice (+) Chinese peony	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
Chinese licorice (+) Chinese peony (+) cinnamon (+) ephedra (+) ginger (+) jujube (+) kudzu	0	(0.0)	3	(0.4)	0	(0.0)	3	(0.2)	0	(0.0)	4	(0.2)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
various												
all other therapeutic products	**35**	**(9.9)**	**70**	**(9.9)**	**77**	**(10.9)**	**147**	**(10.4)**	**24**	**(7.7)**	**225**	**(10.2)**
Chinese rhubarb	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
Echinacea purpurea	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
English ivy	2	(0.6)	1	(0.1)	4	(0.6)	5	(0.4)	0	(0.0)	7	(0.3)
English ivy (+) thyme oil	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	2	(0.1)
English plantain	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
Haematococcus pluvialis	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
Iceland moss	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
Jobs tears	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
Prunus serrulata	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
Sichuan aconite	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
St Johns wort	0	(0.0)	3	(0.4)	0	(0.0)	3	(0.2)	0	(0.0)	3	(0.1)
Streptococcus faecalis	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
[composition unspecified]	7	(2.0)	11	(1.6)	9	(1.3)	20	(1.4)	2	(0.6)	37	(1.7)
achyranthes (+) cang zhu atractylodes (+) Chinese licorice (+) Chinese peony (+) citrus unshiu (+) dong quai (+) fragrant angeli	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
various												
all other therapeutic products	**35**	**(9.9)**	**70**	**(9.9)**	**77**	**(10.9)**	**147**	**(10.4)**	**24**	**(7.7)**	**225**	**(10.2)**
aconite (+) arnica (+) belladonna (+) calendula (+) chamomile (+) comfrey (+) Echinacea angustifolia (+) Echinacea purpurea (+)	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
aconite (+) atropine sulfate (+) mercuric cyanide	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	1	(0.3)	2	(0.1)
aconite (+) belladonna (+) boneset (+) Echinacea angustifolia	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
aconitine	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
adenine (+) carnitine orotate (+) fosfructose magnesium (+) potassium orotate (+) vitamin B complex (+) xanthine	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
various												
all other therapeutic products	**35**	**(9.9)**	**70**	**(9.9)**	**77**	**(10.9)**	**147**	**(10.4)**	**24**	**(7.7)**	**225**	**(10.2)**
agmatine sulfate (+) betaine (+) D-aspartic acid (+) grains of paradise (+) levocarnitine tartrate (+) mangosteen (+) velvet bea	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
alfalfa	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
alfalfa (+) astragalus (+) calcium carbonate (+) celery (+) chocolate (+) cinnamon (+) fennel (+) ginger (+) hawthorn (+) licori	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
alfalfa (+) cellulase (+) Echinacea purpurea (+) ginger (+) hemicellulose (+) lipase (+) mullein (+) protease (+) rose hips	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.0)
algae (unspecified)	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
various												
all other therapeutic products	**35**	**(9.9)**	**70**	**(9.9)**	**77**	**(10.9)**	**147**	**(10.4)**	**24**	**(7.7)**	**225**	**(10.2)**
ambergris (+) Anamirta paniculata (+) Conium maculatum (+) kerosene	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
ammonium glycyrrhizate (+) cysteine (+) glycine	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
ammonium glycyrrhizate (+) cysteine hydrochloride (+) glycine	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.1)	0	(0.0)	2	(0.1)
ammonium glycyrrhizate (+) glycine (+) racemethionine	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
andrographis (+) European elder (+) European vervain (+) garlic (+) gentian (+) linden (+) mullein (+) thyme	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
various												
all other therapeutic products	**35**	**(9.9)**	**70**	**(9.9)**	**77**	**(10.9)**	**147**	**(10.4)**	**24**	**(7.7)**	**225**	**(10.2)**
angelica (+) bitter candytuft (+) caraway (+) celandine (+) chamomile (+) lemon balm (+) licorice (+) milk thistle (+) peppermin	0	(0.0)	0	(0.0)	2	(0.3)	2	(0.1)	1	(0.3)	3	(0.1)
apoaequorin	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
apricot seed (+) Chinese licorice (+) Chinese wild ginger (+) ginger (+) pinellia (+) poria (+) schisandra	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
apricot seed (+) cassia (+) Chinese licorice (+) ephedra	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
arnica (+) Echinacea angustifolia (+) European goldenrod (+) horsetail (+) lily of the valley (+) madder (+) magnesium phosphate	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
various												
all other therapeutic products	**35**	**(9.9)**	**70**	**(9.9)**	**77**	**(10.9)**	**147**	**(10.4)**	**24**	**(7.7)**	**225**	**(10.2)**
arnica (+) calendula (+) horse chestnut	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.0)
artichoke (+) Chinese rhubarb	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
artichoke (+) chromium polynicotinate (+) eicosapentaenoic acid (+) guggul (+) policosanol (+) red yeast (+) soy isoflavones (+)	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
ascorbic acid (+) Chinese chaste tree (+) echinacea (unspecified) (+) forsythia (+) ginger (+) glutamine (+) honeysuckle (+) isa	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	2	(0.1)
ascorbic acid (+) beet (+) grape seeds (+) magnesium oxide (+) quercetin (+) potassium nitrate (+) spinach	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

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	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
various												
all other therapeutic products	**35**	**(9.9)**	**70**	**(9.9)**	**77**	**(10.9)**	**147**	**(10.4)**	**24**	**(7.7)**	**225**	**(10.2)**
ascorbic acid (+) betaine (+) blackberry (+) blueberry (+) cranberry (+) dimethyl sulfone (+) fructooligosaccharides (+) glucosa	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
ascorbic acid (+) chondroitin sulfate sodium (+) collagen (+) dimethyl sulfone (+) glucosamine hydrochloride (+) Indian frankinc	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
ascorbic acid (+) chondroitin sulfate sodium (+) dimethyl sulfone (+) gelatin (+) glucosamine hydrochloride (+) hyaluronic acid	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.0)
ascorbic acid (+) glucosamine sulfate	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)

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Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
various												
all other therapeutic products	**35**	**(9.9)**	**70**	**(9.9)**	**77**	**(10.9)**	**147**	**(10.4)**	**24**	**(7.7)**	**225**	**(10.2)**
ascorbic acid (+) kojic acid	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
ashwagandha (+) epimedium (+) magnolia (+) phosphatidyl serine (+) theanine	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
astragalus	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
bai zhu atractylodes	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
bee, hornet, or wasp larvae	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
black cherry	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
black cohosh	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
black currant	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
butyric acid	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
cabbage palm	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
cabbage palm (+) tea	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
calcium (unspecified) (+) cassia (+) Chinese amomum (+) Chinese licorice (+) Chinese peony (+) Corydalis yanhusuo (+) fennel (+)	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)

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	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
various												
all other therapeutic products	**35**	**(9.9)**	**70**	**(9.9)**	**77**	**(10.9)**	**147**	**(10.4)**	**24**	**(7.7)**	**225**	**(10.2)**
calcium glycinate (+) chromium picolinate (+) folic acid (+) hawthorn (+) higenamine (+) hordenine (+) mate (+) mecobalamin (+)	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
calcium magnesium phytate (+) chondroitin sulfate sodium (+) collagen (+) hyaluronic acid (+) Indian frankincense (+) magnesium	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
camphor (+) horse chestnut	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
camu camu	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
cang zhu atractylodes (+) cassia (+) Chinese licorice (+) Chinese peony (+) dong quai (+) ephedra (+) Jobs tears	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
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	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
various												
all other therapeutic products	**35**	**(9.9)**	**70**	**(9.9)**	**77**	**(10.9)**	**147**	**(10.4)**	**24**	**(7.7)**	**225**	**(10.2)**
capsicum (+) colocynth (+) fragrant everlasting (+) magnesium phosphate, dibasic	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
capsicum (+) guaiac (+) poke	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
cassia (+) Chinese peony (+) peach seed (+) poria (+) tree peony	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
cattle gallstone	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	2	(0.1)
chamomile	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
cherry bark extract	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
choline bitartrate (+) collagen (+) dimethyl sulfone (+) hyaluronic acid (+) inositol (+) minerals (unspecified) (+) tea (+) thi	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
chondroitin	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
chondroitin sulfate sodium (+) dimethyl sulfone (+) glucosamine	0	(0.0)	1	(0.1)	2	(0.3)	3	(0.2)	0	(0.0)	3	(0.1)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
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	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
various												
all other therapeutic products	**35**	**(9.9)**	**70**	**(9.9)**	**77**	**(10.9)**	**147**	**(10.4)**	**24**	**(7.7)**	**225**	**(10.2)**
chondroitin sulfate sodium (+) dimethyl sulfone (+) glucosamine hydrochloride (+) Indian frankincense (+) ubidecarenone	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
chondroitin sulfate sodium (+) glucosamine hydrochloride	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
chondroitin sulfate sodium (+) glucosamine sulfate	1	(0.3)	2	(0.3)	2	(0.3)	4	(0.3)	0	(0.0)	5	(0.2)
cinnamon	0	(0.0)	0	(0.0)	4	(0.6)	4	(0.3)	1	(0.3)	6	(0.3)
cinnamon (+) lemon balm (+) orange (+) passionflower	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.0)
coffee	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
colestilan chloride	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
cowslip	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
cowslip (+) European vervain (+) gentian (+) sambucus (unspecified) (+) sorrel	1	(0.3)	5	(0.7)	8	(1.1)	13	(0.9)	4	(1.3)	18	(0.8)
cowslip (+) thyme	1	(0.3)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	2	(0.1)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
various												
all other therapeutic products	**35**	**(9.9)**	**70**	**(9.9)**	**77**	**(10.9)**	**147**	**(10.4)**	**24**	**(7.7)**	**225**	**(10.2)**
cowslip (+) thyme oil	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
cranberry	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
cyanocobalamin (+) folic acid (+) uridine 5'-monophosphate disodium salt	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.0)
devils claw	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
dimethyl sulfone	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
dong quai	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
earthworm	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
echinacea (unspecified)	1	(0.3)	2	(0.3)	2	(0.3)	4	(0.3)	0	(0.0)	5	(0.2)
eggshell membrane	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
ephedra	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
epimedium (+) Eurycoma longifolia (+) fenugreek (+) forskohlii (+) piperine (+) protease (+) thioctic acid (+) tribulus	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
ethyl cysteine hydrochloride	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
eucalyptus oil	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
various												
all other therapeutic products	**35**	**(9.9)**	**70**	**(9.9)**	**77**	**(10.9)**	**147**	**(10.4)**	**24**	**(7.7)**	**225**	**(10.2)**
eucalyptus oil (+) rosemary oil (+) thyme oil (+) thymol (+) turpentine	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.0)
evening primrose oil	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
garcinia	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
garden nasturtium (+) horseradish	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	2	(0.1)
garlic	1	(0.3)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	3	(0.1)
ginger	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
ginkgo	0	(0.0)	0	(0.0)	2	(0.3)	2	(0.1)	0	(0.0)	2	(0.1)
ginseng (unspecified)	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
glucomannan	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
glucosamine	0	(0.0)	6	(0.9)	5	(0.7)	11	(0.8)	0	(0.0)	12	(0.5)
glucosamine hydrochloride	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
glucosamine sulfate	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.6)	2	(0.1)
glutathione	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
grape seeds	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
helicidine	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
horse chestnut	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
horseradish tree	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
various												
all other therapeutic products	**35**	**(9.9)**	**70**	**(9.9)**	**77**	**(10.9)**	**147**	**(10.4)**	**24**	**(7.7)**	**225**	**(10.2)**
investigational biologic drug (unspecified)	0	(0.0)	2	(0.3)	1	(0.1)	3	(0.2)	0	(0.0)	5	(0.2)
investigational drug (unspecified)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
kava	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.0)
lavender oil	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.0)
marshmallow	1	(0.3)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	2	(0.1)
mercuric cyanide	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
milk thistle	0	(0.0)	3	(0.4)	0	(0.0)	3	(0.2)	0	(0.0)	4	(0.2)
myrtle oil	2	(0.6)	3	(0.4)	3	(0.4)	6	(0.4)	2	(0.6)	10	(0.5)
naloxone hydrochloride	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
neurotropin	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
nitrogen	2	(0.6)	3	(0.4)	0	(0.0)	3	(0.2)	0	(0.0)	6	(0.3)
oregano oil	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
oregano oil (+) vitamin A palmitate	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
oxygen	1	(0.3)	0	(0.0)	3	(0.4)	3	(0.2)	0	(0.0)	4	(0.2)
phospholipids (unspecified)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.0)
prasterone	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
psoralea	1	(0.3)	2	(0.3)	2	(0.3)	4	(0.3)	0	(0.0)	7	(0.3)
raspberry	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
red yeast	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
various												
all other therapeutic products	**35**	**(9.9)**	**70**	**(9.9)**	**77**	**(10.9)**	**147**	**(10.4)**	**24**	**(7.7)**	**225**	**(10.2)**
rhodiola	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
sage	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
saw palmetto	2	(0.6)	2	(0.3)	2	(0.3)	4	(0.3)	2	(0.6)	8	(0.4)
scopolia extract	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
sodium polystyrene sulfonate	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
spirulina	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
tea	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
theanine	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
thioctic acid	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
thyme	0	(0.0)	3	(0.4)	0	(0.0)	3	(0.2)	0	(0.0)	3	(0.1)
turmeric	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
uva ursi	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
white willow	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
yeast	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
zedoary	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
allergens	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.1)**	**1**	**(0.1)**	**0**	**(0.0)**	**1**	**(0.0)**
pollen extract	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
contrast media	**0**	**(0.0)**	**3**	**(0.4)**	**6**	**(0.8)**	**9**	**(0.6)**	**0**	**(0.0)**	**10**	**(0.5)**
iobitridol	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
iohexol	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	2	(0.1)
iopamidol	0	(0.0)	0	(0.0)	3	(0.4)	3	(0.2)	0	(0.0)	3	(0.1)
ioversol	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)

Subjects With Specific Concomitant Medications (Incidence >0% in One or More Treatment Groups)
Phase 2 and 3 Trials Base Period
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100/200 mg		Etanercept 50mg		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
various												
contrast media	**0**	**(0.0)**	**3**	**(0.4)**	**6**	**(0.8)**	**9**	**(0.6)**	**0**	**(0.0)**	**10**	**(0.5)**
magnetic resonance imaging contrast media (unspecified)	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
radiographic contrast medium (unspecified)	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)	0	(0.0)	2	(0.1)
diagnostic agents	**0**	**(0.0)**	**1**	**(0.1)**	**0**	**(0.0)**	**1**	**(0.1)**	**0**	**(0.0)**	**1**	**(0.0)**
tuberculin purified protein derivative	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
diagnostic radiopharmaceuticals	**1**	**(0.3)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.0)**
technetium Tc 99m sulfur colloid	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.0)
general nutrients	**0**	**(0.0)**	**2**	**(0.3)**	**1**	**(0.1)**	**3**	**(0.2)**	**1**	**(0.3)**	**4**	**(0.2)**
dextrose	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
milk	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)	1	(0.0)
papaya (+) pineapple (+) protein (unspecified)	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
protein (unspecified)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)

Every subject is counted a single time for each applicable specific concomitant medication. A subject with multiple concomitant medications 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 in one or more of the columns meets the incidence criterion in the report title, after rounding.

Note: Treatment arms are based on the allocation at baseline. Re-randomization/re-allocation is not reflected in this table.

[Source: 5.3.5.3-10]

付録 2.7.4-9
投与群別に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>0%)
第 I 相試験 - 健常人集団
1 回以上投与された全被験者

	MK-3222		Placebo		Post-Study		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	103		15		118		118	
with one or more adverse events	85	(82.5)	12	(80.0)	0	(0.0)	97	(82.2)
with no adverse events	18	(17.5)	3	(20.0)	118	(100.0)	21	(17.8)
Blood and lymphatic system disorders	**2**	**(1.9)**	**1**	**(6.7)**	**0**	**(0.0)**	**3**	**(2.5)**
Iron deficiency anaemia	0	(0.0)	1	(6.7)	0	(0.0)	1	(0.8)
Neutropenia	2	(1.9)	0	(0.0)	0	(0.0)	2	(1.7)
Ear and labyrinth disorders	**1**	**(1.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.8)**
Ear discomfort	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Eye disorders	**0**	**(0.0)**	**1**	**(6.7)**	**0**	**(0.0)**	**1**	**(0.8)**
Vision blurred	0	(0.0)	1	(6.7)	0	(0.0)	1	(0.8)
Gastrointestinal disorders	**19**	**(18.4)**	**2**	**(13.3)**	**0**	**(0.0)**	**21**	**(17.8)**
Abdominal pain	3	(2.9)	0	(0.0)	0	(0.0)	3	(2.5)
Abdominal pain upper	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Aphthous ulcer	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Diarrhoea	6	(5.8)	1	(6.7)	0	(0.0)	7	(5.9)
Dyspepsia	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Gingival bleeding	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Mouth ulceration	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Nausea	8	(7.8)	1	(6.7)	0	(0.0)	9	(7.6)
Oral mucosal blistering	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Toothache	2	(1.9)	0	(0.0)	0	(0.0)	2	(1.7)
Vomiting	3	(2.9)	0	(0.0)	0	(0.0)	3	(2.5)

Subjects With Specific Adverse Events by Treatment (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Healthy Population All Subjects as Treated

	MK-3222		Placebo		Post-Study		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
General disorders and administration site conditions	**25**	**(24.3)**	**4**	**(26.7)**	**0**	**(0.0)**	**29**	**(24.6)**
Catheter site bruise	1	(1.0)	1	(6.7)	0	(0.0)	2	(1.7)
Catheter site pain	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Chest discomfort	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Infusion site thrombosis	2	(1.9)	0	(0.0)	0	(0.0)	2	(1.7)
Injection site bruising	10	(9.7)	0	(0.0)	0	(0.0)	10	(8.5)
Injection site erythema	5	(4.9)	2	(13.3)	0	(0.0)	7	(5.9)
Injection site pain	7	(6.8)	0	(0.0)	0	(0.0)	7	(5.9)
Injection site reaction	2	(1.9)	0	(0.0)	0	(0.0)	2	(1.7)
Vessel puncture site bruise	4	(3.9)	1	(6.7)	0	(0.0)	5	(4.2)
Immune system disorders	**5**	**(4.9)**	**0**	**(0.0)**	**0**	**(0.0)**	**5**	**(4.2)**
Drug hypersensitivity	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Seasonal allergy	4	(3.9)	0	(0.0)	0	(0.0)	4	(3.4)
Infections and infestations	**39**	**(37.9)**	**8**	**(53.3)**	**0**	**(0.0)**	**47**	**(39.8)**
Appendicitis	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Chikungunya virus infection	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Ear infection	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Enterobiasis	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Gastroenteritis	1	(1.0)	1	(6.7)	0	(0.0)	2	(1.7)
Gastroenteritis viral	2	(1.9)	0	(0.0)	0	(0.0)	2	(1.7)
Gingivitis	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Herpes simplex	0	(0.0)	1	(6.7)	0	(0.0)	1	(0.8)
Influenza	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Nasopharyngitis	2	(1.9)	1	(6.7)	0	(0.0)	3	(2.5)

Subjects With Specific Adverse Events by Treatment (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Healthy Population All Subjects as Treated

	MK-3222		Placebo		Post-Study		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Infections and infestations	**39**	**(37.9)**	**8**	**(53.3)**	**0**	**(0.0)**	**47**	**(39.8)**
Oral herpes	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Pharyngitis	3	(2.9)	1	(6.7)	0	(0.0)	4	(3.4)
Rhinitis	1	(1.0)	2	(13.3)	0	(0.0)	3	(2.5)
Sinusitis	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Tonsillitis	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Upper respiratory tract infection	28	(27.2)	6	(40.0)	0	(0.0)	34	(28.8)
Urinary tract infection	2	(1.9)	0	(0.0)	0	(0.0)	2	(1.7)
Injury, poisoning and procedural complications	**19**	**(18.4)**	**3**	**(20.0)**	**0**	**(0.0)**	**22**	**(18.6)**
Arthropod bite	2	(1.9)	0	(0.0)	0	(0.0)	2	(1.7)
Contusion	8	(7.8)	1	(6.7)	0	(0.0)	9	(7.6)
Eye contusion	0	(0.0)	1	(6.7)	0	(0.0)	1	(0.8)
Face injury	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Fall	0	(0.0)	1	(6.7)	0	(0.0)	1	(0.8)
Infusion related reaction	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Laceration	1	(1.0)	1	(6.7)	0	(0.0)	2	(1.7)
Nail injury	0	(0.0)	1	(6.7)	0	(0.0)	1	(0.8)
Procedural pain	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Scratch	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Skin abrasion	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Soft tissue injury	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Sunburn	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Thermal burn	2	(1.9)	0	(0.0)	0	(0.0)	2	(1.7)
Venomous sting	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)

Subjects With Specific Adverse Events by Treatment (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Healthy Population All Subjects as Treated

	MK-3222		Placebo		Post-Study		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Investigations	**5**	**(4.9)**	**0**	**(0.0)**	**0**	**(0.0)**	**5**	**(4.2)**
Alanine aminotransferase increased	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Blood triglycerides increased	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Body temperature increased	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Eosinophil count increased	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Platelet count decreased	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Musculoskeletal and connective tissue disorders	**15**	**(14.6)**	**0**	**(0.0)**	**0**	**(0.0)**	**15**	**(12.7)**
Back pain	3	(2.9)	0	(0.0)	0	(0.0)	3	(2.5)
Joint stiffness	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Muscle twitching	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Musculoskeletal chest pain	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Myalgia	8	(7.8)	0	(0.0)	0	(0.0)	8	(6.8)
Neck pain	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Pain in extremity	2	(1.9)	0	(0.0)	0	(0.0)	2	(1.7)
Nervous system disorders	**38**	**(36.9)**	**7**	**(46.7)**	**0**	**(0.0)**	**45**	**(38.1)**
Disturbance in attention	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Dizziness	6	(5.8)	0	(0.0)	0	(0.0)	6	(5.1)
Headache	28	(27.2)	6	(40.0)	0	(0.0)	34	(28.8)
Hypoaesthesia	2	(1.9)	0	(0.0)	0	(0.0)	2	(1.7)
Lethargy	3	(2.9)	1	(6.7)	0	(0.0)	4	(3.4)
Migraine	3	(2.9)	2	(13.3)	0	(0.0)	5	(4.2)
Paraesthesia	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Presyncope	2	(1.9)	0	(0.0)	0	(0.0)	2	(1.7)
Somnolence	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)

Subjects With Specific Adverse Events by Treatment (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Healthy Population All Subjects as Treated

	MK-3222		Placebo		Post-Study		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Nervous system disorders	**38**	**(36.9)**	**7**	**(46.7)**	**0**	**(0.0)**	**45**	**(38.1)**
Syncope	2	(1.9)	0	(0.0)	0	(0.0)	2	(1.7)
Psychiatric disorders	**4**	**(3.9)**	**2**	**(13.3)**	**0**	**(0.0)**	**6**	**(5.1)**
Anxiety	0	(0.0)	1	(6.7)	0	(0.0)	1	(0.8)
Depression	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Insomnia	2	(1.9)	1	(6.7)	0	(0.0)	3	(2.5)
Suicidal ideation	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Renal and urinary disorders	**1**	**(1.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.8)**
Pollakiuria	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Reproductive system and breast disorders	**8**	**(7.8)**	**1**	**(6.7)**	**0**	**(0.0)**	**9**	**(7.6)**
Dysmenorrhoea	8	(7.8)	1	(6.7)	0	(0.0)	9	(7.6)
Respiratory, thoracic and mediastinal disorders	**11**	**(10.7)**	**2**	**(13.3)**	**0**	**(0.0)**	**13**	**(11.0)**
Cough	3	(2.9)	1	(6.7)	0	(0.0)	4	(3.4)
Epistaxis	2	(1.9)	0	(0.0)	0	(0.0)	2	(1.7)
Nasal congestion	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Nasal obstruction	0	(0.0)	1	(6.7)	0	(0.0)	1	(0.8)
Oropharyngeal pain	4	(3.9)	0	(0.0)	0	(0.0)	4	(3.4)
Rhinitis allergic	1	(1.0)	1	(6.7)	0	(0.0)	2	(1.7)
Throat irritation	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)

Subjects With Specific Adverse Events by Treatment (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Healthy Population All Subjects as Treated

	MK-3222		Placebo		Post-Study		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Skin and subcutaneous tissue disorders	**20**	**(19.4)**	**0**	**(0.0)**	**0**	**(0.0)**	**20**	**(16.9)**
Acne	2	(1.9)	0	(0.0)	0	(0.0)	2	(1.7)
Cold sweat	2	(1.9)	0	(0.0)	0	(0.0)	2	(1.7)
Dermatitis	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Dry skin	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Erythema	2	(1.9)	0	(0.0)	0	(0.0)	2	(1.7)
Hyperhidrosis	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Pruritus	2	(1.9)	0	(0.0)	0	(0.0)	2	(1.7)
Rash	5	(4.9)	0	(0.0)	0	(0.0)	5	(4.2)
Rash erythematous	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Rash generalised	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Rash maculo-papular	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Rash pruritic	2	(1.9)	0	(0.0)	0	(0.0)	2	(1.7)
Skin irritation	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Swelling face	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Surgical and medical procedures	**1**	**(1.0)**	**1**	**(6.7)**	**0**	**(0.0)**	**2**	**(1.7)**
Nasal septal operation	0	(0.0)	1	(6.7)	0	(0.0)	1	(0.8)
Turbinectomy	0	(0.0)	1	(6.7)	0	(0.0)	1	(0.8)
Wisdom teeth removal	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Vascular disorders	**2**	**(1.9)**	**0**	**(0.0)**	**0**	**(0.0)**	**2**	**(1.7)**
Haematoma	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)
Phlebitis	1	(1.0)	0	(0.0)	0	(0.0)	1	(0.8)

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: [ISSPH1: analysis-adsl] [ISSPH1: tabulations-aeplus] SourceはSASシステム中の電子的データのため5章に含めなかった。

付録 2.7.4-10
投与量別に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 > 0%）
第 I 相試験 - 健常人集団
1 回以上投与された全被験者

	MK-3222 0.1 mg/kg IV		MK-3222 0.5 mg/kg IV		MK-3222 3 mg/kg IV		MK-3222 10 mg/kg IV		MK-3222 50 mg SC		MK-3222 200 mg SC	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	4		4		8		12		30		27	
with one or more adverse events	2	(50.0)	3	(75.0)	7	(87.5)	11	(91.7)	24	(80.0)	24	(88.9)
with no adverse events	2	(50.0)	1	(25.0)	1	(12.5)	1	(8.3)	6	(20.0)	3	(11.1)
Blood and lymphatic system disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(8.3)**	**0**	**(0.0)**	**0**	**(0.0)**
Iron deficiency anaemia	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Neutropenia	0	(0.0)	0	(0.0)	0	(0.0)	1	(8.3)	0	(0.0)	0	(0.0)
Ear and labyrinth disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(8.3)**	**0**	**(0.0)**	**0**	**(0.0)**
Ear discomfort	0	(0.0)	0	(0.0)	0	(0.0)	1	(8.3)	0	(0.0)	0	(0.0)
Eye disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**
Vision blurred	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Gastrointestinal disorders	**1**	**(25.0)**	**1**	**(25.0)**	**1**	**(12.5)**	**2**	**(16.7)**	**4**	**(13.3)**	**7**	**(25.9)**
Abdominal pain	0	(0.0)	0	(0.0)	0	(0.0)	1	(8.3)	1	(3.3)	1	(3.7)
Abdominal pain upper	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.7)
Aphthous ulcer	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.3)	0	(0.0)
Diarrhoea	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	2	(6.7)	2	(7.4)
Dyspepsia	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Gingival bleeding	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Mouth ulceration	0	(0.0)	1	(25.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Nausea	1	(25.0)	0	(0.0)	0	(0.0)	1	(8.3)	2	(6.7)	3	(11.1)

Subjects With Specific Adverse Events by Dose (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Healthy Population All Subjects as Treated

	MK-3222 400 mg SC		Placebo		Post-Study		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	18		15		118		118	
with one or more adverse events	14	(77.8)	12	(80.0)	0	(0.0)	97	(82.2)
with no adverse events	4	(22.2)	3	(20.0)	118	(100.0)	21	(17.8)
Blood and lymphatic system disorders	**1**	**(5.6)**	**1**	**(6.7)**	**0**	**(0.0)**	**3**	**(2.5)**
Iron deficiency anaemia	0	(0.0)	1	(6.7)	0	(0.0)	1	(0.8)
Neutropenia	1	(5.6)	0	(0.0)	0	(0.0)	2	(1.7)
Ear and labyrinth disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.8)**
Ear discomfort	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Eye disorders	**0**	**(0.0)**	**1**	**(6.7)**	**0**	**(0.0)**	**1**	**(0.8)**
Vision blurred	0	(0.0)	1	(6.7)	0	(0.0)	1	(0.8)
Gastrointestinal disorders	**3**	**(16.7)**	**2**	**(13.3)**	**0**	**(0.0)**	**21**	**(17.8)**
Abdominal pain	0	(0.0)	0	(0.0)	0	(0.0)	3	(2.5)
Abdominal pain upper	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Aphthous ulcer	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Diarrhoea	2	(11.1)	1	(6.7)	0	(0.0)	7	(5.9)
Dyspepsia	1	(5.6)	0	(0.0)	0	(0.0)	1	(0.8)
Gingival bleeding	1	(5.6)	0	(0.0)	0	(0.0)	1	(0.8)
Mouth ulceration	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Nausea	1	(5.6)	1	(6.7)	0	(0.0)	9	(7.6)

Subjects With Specific Adverse Events by Dose (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Healthy Population All Subjects as Treated

	MK-3222 0.1 mg/kg IV		MK-3222 0.5 mg/kg IV		MK-3222 3 mg/kg IV		MK-3222 10 mg/kg IV		MK-3222 50 mg SC		MK-3222 200 mg SC	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Gastrointestinal disorders	**1**	**(25.0)**	**1**	**(25.0)**	**1**	**(12.5)**	**2**	**(16.7)**	**4**	**(13.3)**	**7**	**(25.9)**
Oral mucosal blistering	0	(0.0)	0	(0.0)	1	(12.5)	0	(0.0)	0	(0.0)	0	(0.0)
Toothache	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	2	(7.4)
Vomiting	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	2	(7.4)
General disorders and administration site conditions	**0**	**(0.0)**	**0**	**(0.0)**	**2**	**(25.0)**	**3**	**(25.0)**	**3**	**(10.0)**	**10**	**(37.0)**
Catheter site bruise	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.7)
Catheter site pain	0	(0.0)	0	(0.0)	0	(0.0)	1	(8.3)	0	(0.0)	0	(0.0)
Chest discomfort	0	(0.0)	0	(0.0)	1	(12.5)	0	(0.0)	0	(0.0)	0	(0.0)
Infusion site thrombosis	0	(0.0)	0	(0.0)	0	(0.0)	1	(8.3)	0	(0.0)	0	(0.0)
Injection site bruising	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.3)	4	(14.8)
Injection site erythema	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.3)	2	(7.4)
Injection site pain	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.3)	5	(18.5)
Injection site reaction	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	2	(7.4)
Vessel puncture site bruise	0	(0.0)	0	(0.0)	2	(25.0)	1	(8.3)	1	(3.3)	0	(0.0)
Immune system disorders	**1**	**(25.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(8.3)**	**1**	**(3.3)**	**2**	**(7.4)**
Drug hypersensitivity	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.3)	0	(0.0)
Seasonal allergy	1	(25.0)	0	(0.0)	0	(0.0)	1	(8.3)	0	(0.0)	2	(7.4)
Infections and infestations	**1**	**(25.0)**	**3**	**(75.0)**	**6**	**(75.0)**	**5**	**(41.7)**	**11**	**(36.7)**	**9**	**(33.3)**
Appendicitis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.3)	0	(0.0)
Chikungunya virus infection	0	(0.0)	0	(0.0)	0	(0.0)	1	(8.3)	0	(0.0)	0	(0.0)

Subjects With Specific Adverse Events by Dose (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Healthy Population All Subjects as Treated

	MK-3222 400 mg SC		Placebo		Post-Study		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Gastrointestinal disorders	**3**	**(16.7)**	**2**	**(13.3)**	**0**	**(0.0)**	**21**	**(17.8)**
Oral mucosal blistering	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Toothache	0	(0.0)	0	(0.0)	0	(0.0)	2	(1.7)
Vomiting	1	(5.6)	0	(0.0)	0	(0.0)	3	(2.5)
General disorders and administration site conditions	**7**	**(38.9)**	**4**	**(26.7)**	**0**	**(0.0)**	**29**	**(24.6)**
Catheter site bruise	0	(0.0)	1	(6.7)	0	(0.0)	2	(1.7)
Catheter site pain	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Chest discomfort	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Infusion site thrombosis	1	(5.6)	0	(0.0)	0	(0.0)	2	(1.7)
Injection site bruising	5	(27.8)	0	(0.0)	0	(0.0)	10	(8.5)
Injection site erythema	2	(11.1)	2	(13.3)	0	(0.0)	7	(5.9)
Injection site pain	1	(5.6)	0	(0.0)	0	(0.0)	7	(5.9)
Injection site reaction	0	(0.0)	0	(0.0)	0	(0.0)	2	(1.7)
Vessel puncture site bruise	0	(0.0)	1	(6.7)	0	(0.0)	5	(4.2)
Immune system disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**5**	**(4.2)**
Drug hypersensitivity	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Seasonal allergy	0	(0.0)	0	(0.0)	0	(0.0)	4	(3.4)
Infections and infestations	**4**	**(22.2)**	**8**	**(53.3)**	**0**	**(0.0)**	**47**	**(39.8)**
Appendicitis	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Chikungunya virus infection	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)

Subjects With Specific Adverse Events by Dose (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Healthy Population All Subjects as Treated

	MK-3222 0.1 mg/kg IV		MK-3222 0.5 mg/kg IV		MK-3222 3 mg/kg IV		MK-3222 10 mg/kg IV		MK-3222 50 mg SC		MK-3222 200 mg SC	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Infections and infestations	**1**	**(25.0)**	**3**	**(75.0)**	**6**	**(75.0)**	**5**	**(41.7)**	**11**	**(36.7)**	**9**	**(33.3)**
Ear infection	0	(0.0)	0	(0.0)	0	(0.0)	1	(8.3)	0	(0.0)	0	(0.0)
Enterobiasis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.7)
Gastroenteritis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.7)
Gastroenteritis viral	0	(0.0)	0	(0.0)	0	(0.0)	1	(8.3)	1	(3.3)	0	(0.0)
Gingivitis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.3)	0	(0.0)
Herpes simplex	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Influenza	0	(0.0)	0	(0.0)	1	(12.5)	0	(0.0)	0	(0.0)	0	(0.0)
Nasopharyngitis	0	(0.0)	1	(25.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.7)
Oral herpes	0	(0.0)	0	(0.0)	0	(0.0)	1	(8.3)	0	(0.0)	0	(0.0)
Pharyngitis	0	(0.0)	1	(25.0)	0	(0.0)	1	(8.3)	1	(3.3)	0	(0.0)
Rhinitis	0	(0.0)	0	(0.0)	1	(12.5)	0	(0.0)	0	(0.0)	0	(0.0)
Sinusitis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.7)
Tonsillitis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.7)
Upper respiratory tract infection	1	(25.0)	1	(25.0)	4	(50.0)	4	(33.3)	9	(30.0)	5	(18.5)
Urinary tract infection	0	(0.0)	0	(0.0)	1	(12.5)	0	(0.0)	0	(0.0)	1	(3.7)
Injury, poisoning and procedural complications	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(12.5)**	**5**	**(41.7)**	**4**	**(13.3)**	**4**	**(14.8)**
Arthropod bite	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.3)	1	(3.7)
Contusion	0	(0.0)	0	(0.0)	0	(0.0)	3	(25.0)	1	(3.3)	2	(7.4)
Eye contusion	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Face injury	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Fall	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

Subjects With Specific Adverse Events by Dose (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Healthy Population All Subjects as Treated

	MK-3222 400 mg SC		Placebo		Post-Study		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Infections and infestations	**4**	**(22.2)**	**8**	**(53.3)**	**0**	**(0.0)**	**47**	**(39.8)**
Ear infection	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Enterobiasis	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Gastroenteritis	0	(0.0)	1	(6.7)	0	(0.0)	2	(1.7)
Gastroenteritis viral	0	(0.0)	0	(0.0)	0	(0.0)	2	(1.7)
Gingivitis	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Herpes simplex	0	(0.0)	1	(6.7)	0	(0.0)	1	(0.8)
Influenza	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Nasopharyngitis	0	(0.0)	1	(6.7)	0	(0.0)	3	(2.5)
Oral herpes	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Pharyngitis	0	(0.0)	1	(6.7)	0	(0.0)	4	(3.4)
Rhinitis	0	(0.0)	2	(13.3)	0	(0.0)	3	(2.5)
Sinusitis	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Tonsillitis	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Upper respiratory tract infection	4	(22.2)	6	(40.0)	0	(0.0)	34	(28.8)
Urinary tract infection	0	(0.0)	0	(0.0)	0	(0.0)	2	(1.7)
Injury, poisoning and procedural complications	**5**	**(27.8)**	**3**	**(20.0)**	**0**	**(0.0)**	**22**	**(18.6)**
Arthropod bite	0	(0.0)	0	(0.0)	0	(0.0)	2	(1.7)
Contusion	2	(11.1)	1	(6.7)	0	(0.0)	9	(7.6)
Eye contusion	0	(0.0)	1	(6.7)	0	(0.0)	1	(0.8)
Face injury	1	(5.6)	0	(0.0)	0	(0.0)	1	(0.8)
Fall	0	(0.0)	1	(6.7)	0	(0.0)	1	(0.8)

Subjects With Specific Adverse Events by Dose (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Healthy Population All Subjects as Treated

	MK-3222 0.1 mg/kg IV		MK-3222 0.5 mg/kg IV		MK-3222 3 mg/kg IV		MK-3222 10 mg/kg IV		MK-3222 50 mg SC		MK-3222 200 mg SC	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Injury, poisoning and procedural complications	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(12.5)**	**5**	**(41.7)**	**4**	**(13.3)**	**4**	**(14.8)**
Infusion related reaction	0	(0.0)	0	(0.0)	1	(12.5)	0	(0.0)	0	(0.0)	0	(0.0)
Laceration	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Nail injury	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Procedural pain	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.3)	0	(0.0)
Scratch	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.7)
Skin abrasion	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Soft tissue injury	0	(0.0)	0	(0.0)	0	(0.0)	1	(8.3)	0	(0.0)	0	(0.0)
Sunburn	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.7)
Thermal burn	0	(0.0)	0	(0.0)	0	(0.0)	1	(8.3)	1	(3.3)	0	(0.0)
Venomous sting	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Investigations	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(8.3)**	**0**	**(0.0)**	**1**	**(3.7)**
Alanine aminotransferase increased	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Blood triglycerides increased	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Body temperature increased	0	(0.0)	0	(0.0)	0	(0.0)	1	(8.3)	0	(0.0)	0	(0.0)
Eosinophil count increased	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.7)
Platelet count decreased	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

Subjects With Specific Adverse Events by Dose (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Healthy Population All Subjects as Treated

	MK-3222 400 mg SC		Placebo		Post-Study		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Injury, poisoning and procedural complications	**5**	**(27.8)**	**3**	**(20.0)**	**0**	**(0.0)**	**22**	**(18.6)**
Infusion related reaction	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Laceration	1	(5.6)	1	(6.7)	0	(0.0)	2	(1.7)
Nail injury	0	(0.0)	1	(6.7)	0	(0.0)	1	(0.8)
Procedural pain	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Scratch	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Skin abrasion	1	(5.6)	0	(0.0)	0	(0.0)	1	(0.8)
Soft tissue injury	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Sunburn	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Thermal burn	0	(0.0)	0	(0.0)	0	(0.0)	2	(1.7)
Venomous sting	1	(5.6)	0	(0.0)	0	(0.0)	1	(0.8)
Investigations	**3**	**(16.7)**	**0**	**(0.0)**	**0**	**(0.0)**	**5**	**(4.2)**
Alanine aminotransferase increased	1	(5.6)	0	(0.0)	0	(0.0)	1	(0.8)
Blood triglycerides increased	1	(5.6)	0	(0.0)	0	(0.0)	1	(0.8)
Body temperature increased	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Eosinophil count increased	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Platelet count decreased	1	(5.6)	0	(0.0)	0	(0.0)	1	(0.8)

Subjects With Specific Adverse Events by Dose (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Healthy Population All Subjects as Treated

	MK-3222 0.1 mg/kg IV		MK-3222 0.5 mg/kg IV		MK-3222 3 mg/kg IV		MK-3222 10 mg/kg IV		MK-3222 50 mg SC		MK-3222 200 mg SC	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Musculoskeletal and connective tissue disorders	**1**	**(25.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**2**	**(16.7)**	**4**	**(13.3)**	**4**	**(14.8)**
Back pain	1	(25.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.3)	1	(3.7)
Joint stiffness	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Muscle twitching	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.3)	0	(0.0)
Musculoskeletal chest pain	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.3)	0	(0.0)
Myalgia	0	(0.0)	0	(0.0)	0	(0.0)	2	(16.7)	1	(3.3)	2	(7.4)
Neck pain	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Pain in extremity	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.7)
Nervous system disorders	**2**	**(50.0)**	**1**	**(25.0)**	**5**	**(62.5)**	**4**	**(33.3)**	**11**	**(36.7)**	**11**	**(40.7)**
Disturbance in attention	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.7)
Dizziness	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	2	(6.7)	3	(11.1)
Headache	1	(25.0)	1	(25.0)	4	(50.0)	3	(25.0)	7	(23.3)	9	(33.3)
Hypoaesthesia	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.7)
Lethargy	1	(25.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.3)	1	(3.7)
Migraine	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	2	(6.7)	0	(0.0)
Paraesthesia	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Presyncope	0	(0.0)	0	(0.0)	0	(0.0)	1	(8.3)	1	(3.3)	0	(0.0)
Somnolence	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.3)	0	(0.0)
Syncope	0	(0.0)	0	(0.0)	1	(12.5)	0	(0.0)	1	(3.3)	0	(0.0)
Psychiatric disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(3.3)**	**2**	**(7.4)**
Anxiety	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Depression	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.3)	0	(0.0)

Subjects With Specific Adverse Events by Dose (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Healthy Population All Subjects as Treated

	MK-3222 400 mg SC		Placebo		Post-Study		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Musculoskeletal and connective tissue disorders	**4**	**(22.2)**	**0**	**(0.0)**	**0**	**(0.0)**	**15**	**(12.7)**
Back pain	0	(0.0)	0	(0.0)	0	(0.0)	3	(2.5)
Joint stiffness	1	(5.6)	0	(0.0)	0	(0.0)	1	(0.8)
Muscle twitching	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Musculoskeletal chest pain	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Myalgia	3	(16.7)	0	(0.0)	0	(0.0)	8	(6.8)
Neck pain	1	(5.6)	0	(0.0)	0	(0.0)	1	(0.8)
Pain in extremity	1	(5.6)	0	(0.0)	0	(0.0)	2	(1.7)
Nervous system disorders	**4**	**(22.2)**	**7**	**(46.7)**	**0**	**(0.0)**	**45**	**(38.1)**
Disturbance in attention	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Dizziness	1	(5.6)	0	(0.0)	0	(0.0)	6	(5.1)
Headache	3	(16.7)	6	(40.0)	0	(0.0)	34	(28.8)
Hypoaesthesia	1	(5.6)	0	(0.0)	0	(0.0)	2	(1.7)
Lethargy	0	(0.0)	1	(6.7)	0	(0.0)	4	(3.4)
Migraine	1	(5.6)	2	(13.3)	0	(0.0)	5	(4.2)
Paraesthesia	1	(5.6)	0	(0.0)	0	(0.0)	1	(0.8)
Presyncope	0	(0.0)	0	(0.0)	0	(0.0)	2	(1.7)
Somnolence	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Syncope	0	(0.0)	0	(0.0)	0	(0.0)	2	(1.7)
Psychiatric disorders	**1**	**(5.6)**	**2**	**(13.3)**	**0**	**(0.0)**	**6**	**(5.1)**
Anxiety	0	(0.0)	1	(6.7)	0	(0.0)	1	(0.8)
Depression	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)

Subjects With Specific Adverse Events by Dose (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Healthy Population All Subjects as Treated

	MK-3222 0.1 mg/kg IV		MK-3222 0.5 mg/kg IV		MK-3222 3 mg/kg IV		MK-3222 10 mg/kg IV		MK-3222 50 mg SC		MK-3222 200 mg SC	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Psychiatric disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(3.3)**	**2**	**(7.4)**
Insomnia	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	2	(7.4)
Suicidal ideation	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Renal and urinary disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**
Pollakiuria	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Reproductive system and breast disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**3**	**(25.0)**	**0**	**(0.0)**	**5**	**(18.5)**
Dysmenorrhoea	0	(0.0)	0	(0.0)	0	(0.0)	3	(25.0)	0	(0.0)	5	(18.5)
Respiratory, thoracic and mediastinal disorders	**0**	**(0.0)**	**0**	**(0.0)**	**2**	**(25.0)**	**1**	**(8.3)**	**4**	**(13.3)**	**4**	**(14.8)**
Cough	0	(0.0)	0	(0.0)	1	(12.5)	0	(0.0)	1	(3.3)	1	(3.7)
Epistaxis	0	(0.0)	0	(0.0)	1	(12.5)	0	(0.0)	0	(0.0)	1	(3.7)
Nasal congestion	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.7)
Nasal obstruction	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Oropharyngeal pain	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	2	(6.7)	2	(7.4)
Rhinitis allergic	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.3)	0	(0.0)
Throat irritation	0	(0.0)	0	(0.0)	0	(0.0)	1	(8.3)	0	(0.0)	0	(0.0)
Skin and subcutaneous tissue disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**8**	**(26.7)**	**9**	**(33.3)**
Acne	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.3)	1	(3.7)
Cold sweat	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.7)

Subjects With Specific Adverse Events by Dose (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Healthy Population All Subjects as Treated

	MK-3222 400 mg SC		Placebo		Post-Study		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Psychiatric disorders	**1**	**(5.6)**	**2**	**(13.3)**	**0**	**(0.0)**	**6**	**(5.1)**
Insomnia	0	(0.0)	1	(6.7)	0	(0.0)	3	(2.5)
Suicidal ideation	1	(5.6)	0	(0.0)	0	(0.0)	1	(0.8)
Renal and urinary disorders	**1**	**(5.6)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.8)**
Pollakiuria	1	(5.6)	0	(0.0)	0	(0.0)	1	(0.8)
Reproductive system and breast disorders	**0**	**(0.0)**	**1**	**(6.7)**	**0**	**(0.0)**	**9**	**(7.6)**
Dysmenorrhoea	0	(0.0)	1	(6.7)	0	(0.0)	9	(7.6)
Respiratory, thoracic and mediastinal disorders	**0**	**(0.0)**	**2**	**(13.3)**	**0**	**(0.0)**	**13**	**(11.0)**
Cough	0	(0.0)	1	(6.7)	0	(0.0)	4	(3.4)
Epistaxis	0	(0.0)	0	(0.0)	0	(0.0)	2	(1.7)
Nasal congestion	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Nasal obstruction	0	(0.0)	1	(6.7)	0	(0.0)	1	(0.8)
Oropharyngeal pain	0	(0.0)	0	(0.0)	0	(0.0)	4	(3.4)
Rhinitis allergic	0	(0.0)	1	(6.7)	0	(0.0)	2	(1.7)
Throat irritation	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Skin and subcutaneous tissue disorders	**3**	**(16.7)**	**0**	**(0.0)**	**0**	**(0.0)**	**20**	**(16.9)**
Acne	0	(0.0)	0	(0.0)	0	(0.0)	2	(1.7)
Cold sweat	1	(5.6)	0	(0.0)	0	(0.0)	2	(1.7)

Subjects With Specific Adverse Events by Dose (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Healthy Population All Subjects as Treated

	MK-3222 0.1 mg/kg IV		MK-3222 0.5 mg/kg IV		MK-3222 3 mg/kg IV		MK-3222 10 mg/kg IV		MK-3222 50 mg SC		MK-3222 200 mg SC	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Skin and subcutaneous tissue disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**8**	**(26.7)**	**9**	**(33.3)**
Dermatitis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.7)
Dry skin	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.7)
Erythema	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.3)	1	(3.7)
Hyperhidrosis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.3)	0	(0.0)
Pruritus	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	2	(7.4)
Rash	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	2	(6.7)	2	(7.4)
Rash erythematous	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.3)	0	(0.0)
Rash generalised	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.7)
Rash maculo-papular	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.3)	0	(0.0)
Rash pruritic	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.3)	1	(3.7)
Skin irritation	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.3)	0	(0.0)
Swelling face	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Surgical and medical procedures	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(3.3)**	**0**	**(0.0)**
Nasal septal operation	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Turbinectomy	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Wisdom teeth removal	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.3)	0	(0.0)
Vascular disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(8.3)**	**0**	**(0.0)**	**0**	**(0.0)**
Haematoma	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Phlebitis	0	(0.0)	0	(0.0)	0	(0.0)	1	(8.3)	0	(0.0)	0	(0.0)

Subjects With Specific Adverse Events by Dose (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Healthy Population All Subjects as Treated

	MK-3222 400 mg SC		Placebo		Post-Study		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Skin and subcutaneous tissue disorders	**3**	**(16.7)**	**0**	**(0.0)**	**0**	**(0.0)**	**20**	**(16.9)**
Dermatitis	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Dry skin	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Erythema	0	(0.0)	0	(0.0)	0	(0.0)	2	(1.7)
Hyperhidrosis	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Pruritus	0	(0.0)	0	(0.0)	0	(0.0)	2	(1.7)
Rash	1	(5.6)	0	(0.0)	0	(0.0)	5	(4.2)
Rash erythematous	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Rash generalised	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Rash maculo-papular	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Rash pruritic	0	(0.0)	0	(0.0)	0	(0.0)	2	(1.7)
Skin irritation	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Swelling face	1	(5.6)	0	(0.0)	0	(0.0)	1	(0.8)
Surgical and medical procedures	**0**	**(0.0)**	**1**	**(6.7)**	**0**	**(0.0)**	**2**	**(1.7)**
Nasal septal operation	0	(0.0)	1	(6.7)	0	(0.0)	1	(0.8)
Turbinectomy	0	(0.0)	1	(6.7)	0	(0.0)	1	(0.8)
Wisdom teeth removal	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Vascular disorders	**1**	**(5.6)**	**0**	**(0.0)**	**0**	**(0.0)**	**2**	**(1.7)**
Haematoma	1	(5.6)	0	(0.0)	0	(0.0)	1	(0.8)
Phlebitis	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)

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: [ISSPH1: analysis-adsl] [ISSPH1: tabulations-aeplus]　SourceはSASシステム中の電子的データのため5章に含めなかった。

付録 2.7.4-11
投与群別に治験薬との因果関係を否定できない有害事象を発現した被験者（1 投与群以上で発現率 > 0%）
第 I 相試験 - 健常人集団
1 回以上投与された全被験者

	MK-3222		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Subjects in population	103		15		118	
with one or more adverse events	34	(33.0)	6	(40.0)	40	(33.9)
with no adverse events	69	(67.0)	9	(60.0)	78	(66.1)
Eye disorders	**0**	**(0.0)**	**1**	**(6.7)**	**1**	**(0.8)**
Vision blurred	0	(0.0)	1	(6.7)	1	(0.8)
Gastrointestinal disorders	**4**	**(3.9)**	**0**	**(0.0)**	**4**	**(3.4)**
Abdominal pain	1	(1.0)	0	(0.0)	1	(0.8)
Nausea	3	(2.9)	0	(0.0)	3	(2.5)
General disorders and administration site conditions	**18**	**(17.5)**	**2**	**(13.3)**	**20**	**(16.9)**
Injection site bruising	10	(9.7)	0	(0.0)	10	(8.5)
Injection site erythema	5	(4.9)	2	(13.3)	7	(5.9)
Injection site pain	6	(5.8)	0	(0.0)	6	(5.1)
Injection site reaction	2	(1.9)	0	(0.0)	2	(1.7)
Infections and infestations	**4**	**(3.9)**	**3**	**(20.0)**	**7**	**(5.9)**
Gastroenteritis	1	(1.0)	1	(6.7)	2	(1.7)
Nasopharyngitis	1	(1.0)	0	(0.0)	1	(0.8)
Pharyngitis	0	(0.0)	1	(6.7)	1	(0.8)
Rhinitis	0	(0.0)	1	(6.7)	1	(0.8)
Tonsillitis	1	(1.0)	0	(0.0)	1	(0.8)
Upper respiratory tract infection	1	(1.0)	1	(6.7)	2	(1.7)

Subjects With Drug-Related Adverse Events by Treatment (Incidence > 0% in One or More Treatment Groups)
Phase I Trials - Healthy Population All Subjects as Treated

	MK-3222		Placebo		Total	
	n	(%)	n	(%)	n	(%)
Injury, poisoning and procedural complications	**1**	**(1.0)**	**0**	**(0.0)**	**1**	**(0.8)**
Infusion related reaction	1	(1.0)	0	(0.0)	1	(0.8)
Musculoskeletal and connective tissue disorders	**2**	**(1.9)**	**0**	**(0.0)**	**2**	**(1.7)**
Myalgia	2	(1.9)	0	(0.0)	2	(1.7)
Neck pain	1	(1.0)	0	(0.0)	1	(0.8)
Nervous system disorders	**10**	**(9.7)**	**3**	**(20.0)**	**13**	**(11.0)**
Disturbance in attention	1	(1.0)	0	(0.0)	1	(0.8)
Dizziness	1	(1.0)	0	(0.0)	1	(0.8)
Headache	8	(7.8)	3	(20.0)	11	(9.3)
Lethargy	1	(1.0)	0	(0.0)	1	(0.8)
Skin and subcutaneous tissue disorders	**5**	**(4.9)**	**0**	**(0.0)**	**5**	**(4.2)**
Cold sweat	1	(1.0)	0	(0.0)	1	(0.8)
Dry skin	1	(1.0)	0	(0.0)	1	(0.8)
Erythema	1	(1.0)	0	(0.0)	1	(0.8)
Rash	1	(1.0)	0	(0.0)	1	(0.8)
Rash generalised	1	(1.0)	0	(0.0)	1	(0.8)

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: [ISSPH1: analysis-adsl] [ISSPH1: tabulations-aeplus] SourceはSASシステム中の電子的データのため5章に含めなかった。

付録 2.7.4-12
投与量別に治験薬との因果関係を否定できない有害事象を発現した被験者（1 投与群以上で発現率>0%）
第 I 相試験 - 健常人集団
1 回以上投与された全被験者

	MK-3222 0.1 mg/kg IV		MK-3222 0.5 mg/kg IV		MK-3222 3 mg/kg IV		MK-3222 10 mg/kg IV		MK-3222 50 mg SC		MK-3222 200 mg SC	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	4		4		8		12		30		27	
with one or more adverse events	0	(0.0)	1	(25.0)	3	(37.5)	0	(0.0)	5	(16.7)	16	(59.3)
with no adverse events	4	(100.0)	3	(75.0)	5	(62.5)	12	(100.0)	25	(83.3)	11	(40.7)
Eye disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**
Vision blurred	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Gastrointestinal disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**2**	**(6.7)**	**1**	**(3.7)**
Abdominal pain	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.3)	0	(0.0)
Nausea	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.3)	1	(3.7)
General disorders and administration site conditions	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**2**	**(6.7)**	**10**	**(37.0)**
Injection site bruising	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.3)	4	(14.8)
Injection site erythema	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.3)	2	(7.4)
Injection site pain	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.3)	4	(14.8)
Injection site reaction	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	2	(7.4)
Infections and infestations	**0**	**(0.0)**	**1**	**(25.0)**	**1**	**(12.5)**	**0**	**(0.0)**	**0**	**(0.0)**	**2**	**(7.4)**
Gastroenteritis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.7)
Nasopharyngitis	0	(0.0)	1	(25.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Pharyngitis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Rhinitis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Tonsillitis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.7)

Subjects With Drug-Related Adverse Events by Dose (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Healthy Population All Subjects as Treated

	MK-3222 400 mg SC		Placebo		Post-Study		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	18		15		118		118	
with one or more adverse events	9	(50.0)	6	(40.0)	0	(0.0)	40	(33.9)
with no adverse events	9	(50.0)	9	(60.0)	118	(100.0)	78	(66.1)
Eye disorders	**0**	**(0.0)**	**1**	**(6.7)**	**0**	**(0.0)**	**1**	**(0.8)**
Vision blurred	0	(0.0)	1	(6.7)	0	(0.0)	1	(0.8)
Gastrointestinal disorders	**1**	**(5.6)**	**0**	**(0.0)**	**0**	**(0.0)**	**4**	**(3.4)**
Abdominal pain	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Nausea	1	(5.6)	0	(0.0)	0	(0.0)	3	(2.5)
General disorders and administration site conditions	**6**	**(33.3)**	**2**	**(13.3)**	**0**	**(0.0)**	**20**	**(16.9)**
Injection site bruising	5	(27.8)	0	(0.0)	0	(0.0)	10	(8.5)
Injection site erythema	2	(11.1)	2	(13.3)	0	(0.0)	7	(5.9)
Injection site pain	1	(5.6)	0	(0.0)	0	(0.0)	6	(5.1)
Injection site reaction	0	(0.0)	0	(0.0)	0	(0.0)	2	(1.7)
Infections and infestations	**0**	**(0.0)**	**3**	**(20.0)**	**0**	**(0.0)**	**7**	**(5.9)**
Gastroenteritis	0	(0.0)	1	(6.7)	0	(0.0)	2	(1.7)
Nasopharyngitis	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Pharyngitis	0	(0.0)	1	(6.7)	0	(0.0)	1	(0.8)
Rhinitis	0	(0.0)	1	(6.7)	0	(0.0)	1	(0.8)
Tonsillitis	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)

Subjects With Drug-Related Adverse Events by Dose (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Healthy Population All Subjects as Treated

	MK-3222 0.1 mg/kg IV		MK-3222 0.5 mg/kg IV		MK-3222 3 mg/kg IV		MK-3222 10 mg/kg IV		MK-3222 50 mg SC		MK-3222 200 mg SC	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Infections and infestations	**0**	**(0.0)**	**1**	**(25.0)**	**1**	**(12.5)**	**0**	**(0.0)**	**0**	**(0.0)**	**2**	**(7.4)**
Upper respiratory tract infection	0	(0.0)	0	(0.0)	1	(12.5)	0	(0.0)	0	(0.0)	0	(0.0)
Injury, poisoning and procedural complications	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(12.5)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**
Infusion related reaction	0	(0.0)	0	(0.0)	1	(12.5)	0	(0.0)	0	(0.0)	0	(0.0)
Musculoskeletal and connective tissue disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**
Myalgia	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Neck pain	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Nervous system disorders	**0**	**(0.0)**	**0**	**(0.0)**	**2**	**(25.0)**	**0**	**(0.0)**	**2**	**(6.7)**	**5**	**(18.5)**
Disturbance in attention	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.7)
Dizziness	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.3)	0	(0.0)
Headache	0	(0.0)	0	(0.0)	2	(25.0)	0	(0.0)	2	(6.7)	3	(11.1)
Lethargy	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.7)
Skin and subcutaneous tissue disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**4**	**(14.8)**
Cold sweat	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Dry skin	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.7)
Erythema	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.7)

Subjects With Drug-Related Adverse Events by Dose (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Healthy Population All Subjects as Treated

	MK-3222 400 mg SC		Placebo		Post-Study		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Infections and infestations	**0**	**(0.0)**	**3**	**(20.0)**	**0**	**(0.0)**	**7**	**(5.9)**
Upper respiratory tract infection	0	(0.0)	1	(6.7)	0	(0.0)	2	(1.7)
Injury, poisoning and procedural complications	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.8)**
Infusion related reaction	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Musculoskeletal and connective tissue disorders	**2**	**(11.1)**	**0**	**(0.0)**	**0**	**(0.0)**	**2**	**(1.7)**
Myalgia	2	(11.1)	0	(0.0)	0	(0.0)	2	(1.7)
Neck pain	1	(5.6)	0	(0.0)	0	(0.0)	1	(0.8)
Nervous system disorders	**1**	**(5.6)**	**3**	**(20.0)**	**0**	**(0.0)**	**13**	**(11.0)**
Disturbance in attention	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Dizziness	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Headache	1	(5.6)	3	(20.0)	0	(0.0)	11	(9.3)
Lethargy	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Skin and subcutaneous tissue disorders	**1**	**(5.6)**	**0**	**(0.0)**	**0**	**(0.0)**	**5**	**(4.2)**
Cold sweat	1	(5.6)	0	(0.0)	0	(0.0)	1	(0.8)
Dry skin	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Erythema	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Rash	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)
Rash generalised	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.8)

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: [ISSPH1: analysis-adsl] [ISSPH1: tabulations-aeplus]　SourceはSASシステム中の電子的データのため5章に含めなかった。

付録 2.7.4-13
投与群別に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 > 0%）
第 I 相試験 - 乾癬患者集団
1 回以上投与された全被験者

	MK-3222		Other		Placebo		Post-Study		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	75		20		20		96		96	
with one or more adverse events	58	(77.3)	3	(15.0)	15	(75.0)	1	(1.0)	75	(78.1)
with no adverse events	17	(22.7)	17	(85.0)	5	(25.0)	95	(99.0)	21	(21.9)
Blood and lymphatic system disorders	**4**	**(5.3)**	**0**	**(0.0)**	**1**	**(5.0)**	**0**	**(0.0)**	**5**	**(5.2)**
Eosinophilia	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Leukocytosis	0	(0.0)	0	(0.0)	1	(5.0)	0	(0.0)	1	(1.0)
Leukopenia	2	(2.7)	0	(0.0)	0	(0.0)	0	(0.0)	2	(2.1)
Lymphopenia	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Neutrophilia	0	(0.0)	0	(0.0)	1	(5.0)	0	(0.0)	1	(1.0)
Thrombocytopenia	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Cardiac disorders	**1**	**(1.3)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(1.0)**
Ventricular extrasystoles	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Eye disorders	**1**	**(1.3)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(1.0)**
Vision blurred	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Gastrointestinal disorders	**13**	**(17.3)**	**0**	**(0.0)**	**2**	**(10.0)**	**0**	**(0.0)**	**15**	**(15.6)**
Abdominal pain	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Abdominal pain lower	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Aphthous ulcer	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Diarrhoea	1	(1.3)	0	(0.0)	1	(5.0)	0	(0.0)	2	(2.1)
Haemorrhoids	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)

Subjects With Specific Adverse Events by Treatment (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Psoriasis Population All Subjects as Treated

	MK-3222		Other		Placebo		Post-Study		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Gastrointestinal disorders	**13**	**(17.3)**	**0**	**(0.0)**	**2**	**(10.0)**	**0**	**(0.0)**	**15**	**(15.6)**
Large intestine polyp	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Nausea	0	(0.0)	0	(0.0)	1	(5.0)	0	(0.0)	1	(1.0)
Oedema mouth	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Paraesthesia oral	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Rectal polyp	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Tongue pruritus	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Toothache	3	(4.0)	0	(0.0)	0	(0.0)	0	(0.0)	3	(3.1)
Umbilical hernia	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
General disorders and administration site conditions	**7**	**(9.3)**	**0**	**(0.0)**	**2**	**(10.0)**	**0**	**(0.0)**	**9**	**(9.4)**
Application site reaction	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Chest pain	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Fatigue	1	(1.3)	0	(0.0)	2	(10.0)	0	(0.0)	3	(3.1)
Influenza like illness	2	(2.7)	0	(0.0)	0	(0.0)	0	(0.0)	2	(2.1)
Peripheral swelling	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Pyrexia	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Hepatobiliary disorders	**1**	**(1.3)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(1.0)**
Hepatotoxicity	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Immune system disorders	**1**	**(1.3)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(1.0)**
Allergy to arthropod sting	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)

Subjects With Specific Adverse Events by Treatment (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Psoriasis Population All Subjects as Treated

	MK-3222		Other		Placebo		Post-Study		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Infections and infestations	**35**	**(46.7)**	**0**	**(0.0)**	**9**	**(45.0)**	**1**	**(1.0)**	**44**	**(45.8)**
Bronchitis	0	(0.0)	0	(0.0)	1	(5.0)	0	(0.0)	1	(1.0)
Conjunctivitis	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Cytomegalovirus infection	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)	1	(1.0)
Diverticulitis	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Erysipelas	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Furuncle	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Gastroenteritis	3	(4.0)	0	(0.0)	1	(5.0)	0	(0.0)	4	(4.2)
Gingivitis	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Haemorrhoid infection	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Herpes zoster	0	(0.0)	0	(0.0)	1	(5.0)	0	(0.0)	1	(1.0)
Infected dermal cyst	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Laryngitis	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Nasopharyngitis	11	(14.7)	0	(0.0)	2	(10.0)	0	(0.0)	13	(13.5)
Oral herpes	0	(0.0)	0	(0.0)	1	(5.0)	0	(0.0)	1	(1.0)
Pharyngitis	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Pharyngitis streptococcal	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Rhinitis	4	(5.3)	0	(0.0)	0	(0.0)	0	(0.0)	4	(4.2)
Sinusitis	0	(0.0)	0	(0.0)	3	(15.0)	0	(0.0)	3	(3.1)
Staphylococcal skin infection	0	(0.0)	0	(0.0)	1	(5.0)	0	(0.0)	1	(1.0)
Subcutaneous abscess	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Tinea cruris	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Tinea pedis	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Tonsillitis	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Tooth abscess	1	(1.3)	0	(0.0)	1	(5.0)	0	(0.0)	2	(2.1)
Upper respiratory tract infection	11	(14.7)	0	(0.0)	3	(15.0)	0	(0.0)	14	(14.6)

Subjects With Specific Adverse Events by Treatment (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Psoriasis Population All Subjects as Treated

	MK-3222		Other		Placebo		Post-Study		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Infections and infestations	**35**	**(46.7)**	**0**	**(0.0)**	**9**	**(45.0)**	**1**	**(1.0)**	**44**	**(45.8)**
Urinary tract infection	0	(0.0)	0	(0.0)	1	(5.0)	0	(0.0)	1	(1.0)
Vulvovaginal mycotic infection	1	(1.3)	0	(0.0)	1	(5.0)	0	(0.0)	2	(2.1)
Wound infection	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Injury, poisoning and procedural complications	**10**	**(13.3)**	**0**	**(0.0)**	**2**	**(10.0)**	**0**	**(0.0)**	**12**	**(12.5)**
Accident	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Acetabulum fracture	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Ankle fracture	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Contusion	2	(2.7)	0	(0.0)	0	(0.0)	0	(0.0)	2	(2.1)
Facial bones fracture	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Ligament sprain	2	(2.7)	0	(0.0)	1	(5.0)	0	(0.0)	3	(3.1)
Muscle strain	0	(0.0)	0	(0.0)	1	(5.0)	0	(0.0)	1	(1.0)
Procedural pain	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Skin abrasion	1	(1.3)	0	(0.0)	1	(5.0)	0	(0.0)	2	(2.1)
Thermal burn	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Upper limb fracture	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Investigations	**15**	**(20.0)**	**1**	**(5.0)**	**2**	**(10.0)**	**0**	**(0.0)**	**18**	**(18.8)**
Alanine aminotransferase increased	3	(4.0)	0	(0.0)	0	(0.0)	0	(0.0)	3	(3.1)
Aspartate aminotransferase increased	2	(2.7)	0	(0.0)	0	(0.0)	0	(0.0)	2	(2.1)
Blood bilirubin increased	1	(1.3)	1	(5.0)	0	(0.0)	0	(0.0)	2	(2.1)
Blood chloride decreased	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)

Subjects With Specific Adverse Events by Treatment (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Psoriasis Population All Subjects as Treated

	MK-3222		Other		Placebo		Post-Study		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Investigations	**15**	**(20.0)**	**1**	**(5.0)**	**2**	**(10.0)**	**0**	**(0.0)**	**18**	**(18.8)**
Blood creatine phosphokinase increased	4	(5.3)	0	(0.0)	0	(0.0)	0	(0.0)	4	(4.2)
Blood glucose increased	2	(2.7)	0	(0.0)	0	(0.0)	0	(0.0)	2	(2.1)
Blood pressure diastolic increased	0	(0.0)	0	(0.0)	1	(5.0)	0	(0.0)	1	(1.0)
Blood triglycerides increased	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Gamma-glutamyltransferase increased	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Haemoglobin decreased	0	(0.0)	0	(0.0)	1	(5.0)	0	(0.0)	1	(1.0)
Heart rate increased	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Hepatic enzyme increased	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Liver function test increased	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Myocardial necrosis marker increased	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Platelet count decreased	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Metabolism and nutrition disorders	**9**	**(12.0)**	**0**	**(0.0)**	**2**	**(10.0)**	**0**	**(0.0)**	**11**	**(11.5)**
Diabetes mellitus	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Hyperglycaemia	5	(6.7)	0	(0.0)	0	(0.0)	0	(0.0)	5	(5.2)
Hypertriglyceridaemia	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Hyperuricaemia	2	(2.7)	0	(0.0)	1	(5.0)	0	(0.0)	3	(3.1)
Hypokalaemia	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Type 2 diabetes mellitus	1	(1.3)	0	(0.0)	1	(5.0)	0	(0.0)	2	(2.1)

Subjects With Specific Adverse Events by Treatment (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Psoriasis Population All Subjects as Treated

	MK-3222		Other		Placebo		Post-Study		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Musculoskeletal and connective tissue disorders	**13**	**(17.3)**	**0**	**(0.0)**	**6**	**(30.0)**	**0**	**(0.0)**	**19**	**(19.8)**
Arthralgia	3	(4.0)	0	(0.0)	3	(15.0)	0	(0.0)	6	(6.3)
Back pain	3	(4.0)	0	(0.0)	1	(5.0)	0	(0.0)	4	(4.2)
Flank pain	0	(0.0)	0	(0.0)	1	(5.0)	0	(0.0)	1	(1.0)
Muscle spasms	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Musculoskeletal chest pain	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Musculoskeletal pain	2	(2.7)	0	(0.0)	0	(0.0)	0	(0.0)	2	(2.1)
Myalgia	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Myositis	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Pain in extremity	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Psoriatic arthropathy	1	(1.3)	0	(0.0)	1	(5.0)	0	(0.0)	2	(2.1)
Rotator cuff syndrome	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Spinal osteoarthritis	0	(0.0)	0	(0.0)	1	(5.0)	0	(0.0)	1	(1.0)
Tendon disorder	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**1**	**(1.3)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(1.0)**
Fibroadenoma of breast	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Nervous system disorders	**19**	**(25.3)**	**2**	**(10.0)**	**4**	**(20.0)**	**0**	**(0.0)**	**25**	**(26.0)**
Cervicobrachial syndrome	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Dizziness	2	(2.7)	1	(5.0)	1	(5.0)	0	(0.0)	4	(4.2)
Dysgeusia	1	(1.3)	0	(0.0)	1	(5.0)	0	(0.0)	2	(2.1)
Head discomfort	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)

Subjects With Specific Adverse Events by Treatment (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Psoriasis Population All Subjects as Treated

	MK-3222		Other		Placebo		Post-Study		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Nervous system disorders	**19**	**(25.3)**	**2**	**(10.0)**	**4**	**(20.0)**	**0**	**(0.0)**	**25**	**(26.0)**
Headache	13	(17.3)	1	(5.0)	3	(15.0)	0	(0.0)	17	(17.7)
Hypoaesthesia	1	(1.3)	0	(0.0)	1	(5.0)	0	(0.0)	2	(2.1)
Paraesthesia	2	(2.7)	0	(0.0)	0	(0.0)	0	(0.0)	2	(2.1)
Sciatica	2	(2.7)	0	(0.0)	0	(0.0)	0	(0.0)	2	(2.1)
Seizure	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Psychiatric disorders	**3**	**(4.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**3**	**(3.1)**
Insomnia	2	(2.7)	0	(0.0)	0	(0.0)	0	(0.0)	2	(2.1)
Libido decreased	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Reproductive system and breast disorders	**1**	**(1.3)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(1.0)**
Menopausal symptoms	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Respiratory, thoracic and mediastinal disorders	**13**	**(17.3)**	**0**	**(0.0)**	**4**	**(20.0)**	**0**	**(0.0)**	**17**	**(17.7)**
Cough	9	(12.0)	0	(0.0)	3	(15.0)	0	(0.0)	12	(12.5)
Dyspnoea	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Nasal congestion	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Oropharyngeal pain	3	(4.0)	0	(0.0)	1	(5.0)	0	(0.0)	4	(4.2)
Pneumothorax	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Pulmonary embolism	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Pulmonary hypertension	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Rhinitis allergic	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Sinus congestion	1	(1.3)	0	(0.0)	1	(5.0)	0	(0.0)	2	(2.1)

Subjects With Specific Adverse Events by Treatment (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Psoriasis Population All Subjects as Treated

	MK-3222		Other		Placebo		Post-Study		Total	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Respiratory, thoracic and mediastinal disorders	**13**	**(17.3)**	**0**	**(0.0)**	**4**	**(20.0)**	**0**	**(0.0)**	**17**	**(17.7)**
Tonsillar ulcer	0	(0.0)	0	(0.0)	1	(5.0)	0	(0.0)	1	(1.0)
Skin and subcutaneous tissue disorders	**11**	**(14.7)**	**0**	**(0.0)**	**5**	**(25.0)**	**0**	**(0.0)**	**16**	**(16.7)**
Alopecia	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Dermatitis acneiform	2	(2.7)	0	(0.0)	0	(0.0)	0	(0.0)	2	(2.1)
Dermatitis contact	0	(0.0)	0	(0.0)	1	(5.0)	0	(0.0)	1	(1.0)
Eczema	3	(4.0)	0	(0.0)	0	(0.0)	0	(0.0)	3	(3.1)
Erythema	2	(2.7)	0	(0.0)	0	(0.0)	0	(0.0)	2	(2.1)
Hypersensitivity vasculitis	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Pruritus	2	(2.7)	0	(0.0)	1	(5.0)	0	(0.0)	3	(3.1)
Pruritus generalised	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Psoriasis	0	(0.0)	0	(0.0)	2	(10.0)	0	(0.0)	2	(2.1)
Rash macular	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Rash maculo-papular	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Seborrhoeic dermatitis	0	(0.0)	0	(0.0)	1	(5.0)	0	(0.0)	1	(1.0)
Surgical and medical procedures	**3**	**(4.0)**	**0**	**(0.0)**	**1**	**(5.0)**	**0**	**(0.0)**	**4**	**(4.2)**
Endodontic procedure	2	(2.7)	0	(0.0)	0	(0.0)	0	(0.0)	2	(2.1)
Polypectomy	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Tooth extraction	0	(0.0)	0	(0.0)	1	(5.0)	0	(0.0)	1	(1.0)
Vascular disorders	**4**	**(5.3)**	**0**	**(0.0)**	**1**	**(5.0)**	**0**	**(0.0)**	**5**	**(5.2)**
Deep vein thrombosis	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)
Hypertension	3	(4.0)	0	(0.0)	1	(5.0)	0	(0.0)	4	(4.2)
Thrombophlebitis	1	(1.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.0)

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.

MK-3222 includes subjects who received CYP probe on top of MK-3222 in P009.

Source: [ISSPH1: analysis-adsl] [ISSPH1: tabulations-aeplus]　SourceはSASシステム中の電子的データのため5章に含めなかった。

付録 2.7.4-14
投与量別に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 > 0%）
第 I 相試験 - 乾癬患者集団
1 回以上投与された全被験者

	MK-3222 0.05 mg/kg IV		MK-3222 0.1 mg/kg IV		MK-3222 0.5 mg/kg IV		MK-3222 3 mg/kg IV		MK-3222 5 mg/kg IV		MK-3222 10 mg/kg IV	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	6		6		3		21		3		17	
with one or more adverse events	6	(100.0)	4	(66.7)	3	(100.0)	20	(95.2)	3	(100.0)	11	(64.7)
with no adverse events	0	(0.0)	2	(33.3)	0	(0.0)	1	(4.8)	0	(0.0)	6	(35.3)
Blood and lymphatic system disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**2**	**(9.5)**	**0**	**(0.0)**	**2**	**(11.8)**
Eosinophilia	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)
Leukocytosis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Leukopenia	0	(0.0)	0	(0.0)	0	(0.0)	2	(9.5)	0	(0.0)	0	(0.0)
Lymphopenia	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)
Neutrophilia	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Thrombocytopenia	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)
Cardiac disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(5.9)**
Ventricular extrasystoles	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)
Eye disorders	**0**	**(0.0)**	**1**	**(16.7)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**
Vision blurred	0	(0.0)	1	(16.7)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Gastrointestinal disorders	**2**	**(33.3)**	**0**	**(0.0)**	**1**	**(33.3)**	**5**	**(23.8)**	**1**	**(33.3)**	**3**	**(17.6)**
Abdominal pain	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)
Abdominal pain lower	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)
Aphthous ulcer	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)
Diarrhoea	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)
Haemorrhoids	1	(16.7)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

Subjects With Specific Adverse Events by Dose (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Psoriasis Population All Subjects as Treated

	MK-3222 200 mg SC		Placebo		Post-Study		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	19		20		95		95	
with one or more adverse events	9	(47.4)	15	(75.0)	1	(1.1)	71	(74.7)
with no adverse events	10	(52.6)	5	(25.0)	94	(98.9)	24	(25.3)
Blood and lymphatic system disorders	**0**	**(0.0)**	**1**	**(5.0)**	**0**	**(0.0)**	**5**	**(5.3)**
Eosinophilia	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Leukocytosis	0	(0.0)	1	(5.0)	0	(0.0)	1	(1.1)
Leukopenia	0	(0.0)	0	(0.0)	0	(0.0)	2	(2.1)
Lymphopenia	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Neutrophilia	0	(0.0)	1	(5.0)	0	(0.0)	1	(1.1)
Thrombocytopenia	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Cardiac disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(1.1)**
Ventricular extrasystoles	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Eye disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(1.1)**
Vision blurred	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Gastrointestinal disorders	**1**	**(5.3)**	**2**	**(10.0)**	**0**	**(0.0)**	**15**	**(15.8)**
Abdominal pain	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Abdominal pain lower	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Aphthous ulcer	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Diarrhoea	0	(0.0)	1	(5.0)	0	(0.0)	2	(2.1)
Haemorrhoids	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)

Subjects With Specific Adverse Events by Dose (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Psoriasis Population All Subjects as Treated

	MK-3222 0.05 mg/kg IV		MK-3222 0.1 mg/kg IV		MK-3222 0.5 mg/kg IV		MK-3222 3 mg/kg IV		MK-3222 5 mg/kg IV		MK-3222 10 mg/kg IV	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Gastrointestinal disorders	**2**	**(33.3)**	**0**	**(0.0)**	**1**	**(33.3)**	**5**	**(23.8)**	**1**	**(33.3)**	**3**	**(17.6)**
Large intestine polyp	0	(0.0)	0	(0.0)	1	(33.3)	0	(0.0)	0	(0.0)	0	(0.0)
Nausea	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Oedema mouth	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)
Paraesthesia oral	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)
Rectal polyp	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(33.3)	0	(0.0)
Tongue pruritus	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)
Toothache	1	(16.7)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)
Umbilical hernia	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)
General disorders and administration site conditions	**1**	**(16.7)**	**1**	**(16.7)**	**0**	**(0.0)**	**4**	**(19.0)**	**0**	**(0.0)**	**1**	**(5.9)**
Application site reaction	0	(0.0)	1	(16.7)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Chest pain	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)
Fatigue	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)
Influenza like illness	1	(16.7)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)
Peripheral swelling	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)
Pyrexia	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)
Immune system disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(4.8)**	**0**	**(0.0)**	**0**	**(0.0)**
Allergy to arthropod sting	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)
Infections and infestations	**3**	**(50.0)**	**3**	**(50.0)**	**2**	**(66.7)**	**12**	**(57.1)**	**3**	**(100.0)**	**8**	**(47.1)**
Bronchitis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Conjunctivitis	0	(0.0)	0	(0.0)	1	(33.3)	0	(0.0)	0	(0.0)	0	(0.0)

Subjects With Specific Adverse Events by Dose (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Psoriasis Population All Subjects as Treated

	MK-3222 200 mg SC		Placebo		Post-Study		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Gastrointestinal disorders	**1**	**(5.3)**	**2**	**(10.0)**	**0**	**(0.0)**	**15**	**(15.8)**
Large intestine polyp	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Nausea	0	(0.0)	1	(5.0)	0	(0.0)	1	(1.1)
Oedema mouth	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Paraesthesia oral	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Rectal polyp	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Tongue pruritus	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Toothache	1	(5.3)	0	(0.0)	0	(0.0)	3	(3.2)
Umbilical hernia	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
General disorders and administration site conditions	**0**	**(0.0)**	**2**	**(10.0)**	**0**	**(0.0)**	**9**	**(9.5)**
Application site reaction	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Chest pain	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Fatigue	0	(0.0)	2	(10.0)	0	(0.0)	3	(3.2)
Influenza like illness	0	(0.0)	0	(0.0)	0	(0.0)	2	(2.1)
Peripheral swelling	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Pyrexia	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Immune system disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(1.1)**
Allergy to arthropod sting	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Infections and infestations	**4**	**(21.1)**	**9**	**(45.0)**	**1**	**(1.1)**	**44**	**(46.3)**
Bronchitis	0	(0.0)	1	(5.0)	0	(0.0)	1	(1.1)
Conjunctivitis	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)

Subjects With Specific Adverse Events by Dose (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Psoriasis Population All Subjects as Treated

	MK-3222 0.05 mg/kg IV		MK-3222 0.1 mg/kg IV		MK-3222 0.5 mg/kg IV		MK-3222 3 mg/kg IV		MK-3222 5 mg/kg IV		MK-3222 10 mg/kg IV	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Infections and infestations	**3**	**(50.0)**	**3**	**(50.0)**	**2**	**(66.7)**	**12**	**(57.1)**	**3**	**(100.0)**	**8**	**(47.1)**
Cytomegalovirus infection	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Diverticulitis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(33.3)	0	(0.0)
Erysipelas	1	(16.7)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Furuncle	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)
Gastroenteritis	1	(16.7)	1	(16.7)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)
Gingivitis	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)
Haemorrhoid infection	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)
Herpes zoster	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Infected dermal cyst	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Laryngitis	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)
Nasopharyngitis	0	(0.0)	1	(16.7)	0	(0.0)	5	(23.8)	0	(0.0)	4	(23.5)
Oral herpes	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Pharyngitis	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)
Pharyngitis streptococcal	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Rhinitis	1	(16.7)	0	(0.0)	0	(0.0)	2	(9.5)	0	(0.0)	1	(5.9)
Sinusitis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Staphylococcal skin infection	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Subcutaneous abscess	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)
Tinea cruris	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)
Tinea pedis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)
Tonsillitis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)
Tooth abscess	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)
Upper respiratory tract infection	1	(16.7)	2	(33.3)	1	(33.3)	2	(9.5)	2	(66.7)	3	(17.6)

Subjects With Specific Adverse Events by Dose (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Psoriasis Population All Subjects as Treated

	MK-3222 200 mg SC		Placebo		Post-Study		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Infections and infestations	**4**	**(21.1)**	**9**	**(45.0)**	**1**	**(1.1)**	**44**	**(46.3)**
Cytomegalovirus infection	0	(0.0)	0	(0.0)	1	(1.1)	1	(1.1)
Diverticulitis	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Erysipelas	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Furuncle	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Gastroenteritis	0	(0.0)	1	(5.0)	0	(0.0)	4	(4.2)
Gingivitis	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Haemorrhoid infection	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Herpes zoster	0	(0.0)	1	(5.0)	0	(0.0)	1	(1.1)
Infected dermal cyst	1	(5.3)	0	(0.0)	0	(0.0)	1	(1.1)
Laryngitis	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Nasopharyngitis	1	(5.3)	2	(10.0)	0	(0.0)	13	(13.7)
Oral herpes	0	(0.0)	1	(5.0)	0	(0.0)	1	(1.1)
Pharyngitis	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Pharyngitis streptococcal	1	(5.3)	0	(0.0)	0	(0.0)	1	(1.1)
Rhinitis	0	(0.0)	0	(0.0)	0	(0.0)	4	(4.2)
Sinusitis	0	(0.0)	3	(15.0)	0	(0.0)	3	(3.2)
Staphylococcal skin infection	0	(0.0)	1	(5.0)	0	(0.0)	1	(1.1)
Subcutaneous abscess	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Tinea cruris	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Tinea pedis	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Tonsillitis	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Tooth abscess	0	(0.0)	1	(5.0)	0	(0.0)	2	(2.1)
Upper respiratory tract infection	0	(0.0)	3	(15.0)	0	(0.0)	14	(14.7)

Subjects With Specific Adverse Events by Dose (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Psoriasis Population All Subjects as Treated

	MK-3222 0.05 mg/kg IV		MK-3222 0.1 mg/kg IV		MK-3222 0.5 mg/kg IV		MK-3222 3 mg/kg IV		MK-3222 5 mg/kg IV		MK-3222 10 mg/kg IV	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Infections and infestations	**3**	**(50.0)**	**3**	**(50.0)**	**2**	**(66.7)**	**12**	**(57.1)**	**3**	**(100.0)**	**8**	**(47.1)**
Urinary tract infection	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Vulvovaginal mycotic infection	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Wound infection	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)
Injury, poisoning and procedural complications	**2**	**(33.3)**	**0**	**(0.0)**	**1**	**(33.3)**	**2**	**(9.5)**	**0**	**(0.0)**	**3**	**(17.6)**
Accident	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)
Ankle fracture	1	(16.7)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Contusion	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)
Facial bones fracture	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)
Ligament sprain	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)
Muscle strain	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Procedural pain	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)
Skin abrasion	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)
Thermal burn	0	(0.0)	0	(0.0)	1	(33.3)	0	(0.0)	0	(0.0)	0	(0.0)
Upper limb fracture	1	(16.7)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Investigations	**0**	**(0.0)**	**1**	**(16.7)**	**0**	**(0.0)**	**4**	**(19.0)**	**2**	**(66.7)**	**4**	**(23.5)**
Alanine aminotransferase increased	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Aspartate aminotransferase increased	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

Subjects With Specific Adverse Events by Dose (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Psoriasis Population All Subjects as Treated

	MK-3222 200 mg SC		Placebo		Post-Study		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Infections and infestations	**4**	**(21.1)**	**9**	**(45.0)**	**1**	**(1.1)**	**44**	**(46.3)**
Urinary tract infection	0	(0.0)	1	(5.0)	0	(0.0)	1	(1.1)
Vulvovaginal mycotic infection	1	(5.3)	1	(5.0)	0	(0.0)	2	(2.1)
Wound infection	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Injury, poisoning and procedural complications	**0**	**(0.0)**	**2**	**(10.0)**	**0**	**(0.0)**	**10**	**(10.5)**
Accident	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Ankle fracture	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Contusion	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Facial bones fracture	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Ligament sprain	0	(0.0)	1	(5.0)	0	(0.0)	2	(2.1)
Muscle strain	0	(0.0)	1	(5.0)	0	(0.0)	1	(1.1)
Procedural pain	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Skin abrasion	0	(0.0)	1	(5.0)	0	(0.0)	2	(2.1)
Thermal burn	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Upper limb fracture	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Investigations	**3**	**(15.8)**	**2**	**(10.0)**	**0**	**(0.0)**	**16**	**(16.8)**
Alanine aminotransferase increased	2	(10.5)	0	(0.0)	0	(0.0)	2	(2.1)
Aspartate aminotransferase increased	1	(5.3)	0	(0.0)	0	(0.0)	1	(1.1)

Subjects With Specific Adverse Events by Dose (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Psoriasis Population All Subjects as Treated

	MK-3222 0.05 mg/kg IV		MK-3222 0.1 mg/kg IV		MK-3222 0.5 mg/kg IV		MK-3222 3 mg/kg IV		MK-3222 5 mg/kg IV		MK-3222 10 mg/kg IV	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Investigations	**0**	**(0.0)**	**1**	**(16.7)**	**0**	**(0.0)**	**4**	**(19.0)**	**2**	**(66.7)**	**4**	**(23.5)**
Blood bilirubin increased	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Blood chloride decreased	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)
Blood creatine phosphokinase increased	0	(0.0)	0	(0.0)	0	(0.0)	2	(9.5)	1	(33.3)	1	(5.9)
Blood glucose increased	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.8)	1	(33.3)	0	(0.0)
Blood pressure diastolic increased	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Blood triglycerides increased	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(33.3)	0	(0.0)
Gamma-glutamyltransferase increased	0	(0.0)	1	(16.7)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Haemoglobin decreased	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Heart rate increased	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)
Hepatic enzyme increased	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)
Liver function test increased	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)
Myocardial necrosis marker increased	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)
Platelet count decreased	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)
Metabolism and nutrition disorders	**1**	**(16.7)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(4.8)**	**0**	**(0.0)**	**2**	**(11.8)**
Diabetes mellitus	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)

Subjects With Specific Adverse Events by Dose (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Psoriasis Population All Subjects as Treated

	MK-3222 200 mg SC		Placebo		Post-Study		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Investigations	**3**	**(15.8)**	**2**	**(10.0)**	**0**	**(0.0)**	**16**	**(16.8)**
Blood bilirubin increased	1	(5.3)	0	(0.0)	0	(0.0)	1	(1.1)
Blood chloride decreased	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Blood creatine phosphokinase increased	0	(0.0)	0	(0.0)	0	(0.0)	4	(4.2)
Blood glucose increased	0	(0.0)	0	(0.0)	0	(0.0)	2	(2.1)
Blood pressure diastolic increased	0	(0.0)	1	(5.0)	0	(0.0)	1	(1.1)
Blood triglycerides increased	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Gamma-glutamyltransferase increased	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Haemoglobin decreased	0	(0.0)	1	(5.0)	0	(0.0)	1	(1.1)
Heart rate increased	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Hepatic enzyme increased	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Liver function test increased	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Myocardial necrosis marker increased	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Platelet count decreased	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Metabolism and nutrition disorders	**4**	**(21.1)**	**2**	**(10.0)**	**0**	**(0.0)**	**10**	**(10.5)**
Diabetes mellitus	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)

Subjects With Specific Adverse Events by Dose (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Psoriasis Population All Subjects as Treated

	MK-3222 0.05 mg/kg IV		MK-3222 0.1 mg/kg IV		MK-3222 0.5 mg/kg IV		MK-3222 3 mg/kg IV		MK-3222 5 mg/kg IV		MK-3222 10 mg/kg IV	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Metabolism and nutrition disorders	**1**	**(16.7)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(4.8)**	**0**	**(0.0)**	**2**	**(11.8)**
Hyperglycaemia	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Hypertriglyceridaemia	1	(16.7)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Hyperuricaemia	1	(16.7)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)
Hypokalaemia	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)
Type 2 diabetes mellitus	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Musculoskeletal and connective tissue disorders	**2**	**(33.3)**	**0**	**(0.0)**	**0**	**(0.0)**	**9**	**(42.9)**	**1**	**(33.3)**	**1**	**(5.9)**
Arthralgia	0	(0.0)	0	(0.0)	0	(0.0)	2	(9.5)	0	(0.0)	1	(5.9)
Back pain	0	(0.0)	0	(0.0)	0	(0.0)	3	(14.3)	0	(0.0)	0	(0.0)
Flank pain	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Muscle spasms	1	(16.7)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Musculoskeletal chest pain	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(33.3)	0	(0.0)
Musculoskeletal pain	1	(16.7)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)
Myalgia	1	(16.7)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Myositis	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)
Pain in extremity	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)
Psoriatic arthropathy	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)
Rotator cuff syndrome	1	(16.7)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Spinal osteoarthritis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Tendon disorder	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)

Subjects With Specific Adverse Events by Dose (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Psoriasis Population All Subjects as Treated

	MK-3222 200 mg SC		Placebo		Post-Study		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Metabolism and nutrition disorders	**4**	**(21.1)**	**2**	**(10.0)**	**0**	**(0.0)**	**10**	**(10.5)**
Hyperglycaemia	4	(21.1)	0	(0.0)	0	(0.0)	4	(4.2)
Hypertriglyceridaemia	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Hyperuricaemia	0	(0.0)	1	(5.0)	0	(0.0)	3	(3.2)
Hypokalaemia	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Type 2 diabetes mellitus	0	(0.0)	1	(5.0)	0	(0.0)	1	(1.1)
Musculoskeletal and connective tissue disorders	**0**	**(0.0)**	**6**	**(30.0)**	**0**	**(0.0)**	**19**	**(20.0)**
Arthralgia	0	(0.0)	3	(15.0)	0	(0.0)	6	(6.3)
Back pain	0	(0.0)	1	(5.0)	0	(0.0)	4	(4.2)
Flank pain	0	(0.0)	1	(5.0)	0	(0.0)	1	(1.1)
Muscle spasms	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Musculoskeletal chest pain	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Musculoskeletal pain	0	(0.0)	0	(0.0)	0	(0.0)	2	(2.1)
Myalgia	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Myositis	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Pain in extremity	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Psoriatic arthropathy	0	(0.0)	1	(5.0)	0	(0.0)	2	(2.1)
Rotator cuff syndrome	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Spinal osteoarthritis	0	(0.0)	1	(5.0)	0	(0.0)	1	(1.1)
Tendon disorder	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)

Subjects With Specific Adverse Events by Dose (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Psoriasis Population All Subjects as Treated

	MK-3222 0.05 mg/kg IV		MK-3222 0.1 mg/kg IV		MK-3222 0.5 mg/kg IV		MK-3222 3 mg/kg IV		MK-3222 5 mg/kg IV		MK-3222 10 mg/kg IV	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**
Fibroadenoma of breast	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Nervous system disorders	**1**	**(16.7)**	**2**	**(33.3)**	**2**	**(66.7)**	**8**	**(38.1)**	**2**	**(66.7)**	**3**	**(17.6)**
Cervicobrachial syndrome	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)
Dizziness	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.8)	1	(33.3)	0	(0.0)
Dysgeusia	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)
Head discomfort	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)
Headache	1	(16.7)	2	(33.3)	1	(33.3)	5	(23.8)	1	(33.3)	2	(11.8)
Hypoaesthesia	0	(0.0)	0	(0.0)	1	(33.3)	0	(0.0)	0	(0.0)	0	(0.0)
Paraesthesia	0	(0.0)	0	(0.0)	0	(0.0)	2	(9.5)	0	(0.0)	0	(0.0)
Sciatica	0	(0.0)	0	(0.0)	0	(0.0)	2	(9.5)	0	(0.0)	0	(0.0)
Seizure	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)
Psychiatric disorders	**1**	**(16.7)**	**2**	**(33.3)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**
Insomnia	0	(0.0)	2	(33.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Libido decreased	1	(16.7)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Reproductive system and breast disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(4.8)**	**0**	**(0.0)**	**0**	**(0.0)**
Menopausal symptoms	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)

Subjects With Specific Adverse Events by Dose (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Psoriasis Population All Subjects as Treated

	MK-3222 200 mg SC		Placebo		Post-Study		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**1**	**(5.3)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(1.1)**
Fibroadenoma of breast	1	(5.3)	0	(0.0)	0	(0.0)	1	(1.1)
Nervous system disorders	**1**	**(5.3)**	**4**	**(20.0)**	**0**	**(0.0)**	**23**	**(24.2)**
Cervicobrachial syndrome	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Dizziness	0	(0.0)	1	(5.0)	0	(0.0)	3	(3.2)
Dysgeusia	0	(0.0)	1	(5.0)	0	(0.0)	2	(2.1)
Head discomfort	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Headache	1	(5.3)	3	(15.0)	0	(0.0)	16	(16.8)
Hypoaesthesia	0	(0.0)	1	(5.0)	0	(0.0)	2	(2.1)
Paraesthesia	0	(0.0)	0	(0.0)	0	(0.0)	2	(2.1)
Sciatica	0	(0.0)	0	(0.0)	0	(0.0)	2	(2.1)
Seizure	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Psychiatric disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**3**	**(3.2)**
Insomnia	0	(0.0)	0	(0.0)	0	(0.0)	2	(2.1)
Libido decreased	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Reproductive system and breast disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(1.1)**
Menopausal symptoms	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)

Subjects With Specific Adverse Events by Dose (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Psoriasis Population All Subjects as Treated

	MK-3222 0.05 mg/kg IV		MK-3222 0.1 mg/kg IV		MK-3222 0.5 mg/kg IV		MK-3222 3 mg/kg IV		MK-3222 5 mg/kg IV		MK-3222 10 mg/kg IV	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Respiratory, thoracic and mediastinal disorders	**1**	**(16.7)**	**2**	**(33.3)**	**0**	**(0.0)**	**7**	**(33.3)**	**0**	**(0.0)**	**3**	**(17.6)**
Cough	0	(0.0)	1	(16.7)	0	(0.0)	5	(23.8)	0	(0.0)	3	(17.6)
Dyspnoea	1	(16.7)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Nasal congestion	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)
Oropharyngeal pain	0	(0.0)	0	(0.0)	0	(0.0)	2	(9.5)	0	(0.0)	1	(5.9)
Pneumothorax	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)
Pulmonary embolism	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)
Pulmonary hypertension	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)
Rhinitis allergic	0	(0.0)	1	(16.7)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Sinus congestion	0	(0.0)	1	(16.7)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Tonsillar ulcer	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Skin and subcutaneous tissue disorders	**1**	**(16.7)**	**1**	**(16.7)**	**0**	**(0.0)**	**6**	**(28.6)**	**0**	**(0.0)**	**3**	**(17.6)**
Alopecia	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)
Dermatitis acneiform	0	(0.0)	1	(16.7)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)
Dermatitis contact	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Eczema	0	(0.0)	0	(0.0)	0	(0.0)	2	(9.5)	0	(0.0)	1	(5.9)
Erythema	1	(16.7)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)
Hypersensitivity vasculitis	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)
Pruritus	0	(0.0)	0	(0.0)	0	(0.0)	2	(9.5)	0	(0.0)	0	(0.0)
Pruritus generalised	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)
Psoriasis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Rash macular	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)
Rash maculo-papular	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)

Subjects With Specific Adverse Events by Dose (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Psoriasis Population All Subjects as Treated

	MK-3222 200 mg SC		Placebo		Post-Study		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Respiratory, thoracic and mediastinal disorders	**0**	**(0.0)**	**4**	**(20.0)**	**0**	**(0.0)**	**17**	**(17.9)**
Cough	0	(0.0)	3	(15.0)	0	(0.0)	12	(12.6)
Dyspnoea	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Nasal congestion	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Oropharyngeal pain	0	(0.0)	1	(5.0)	0	(0.0)	4	(4.2)
Pneumothorax	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Pulmonary embolism	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Pulmonary hypertension	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Rhinitis allergic	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Sinus congestion	0	(0.0)	1	(5.0)	0	(0.0)	2	(2.1)
Tonsillar ulcer	0	(0.0)	1	(5.0)	0	(0.0)	1	(1.1)
Skin and subcutaneous tissue disorders	**0**	**(0.0)**	**5**	**(25.0)**	**0**	**(0.0)**	**16**	**(16.8)**
Alopecia	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Dermatitis acneiform	0	(0.0)	0	(0.0)	0	(0.0)	2	(2.1)
Dermatitis contact	0	(0.0)	1	(5.0)	0	(0.0)	1	(1.1)
Eczema	0	(0.0)	0	(0.0)	0	(0.0)	3	(3.2)
Erythema	0	(0.0)	0	(0.0)	0	(0.0)	2	(2.1)
Hypersensitivity vasculitis	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Pruritus	0	(0.0)	1	(5.0)	0	(0.0)	3	(3.2)
Pruritus generalised	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Psoriasis	0	(0.0)	2	(10.0)	0	(0.0)	2	(2.1)
Rash macular	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Rash maculo-papular	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)

Subjects With Specific Adverse Events by Dose (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Psoriasis Population All Subjects as Treated

	MK-3222 0.05 mg/kg IV		MK-3222 0.1 mg/kg IV		MK-3222 0.5 mg/kg IV		MK-3222 3 mg/kg IV		MK-3222 5 mg/kg IV		MK-3222 10 mg/kg IV	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Skin and subcutaneous tissue disorders	**1**	**(16.7)**	**1**	**(16.7)**	**0**	**(0.0)**	**6**	**(28.6)**	**0**	**(0.0)**	**3**	**(17.6)**
Seborrhoeic dermatitis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Surgical and medical procedures	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(33.3)**	**1**	**(4.8)**	**0**	**(0.0)**	**1**	**(5.9)**
Endodontic procedure	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	1	(5.9)
Polypectomy	0	(0.0)	0	(0.0)	1	(33.3)	0	(0.0)	0	(0.0)	0	(0.0)
Tooth extraction	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Vascular disorders	**2**	**(33.3)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(4.8)**	**0**	**(0.0)**	**1**	**(5.9)**
Deep vein thrombosis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)
Hypertension	2	(33.3)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)
Thrombophlebitis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)

Subjects With Specific Adverse Events by Dose (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Psoriasis Population All Subjects as Treated

	MK-3222 200 mg SC		Placebo		Post-Study		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Skin and subcutaneous tissue disorders	**0**	**(0.0)**	**5**	**(25.0)**	**0**	**(0.0)**	**16**	**(16.8)**
Seborrhoeic dermatitis	0	(0.0)	1	(5.0)	0	(0.0)	1	(1.1)
Surgical and medical procedures	**0**	**(0.0)**	**1**	**(5.0)**	**0**	**(0.0)**	**4**	**(4.2)**
Endodontic procedure	0	(0.0)	0	(0.0)	0	(0.0)	2	(2.1)
Polypectomy	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Tooth extraction	0	(0.0)	1	(5.0)	0	(0.0)	1	(1.1)
Vascular disorders	**0**	**(0.0)**	**1**	**(5.0)**	**0**	**(0.0)**	**5**	**(5.3)**
Deep vein thrombosis	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Hypertension	0	(0.0)	1	(5.0)	0	(0.0)	4	(4.2)
Thrombophlebitis	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)

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: [ISSPH1: analysis-adsl] [ISSPH1: tabulations-aeplus]　SourceはSASシステム中の電子的データのため5章に含めなかった。

付録 2.7.4-15
投与群別に治験薬との因果関係を否定できない有害事象を発現した被験者（1 投与群以上で発現率 > 0%）
第 I 相試験 - 乾癬患者集団
1 回以上投与された全被験者

	MK-3222		Other		Placebo		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	75		20		20		96	
with one or more adverse events	17	(22.7)	0	(0.0)	3	(15.0)	20	(20.8)
with no adverse events	58	(77.3)	20	(100.0)	17	(85.0)	76	(79.2)
Blood and lymphatic system disorders	**1**	**(1.3)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(1.0)**
Thrombocytopenia	1	(1.3)	0	(0.0)	0	(0.0)	1	(1.0)
Gastrointestinal disorders	**1**	**(1.3)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(1.0)**
Paraesthesia oral	1	(1.3)	0	(0.0)	0	(0.0)	1	(1.0)
General disorders and administration site conditions	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(5.0)**	**1**	**(1.0)**
Fatigue	0	(0.0)	0	(0.0)	1	(5.0)	1	(1.0)
Infections and infestations	**7**	**(9.3)**	**0**	**(0.0)**	**0**	**(0.0)**	**7**	**(7.3)**
Conjunctivitis	1	(1.3)	0	(0.0)	0	(0.0)	1	(1.0)
Erysipelas	1	(1.3)	0	(0.0)	0	(0.0)	1	(1.0)
Infected dermal cyst	1	(1.3)	0	(0.0)	0	(0.0)	1	(1.0)
Nasopharyngitis	1	(1.3)	0	(0.0)	0	(0.0)	1	(1.0)
Pharyngitis streptococcal	1	(1.3)	0	(0.0)	0	(0.0)	1	(1.0)
Rhinitis	1	(1.3)	0	(0.0)	0	(0.0)	1	(1.0)
Vulvovaginal mycotic infection	1	(1.3)	0	(0.0)	0	(0.0)	1	(1.0)
Investigations	**6**	**(8.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**6**	**(6.3)**
Alanine aminotransferase increased	2	(2.7)	0	(0.0)	0	(0.0)	2	(2.1)
Aspartate aminotransferase increased	1	(1.3)	0	(0.0)	0	(0.0)	1	(1.0)

Subjects With Drug-Related Adverse Events by Treatment (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Psoriasis Population All Subjects as Treated

	MK-3222		Other		Placebo		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Investigations	**6**	**(8.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**6**	**(6.3)**
Blood bilirubin increased	1	(1.3)	0	(0.0)	0	(0.0)	1	(1.0)
Blood chloride decreased	1	(1.3)	0	(0.0)	0	(0.0)	1	(1.0)
Blood creatine phosphokinase increased	2	(2.7)	0	(0.0)	0	(0.0)	2	(2.1)
Liver function test increased	1	(1.3)	0	(0.0)	0	(0.0)	1	(1.0)
Platelet count decreased	1	(1.3)	0	(0.0)	0	(0.0)	1	(1.0)
Metabolism and nutrition disorders	**1**	**(1.3)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(1.0)**
Hypokalaemia	1	(1.3)	0	(0.0)	0	(0.0)	1	(1.0)
Musculoskeletal and connective tissue disorders	**1**	**(1.3)**	**0**	**(0.0)**	**1**	**(5.0)**	**2**	**(2.1)**
Arthralgia	1	(1.3)	0	(0.0)	1	(5.0)	2	(2.1)
Nervous system disorders	**3**	**(4.0)**	**0**	**(0.0)**	**3**	**(15.0)**	**6**	**(6.3)**
Dizziness	0	(0.0)	0	(0.0)	1	(5.0)	1	(1.0)
Headache	1	(1.3)	0	(0.0)	1	(5.0)	2	(2.1)
Hypoaesthesia	0	(0.0)	0	(0.0)	1	(5.0)	1	(1.0)
Paraesthesia	1	(1.3)	0	(0.0)	0	(0.0)	1	(1.0)
Seizure	1	(1.3)	0	(0.0)	0	(0.0)	1	(1.0)
Psychiatric disorders	**1**	**(1.3)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(1.0)**
Libido decreased	1	(1.3)	0	(0.0)	0	(0.0)	1	(1.0)

Subjects With Drug-Related Adverse Events by Treatment (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Psoriasis Population All Subjects as Treated

	MK-3222		Other		Placebo		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Respiratory, thoracic and mediastinal disorders	**1**	**(1.3)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(1.0)**
Cough	1	(1.3)	0	(0.0)	0	(0.0)	1	(1.0)
Skin and subcutaneous tissue disorders	**1**	**(1.3)**	**0**	**(0.0)**	**1**	**(5.0)**	**2**	**(2.1)**
Pruritus	1	(1.3)	0	(0.0)	0	(0.0)	1	(1.0)
Psoriasis	0	(0.0)	0	(0.0)	1	(5.0)	1	(1.0)
Vascular disorders	**1**	**(1.3)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(1.0)**
Thrombophlebitis	1	(1.3)	0	(0.0)	0	(0.0)	1	(1.0)

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.
MK-3222 includes subjects who received CYP probe on top of MK-3222 in P009.

Source: [ISSPH1: analysis-adsl] [ISSPH1: tabulations-aeplus]　SourceはSASシステム中の電子的データのため5章に含めなかった。

付録 2.7.4-16
投与量別に治験薬との因果関係を否定できない有害事象を発現した被験者（1 投与群以上で発現率 > 0%）
第 I 相試験 - 乾癬患者集団
1 回以上投与された全被験者

	MK-3222 0.05 mg/kg IV		MK-3222 0.1 mg/kg IV		MK-3222 0.5 mg/kg IV		MK-3222 3 mg/kg IV		MK-3222 5 mg/kg IV		MK-3222 10 mg/kg IV	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	6		6		3		21		3		17	
with one or more adverse events	2	(33.3)	0	(0.0)	1	(33.3)	5	(23.8)	0	(0.0)	4	(23.5)
with no adverse events	4	(66.7)	6	(100.0)	2	(66.7)	16	(76.2)	3	(100.0)	13	(76.5)
Blood and lymphatic system disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(5.9)**
Thrombocytopenia	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)
Gastrointestinal disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(4.8)**	**0**	**(0.0)**	**0**	**(0.0)**
Paraesthesia oral	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)
General disorders and administration site conditions	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**
Fatigue	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Infections and infestations	**1**	**(16.7)**	**0**	**(0.0)**	**1**	**(33.3)**	**1**	**(4.8)**	**0**	**(0.0)**	**1**	**(5.9)**
Conjunctivitis	0	(0.0)	0	(0.0)	1	(33.3)	0	(0.0)	0	(0.0)	0	(0.0)
Erysipelas	1	(16.7)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Infected dermal cyst	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Nasopharyngitis	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)
Pharyngitis streptococcal	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Rhinitis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)
Vulvovaginal mycotic infection	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

Subjects With Drug-Related Adverse Events by Dose (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Psoriasis Population All Subjects as Treated

	MK-3222 200 mg SC		Placebo		Post-Study		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	19		20		95		95	
with one or more adverse events	5	(26.3)	3	(15.0)	0	(0.0)	20	(21.1)
with no adverse events	14	(73.7)	17	(85.0)	95	(100.0)	75	(78.9)
Blood and lymphatic system disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(1.1)**
Thrombocytopenia	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Gastrointestinal disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(1.1)**
Paraesthesia oral	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
General disorders and administration site conditions	**0**	**(0.0)**	**1**	**(5.0)**	**0**	**(0.0)**	**1**	**(1.1)**
Fatigue	0	(0.0)	1	(5.0)	0	(0.0)	1	(1.1)
Infections and infestations	**3**	**(15.8)**	**0**	**(0.0)**	**0**	**(0.0)**	**7**	**(7.4)**
Conjunctivitis	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Erysipelas	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Infected dermal cyst	1	(5.3)	0	(0.0)	0	(0.0)	1	(1.1)
Nasopharyngitis	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Pharyngitis streptococcal	1	(5.3)	0	(0.0)	0	(0.0)	1	(1.1)
Rhinitis	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Vulvovaginal mycotic infection	1	(5.3)	0	(0.0)	0	(0.0)	1	(1.1)

Subjects With Drug-Related Adverse Events by Dose (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Psoriasis Population All Subjects as Treated

	MK-3222 0.05 mg/kg IV		MK-3222 0.1 mg/kg IV		MK-3222 0.5 mg/kg IV		MK-3222 3 mg/kg IV		MK-3222 5 mg/kg IV		MK-3222 10 mg/kg IV	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Investigations	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**2**	**(9.5)**	**0**	**(0.0)**	**1**	**(5.9)**
Alanine aminotransferase increased	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Aspartate aminotransferase increased	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Blood bilirubin increased	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Blood chloride decreased	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)
Blood creatine phosphokinase increased	0	(0.0)	0	(0.0)	0	(0.0)	2	(9.5)	0	(0.0)	0	(0.0)
Liver function test increased	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)
Platelet count decreased	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)
Metabolism and nutrition disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(5.9)**
Hypokalaemia	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)
Musculoskeletal and connective tissue disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(4.8)**	**0**	**(0.0)**	**0**	**(0.0)**
Arthralgia	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)
Nervous system disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(4.8)**	**0**	**(0.0)**	**1**	**(5.9)**
Dizziness	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

Subjects With Drug-Related Adverse Events by Dose (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Psoriasis Population All Subjects as Treated

	MK-3222 200 mg SC		Placebo		Post-Study		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Investigations	**3**	**(15.8)**	**0**	**(0.0)**	**0**	**(0.0)**	**6**	**(6.3)**
Alanine aminotransferase increased	2	(10.5)	0	(0.0)	0	(0.0)	2	(2.1)
Aspartate aminotransferase increased	1	(5.3)	0	(0.0)	0	(0.0)	1	(1.1)
Blood bilirubin increased	1	(5.3)	0	(0.0)	0	(0.0)	1	(1.1)
Blood chloride decreased	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Blood creatine phosphokinase increased	0	(0.0)	0	(0.0)	0	(0.0)	2	(2.1)
Liver function test increased	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Platelet count decreased	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Metabolism and nutrition disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(1.1)**
Hypokalaemia	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Musculoskeletal and connective tissue disorders	**0**	**(0.0)**	**1**	**(5.0)**	**0**	**(0.0)**	**2**	**(2.1)**
Arthralgia	0	(0.0)	1	(5.0)	0	(0.0)	2	(2.1)
Nervous system disorders	**1**	**(5.3)**	**3**	**(15.0)**	**0**	**(0.0)**	**6**	**(6.3)**
Dizziness	0	(0.0)	1	(5.0)	0	(0.0)	1	(1.1)

Subjects With Drug-Related Adverse Events by Dose (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Psoriasis Population All Subjects as Treated

	MK-3222 0.05 mg/kg IV		MK-3222 0.1 mg/kg IV		MK-3222 0.5 mg/kg IV		MK-3222 3 mg/kg IV		MK-3222 5 mg/kg IV		MK-3222 10 mg/kg IV	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Nervous system disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(4.8)**	**0**	**(0.0)**	**1**	**(5.9)**
Headache	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Hypoaesthesia	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Paraesthesia	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)
Seizure	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)
Psychiatric disorders	**1**	**(16.7)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**
Libido decreased	1	(16.7)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Respiratory, thoracic and mediastinal disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(4.8)**	**0**	**(0.0)**	**0**	**(0.0)**
Cough	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)
Skin and subcutaneous tissue disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(4.8)**	**0**	**(0.0)**	**0**	**(0.0)**
Pruritus	0	(0.0)	0	(0.0)	0	(0.0)	1	(4.8)	0	(0.0)	0	(0.0)
Psoriasis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Vascular disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(5.9)**
Thrombophlebitis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(5.9)

Subjects With Drug-Related Adverse Events by Dose (Incidence > 0% in One or More Treatment Groups)
Phase 1 Trials- Psoriasis Population All Subjects as Treated

	MK-3222 200 mg SC		Placebo		Post-Study		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Nervous system disorders	**1**	**(5.3)**	**3**	**(15.0)**	**0**	**(0.0)**	**6**	**(6.3)**
Headache	1	(5.3)	1	(5.0)	0	(0.0)	2	(2.1)
Hypoaesthesia	0	(0.0)	1	(5.0)	0	(0.0)	1	(1.1)
Paraesthesia	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Seizure	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Psychiatric disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(1.1)**
Libido decreased	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Respiratory, thoracic and mediastinal disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(1.1)**
Cough	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Skin and subcutaneous tissue disorders	**0**	**(0.0)**	**1**	**(5.0)**	**0**	**(0.0)**	**2**	**(2.1)**
Pruritus	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)
Psoriasis	0	(0.0)	1	(5.0)	0	(0.0)	1	(1.1)
Vascular disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(1.1)**
Thrombophlebitis	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.1)

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: [ISSPH1: analysis-adsl] [ISSPH1: tabulations-aeplus]　SourceはSASシステム中の電子的データのため5章に含めなかった。

付録 2.7.4-17
重篤な有害事象を発現した被験者の一覧表 第 I 相試験 - 健常人集団

Subject ID	Onset Epoch	Onset Epoch Rel Day	Adverse Event	Duration	Intensity	Serious	Related	Action Taken	Outcome
MK-3222 10 mg/kg IV									
Trial Number=3222-004, Site Number=0001, Subject ID=[redacted], Gender=M, Race=White, Age=2[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=1									
[redacted]	Treatment	4	Chikungunya virus infection	1 Weeks	Severe	Y	N	N/A	Resolved
MK-3222 50 mg SC									
Trial Number=3222-007, Site Number=0001, Subject ID=[redacted], Gender=M, Race=White, Age=2[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=1									
[redacted]	Treatment	86	Appendicitis	3 Days	Severe	Y	N	N/A	Resolved
MK-3222 400 mg SC									
Trial Number=3222-007, Site Number=0001, Subject ID=[redacted], Gender=M, Race=Asian, Age=2[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=1									
[redacted]	Treatment	63	Suicidal ideation	5 Days	Severe	Y	N	Discontinued	Resolved
Placebo									
Trial Number=3222-004, Site Number=0001, Subject ID=[redacted], Gender=F, Race=White, Age=2[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=1									
[redacted]	Treatment	72	Nasal obstruction	2.86 Weeks	Moderate	Y	N	N/A	Resolved
		72	Rhinitis	2.86 Weeks	Moderate	Y	N	N/A	Resolved
		84	Nasal septal operation	1 Days	Moderate	Y	N	N/A	Resolved

Listing of Subjects with Serious Adverse Events (Phase 1 Trials) Healthy Population

Subject ID	Onset Epoch	Onset Epoch Rel Day	Adverse Event	Duration	Intensity	Serious	Related	Action Taken	Outcome
Placebo									
Trial Number=3222-004, Site Number=0001, Subject ID=[redacted], Gender=F, Race=White, Age=2[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=1									
[redacted]	Treatment	84	Turbinectomy	1 Days	Moderate	Y	N	N/A	Resolved

Related: Investigator-assessed relationship of the adverse event to study medication. Y = RELATED, N = NOT RELATED

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

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

Source: [ISSPH1: analysis-adsl] [ISSPH1: tabulations-aeplus; explus] SourceはSASシステム中の電子的データのため5章に含めなかった。

付録 2.7.4-18
重篤な有害事象を発現した被験者の一覧表（第 I 相試験）乾癬患者集団

Subject ID	Onset Epoch	Onset Epoch Rel Day	Adverse Event	Duration	Intensity	Serious	Related	Action Taken	Outcome
MK-3222 0.05 mg/kg IV									
Trial Number=3222-001, Site Number=0005, Subject ID=[redacted], Gender=F, Race=White, Age=5[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=84									
[redacted]	Treatment	305	Upper limb fracture	3.57 Weeks	Moderate	Y	N	N/A	Resolved
Trial Number=3222-001, Site Number=0010, Subject ID=[redacted], Gender=M, Race=White, Age=4[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=85									
[redacted]	Treatment	168	Ankle fracture	2 Days	Severe	Y	N	N/A	Resolved
MK-3222 3 mg/kg IV									
Trial Number=3222-001, Site Number=0005, Subject ID=[redacted], Gender=M, Race=White, Age=6[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=57									
[redacted]	Treatment	186	Pneumothorax	1.14 Weeks	Severe	Y	N	N/A	Resolved
Trial Number=3222-001, Site Number=0006, Subject ID=[redacted], Gender=F, Race=White, Age=4[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=57									
[redacted]	Treatment	309	Skin abrasion	2 Days	Severe	Y	N	N/A	Resolved
Trial Number=3222-001, Site Number=0006, Subject ID=[redacted], Gender=F, Race=White, Age=6[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=57									
[redacted]	Treatment	4	Myocardial necrosis marker increased	5.91 Months	Severe	Y	N	N/A	Resolved
		99	Myositis	1.25 Months	Severe	Y	N	N/A	Resolved
MK-3222 10 mg/kg IV									
Trial Number=3222-001, Site Number=0002, Subject ID=[redacted], Gender=M, Race=White, Age=4[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=58									
[redacted]	Treatment	75	Seizure	1 Days	Severe	Y	Y	Discontinued	Resolved
Trial Number=3222-001, Site Number=0005, Subject ID=[redacted], Gender=M, Race=White, Age=5[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=57									

Listing of Subjects with Serious Adverse Events (Phase 1 Trials) Psoriasis Population

Subject ID	Onset Epoch	Onset Epoch Rel Day	Adverse Event	Duration	Intensity	Serious	Related	Action Taken	Outcome
MK-3222 10 mg/kg IV									
Trial Number=3222-001, Site Number=0005, Subject ID=[redacted], Gender=M, Race=White, Age=5[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=57									
[redacted]	Treatment	189	Pulmonary embolism	Continuing	Severe	Y	N	N/A	Not Resolved
		190	Pulmonary hypertension	Continuing	Severe	Y	N	N/A	Not Resolved
Trial Number=3222-001, Site Number=0006, Subject ID=[redacted], Gender=M, Race=White, Age=4[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=57									
[redacted]	Treatment	151	Facial bones fracture	3 Days	Severe	Y	N	N/A	Resolved
MK-3222 200 mg SC									
Trial Number=3222-009, Site Number=0002, Subject ID=[redacted], Gender=F, Race=White, Age=4[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=18									
[redacted]	Treatment Period 2 Day1	19	Infected dermal cyst	3 Weeks	Moderate	Y	Y	Discontinued	Resolved
Post-Study									
Trial Number=3222-001, Site Number=0006, Subject ID=[redacted], Gender=F, Race=White, Age=6[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=57									
[redacted]	Follow up	111	Cytomegalovirus infection	4.43 Weeks	Severe	Y	N	N/A	Resolved

Related: Investigator-assessed relationship of the adverse event to study medication. Y = RELATED, N = NOT RELATED

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

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

For Trial MK-3222-001, Action Taken of N/A = No Action Taken with Study Medication. Refer to study data reviewers' guide (SDRG) for details on this mapping convention

Listing of Subjects with Serious Adverse Events (Phase 1 Trials) Psoriasis Population

Subject ID	Onset Epoch	Onset Epoch Rel Day	Adverse Event	Duration	Intensity	Serious	Related	Action Taken	Outcome
MK-3222 10 mg/kg IV									
Trial Number=3222-001, Site Number=0005, Subject ID=[redacted], Gender=M, Race=White, Age=5[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=57									
[redacted]	Treatment	189	Pulmonary embolism	Continuing	Severe	Y	N	N/A	Not Resolved
		190	Pulmonary hypertension	Continuing	Severe	Y	N	N/A	Not Resolved
Trial Number=3222-001, Site Number=0006, Subject ID=[redacted], Gender=M, Race=White, Age=4[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=57									
[redacted]	Treatment	151	Facial bones fracture	3 Days	Severe	Y	N	N/A	Resolved
MK-3222 200 mg SC									
Trial Number=3222-009, Site Number=0002, Subject ID=[redacted], Gender=F, Race=White, Age=4[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=18									
[redacted]	Treatment Period 2 Day1	19	Infected dermal cyst	3 Weeks	Moderate	Y	Y	Discontinued	Resolved
Post-Study									
Trial Number=3222-001, Site Number=0006, Subject ID=[redacted], Gender=F, Race=White, Age=6[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=57									
[redacted]	Follow up	111	Cytomegalovirus infection	4.43 Weeks	Severe	Y	N	N/A	Resolved

Related: Investigator-assessed relationship of the adverse event to study medication. Y = RELATED, N = NOT RELATED

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

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

Source: [ISSPH1: analysis-adsl] [ISSPH1: tabulations-aeplus; explus] SourceはSASシステム中の電子的データのため5章に含めなかった。

付録 2.7.4-19
治験中止に至った有害事象を発現した被験者の一覧表（第 I 相試験）健常人集団

Subject ID	Onset Epoch	Onset Epoch Rel Day	Adverse Event	Duration	Intensity	Serious	Related	Action Taken	Outcome
Pre-Study									
Trial Number=3222-005, Site Number=0001, Subject ID=[redacted], Gender=F, Race=White, Age=4[redacted] Years									
[redacted]	Screening	16035	Vulvovaginal candidiasis	5 Days	Mild	N	N	Discontinued	Resolved
Trial Number=3222-005, Site Number=0001, Subject ID=[redacted], Gender=F, Race=Asian, Age=2[redacted] Years									
[redacted]	Screening	7960	Sterile pyuria	Unknown	Mild	N	N	Discontinued	
Trial Number=3222-005, Site Number=0001, Subject ID=[redacted], Gender=M, Race=Asian, Age=3[redacted] Years									
[redacted]	Screening	11798	Upper respiratory tract infection	2.29 Weeks	Mild	N	N	Discontinued	Resolved
MK-3222 400 mg SC									
Trial Number=3222-007, Site Number=0001, Subject ID=[redacted], Gender=M, Race=Asian, Age=2[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=1									
[redacted]	Treatment	63	Suicidal ideation	5 Days	Severe	Y	N	Discontinued	Resolved

Related: Investigator-assessed relationship of the adverse event to study medication. Y = RELATED, N = NOT RELATED

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

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

Source: [ISSPH1: analysis-adsl] [ISSPH1: tabulations-aeplus; explus]　SourceはSASシステム中の電子的データのため5章に含めなかった。

付録 2.7.4-20
治験中止に至った有害事象を発現した被験者の一覧表（第 I 相試験）乾癬患者集団

Subject ID	Onset Epoch	Onset Epoch Rel Day	Adverse Event	Duration	Intensity	Serious	Related	Action Taken	Outcome
MK-3222 10 mg/kg IV									
Trial Number=3222-001, Site Number=0002, Subject ID=[redacted], Gender=M, Race=White, Age=4[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=58									
[redacted]	Treatment	75	Seizure	1 Days	Severe	Y	Y	Discontinued	Resolved
MK-3222 200 mg SC									
Trial Number=3222-009, Site Number=0002, Subject ID=[redacted], Gender=F, Race=White, Age=4[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=18									
[redacted]	Treatment Period 2 Day1	19	Infected dermal cyst	3 Weeks	Moderate	Y	Y	Discontinued	Resolved
Placebo									
Trial Number=3222-001, Site Number=0009, Subject ID=[redacted], Gender=M, Race=White, Age=4[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=20									
[redacted]	Treatment	43	Arthralgia	Continuing	Moderate	N	Y	Discontinued	Not Resolved
		43	Psoriasis	Continuing	Moderate	N	Y	Discontinued	Not Resolved

Related: Investigator-assessed relationship of the adverse event to study medication. Y = RELATED, N = NOT RELATED

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

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

Source: [ISSPH1: analysis-adsl] [ISSPH1: tabulations-aeplus; explus]　SourceはSASシステム中の電子的データのため5章に含めなかった。

付録 2.7.4-21
注射部位反応を発現した被験者の一覧表（第 I 相試験）健常人集団
実際に投薬を受けた被験者（皮下投与）

Subject ID	Onset Epoch	Onset Epoch Rel Day	Adverse Event	Duration	Intensity	Serious	Related	Action Taken	Outcome
MK-3222 50 mg SC									
Trial Number=3222-007, Site Number=0001, Subject ID=[redacted], Gender=F, Race=Asian, Age=2[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=1									
[redacted]	Treatment	1	Injection site pain	1 Days	Mild	N	Y	N/A	Resolved
		2	Injection site erythema	2 Days	Mild	N	Y	N/A	Resolved
Trial Number=3222-007, Site Number=0001, Subject ID=[redacted], Gender=F, Race=Asian, Age=2[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=1									
[redacted]	Treatment	3	Injection site bruising	1.14 Weeks	Mild	N	Y	N/A	Resolved
MK-3222 200 mg SC									
Trial Number=3222-005, Site Number=0001, Subject ID=[redacted], Gender=F, Race=White, Age=2[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=1									
[redacted]	Treatment	1	Injection site bruising	2 Days	Mild	N	Y	N/A	Resolved
Trial Number=3222-007, Site Number=0001, Subject ID=[redacted], Gender=F, Race=Asian, Age=2[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=1									
[redacted]	Treatment	2	Injection site erythema	2 Days	Mild	N	Y	N/A	Resolved
		2	Injection site pain	2 Days	Mild	N	Y	N/A	Resolved
		2	Injection site pain	1.14 Weeks	Mild	N	Y	N/A	Resolved
Trial Number=3222-007, Site Number=0001, Subject ID=[redacted], Gender=F, Race=Asian, Age=2[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=1									
[redacted]	Treatment	4	Injection site bruising	1.57 Weeks	Mild	N	Y	N/A	Resolved
Trial Number=3222-007, Site Number=0001, Subject ID=[redacted], Gender=F, Race=White, Age=2[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=1									
[redacted]	Treatment	2	Injection site pain	3 Days	Mild	N	Y	N/A	Resolved
Trial Number=3222-007, Site Number=0001, Subject ID=[redacted], Gender=F, Race=White, Age=2[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=1									
[redacted]	Treatment	1	Injection site reaction	3 Days	Mild	N	Y	N/A	Resolved

Listing of Subjects With Injection Site Reaction Adverse Events (Phase 1 Trials) Healthy Population
All Subjects as Treated (Subcutaneous Administration)

Subject ID	Onset Epoch	Onset Epoch Rel Day	Adverse Event	Duration	Intensity	Serious	Related	Action Taken	Outcome
MK-3222 200 mg SC									
Trial Number=3222-007, Site Number=0001, Subject ID=[redacted], Gender=F, Race=White, Age=1[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=1									
[redacted]	Treatment	3	Injection site bruising	2 Days	Mild	N	Y	N/A	Resolved
		40	Injection site pain	2 Days	Mild	N	N	N/A	Resolved
Trial Number=3222-007, Site Number=0001, Subject ID=[redacted], Gender=F, Race=White, Age=2[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=1									
[redacted]	Treatment	2	Injection site pain	2 Days	Mild	N	Y	N/A	Resolved
		2	Injection site pain	2 Days	Mild	N	Y	N/A	Resolved
Trial Number=3222-007, Site Number=0001, Subject ID=[redacted], Gender=F, Race=Asian, Age=1[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=1									
[redacted]	Treatment	1	Injection site bruising	1.57 Weeks	Mild	N	Y	N/A	Resolved
		1	Injection site pain	1.57 Weeks	Mild	N	Y	N/A	Resolved
		1	Injection site pain	1 Days	Mild	N	Y	N/A	Resolved
Trial Number=3222-007, Site Number=0001, Subject ID=[redacted], Gender=F, Race=Asian, Age=2[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=1									
[redacted]	Treatment	7	Injection site erythema	1.86 Weeks	Mild	N	Y	N/A	Resolved
		9	Injection site erythema	1.57 Weeks	Mild	N	Y	N/A	Resolved
Trial Number=3222-007, Site Number=0001, Subject ID=[redacted], Gender=F, Race=Asian, Age=2[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=1									
[redacted]	Treatment	12	Injection site reaction	6 Days	Mild	N	Y	N/A	Resolved
		12	Injection site reaction	6 Days	Mild	N	Y	N/A	Resolved
MK-3222 400 mg SC									
Trial Number=3222-007, Site Number=0001, Subject ID=[redacted], Gender=F, Race=Asian, Age=3[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=1									
[redacted]	Treatment	2	Injection site bruising	3 Days	Mild	N	Y	N/A	Resolved

Listing of Subjects With Injection Site Reaction Adverse Events (Phase 1 Trials) Healthy Population
All Subjects as Treated (Subcutaneous Administration)

Subject ID	Onset Epoch	Onset Epoch Rel Day	Adverse Event	Duration	Intensity	Serious	Related	Action Taken	Outcome
MK-3222 400 mg SC									
Trial Number=3222-007, Site Number=0001, Subject ID=[redacted], Gender=F, Race=Asian, Age=3[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=1									
[redacted]	Treatment	2	Injection site bruising	2 Days	Mild	N	Y	N/A	Resolved
		2	Injection site erythema	2 Days	Mild	N	Y	N/A	Resolved
		2	Injection site erythema	2 Days	Mild	N	Y	N/A	Resolved
		3	Injection site bruising	2 Days	Mild	N	Y	N/A	Resolved
		3	Injection site erythema	2 Days	Mild	N	Y	N/A	Resolved
Trial Number=3222-007, Site Number=0001, Subject ID=[redacted], Gender=M, Race=Asian, Age=2[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=1									
[redacted]	Treatment	4	Injection site bruising	3.57 Weeks	Mild	N	Y	N/A	Resolved
Trial Number=3222-007, Site Number=0001, Subject ID=[redacted], Gender=M, Race=White, Age=4[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=1									
[redacted]	Treatment	3	Injection site bruising	5 Days	Mild	N	Y	N/A	Resolved
Trial Number=3222-007, Site Number=0001, Subject ID=[redacted], Gender=M, Race=White, Age=2[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=1									
[redacted]	Treatment	1	Injection site bruising	1.43 Weeks	Mild	N	Y	N/A	Resolved
Trial Number=3222-007, Site Number=0001, Subject ID=[redacted], Gender=F, Race=Asian, Age=2[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=1									
[redacted]	Treatment	2	Injection site erythema	2 Days	Mild	N	Y	N/A	Resolved
		2	Injection site pain	2 Days	Mild	N	Y	N/A	Resolved
Trial Number=3222-007, Site Number=0001, Subject ID=[redacted], Gender=M, Race=Asian, Age=2[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=1									
[redacted]	Treatment	1	Injection site bruising	1 Weeks	Mild	N	Y	N/A	Resolved
Placebo									

Listing of Subjects With Injection Site Reaction Adverse Events (Phase 1 Trials) Healthy Population
All Subjects as Treated (Subcutaneous Administration)

Subject ID	Onset Epoch	Onset Epoch Rel Day	Adverse Event	Duration	Intensity	Serious	Related	Action Taken	Outcome
Placebo									
Trial Number=3222-005, Site Number=0001, Subject ID=[redacted], Gender=M, Race=White, Age=2[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=1									
[redacted]	Treatment	1	Injection site erythema	3 Days	Mild	N	Y	N/A	Resolved
Trial Number=3222-005, Site Number=0001, Subject ID=[redacted], Gender=M, Race=White, Age=2[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=1									
[redacted]	Treatment	1	Injection site erythema	2 Days	Mild	N	Y	N/A	Resolved

Related: Investigator-assessed relationship of the adverse event to study medication. Y = RELATED, N = NOT RELATED

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

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

Source: [ISSPH1: analysis-adsl] [ISSPH1: tabulations-aeplus; explus]　SourceはSASシステム中の電子的データのため5章に含めなかった。

付録 2.7.4-22
ADA 発現有無別の注射部位反応の統合要約 第 I 相試験 - 健常人集団
実際に MK-3222 の投与を受けた被験者（皮下投与）

	Subjects in population (N1=75)		ADA Evaluable (N2=74)			
			Treatment Emergent Positive		Negative or Inconclusive	
	(n)	n/N1(%)	n1	n1/N2 (%)	n2	n2/N2(%)
Subjects in population	75	100.0	8	10.8	57	77.0
Adverse Event Category			n	n/n1 (%)	n	n/n2 (%)
with one or more adverse events	18	24.0	3	37.5	13	22.8
with no adverse event	57	76.0	5	62.5	44	77.2
with drug-related adverse events	18	24.0	3	37.5	13	22.8
with serious adverse events	0	0.0	0	0.0	0	0.0
with serious drug-related adverse events	0	0.0	0	0.0	0	0.0
who died	0	0.0	0	0.0	0	0.0
discontinued due to an adverse event	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
discontinued due to a serious adverse event	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

Subjects in Population (N1) = Subjects treated with MK-3222

ADA Evaluable (N2) = Subjects evaluable for immunogenicity (ADA=anti-drug antibody) analysis are those with one or more samples obtained after MK-3222 administration.

Treatment emergent positive (n1) = subjects who had a negative pre-treatment (baseline) sample and at least 1 (treatment induced) positive post-dose sample and subjects who had a positive pre-treatment and post-dose samples in which the titer increased post-dose by >= 2-fold (treatment boosted positive).

Negative = subjects who had negative pre-treatment and post-dose samples with the MK-3222 concentration in the last post-dose sample below the drug tolerance limit for the ADA assay

Inconclusive = subjects who had negative pre-treatment and post-dose samples with the MK-3222 concentration in the last post-dose sample equal to or above the drug tolerance limit for the ADA assay.

Negative and inconclusive subjects combined= n2.

Non-treatment emergent positive subjects are not reported.

Source: [ISSV01: analysis-adsl; adpada01] [ISSV01: tabulations-aeplus]　SourceはSASシステム中の電子的データのため5章に含めなかった。

付録 2.7.4-23
ADA 発現有無別の有害事象の要約 第 I 相試験 - 健常人集団
実際に MK-3222 の投与を受けた被験者

	Subjects in Population (N=103)		ADA Evaluable (N2=101)			
			Treatment Emergent Positive		Negative or Inconclusive	
	(n)	n/N1(%)	n1	n1/N2 (%)	n2	n2/N2(%)
Subjects in population	103	100.0	10	9.9	79	78.2
Adverse Event Category			n	n/n1 (%)	n	n/n2 (%)
with one or more adverse events	85	82.5	9	90.0	64	81.0
with no adverse event	18	17.5	1	10.0	15	19.0
with drug-related adverse events	34	33.0	3	30.0	28	35.4
with serious adverse events	3	2.9	1	10.0	1	1.3
with serious drug-related adverse events	0	0.0	0	0.0	0	0.0
who died	0	0.0	0	0.0	0	0.0
discontinued due to an adverse event	1	1.0	0	0.0	0	0.0
discontinued due to a drug-related adverse event	0	0.0	0	0.0	0	0.0
discontinued due to a serious adverse event	1	1.0	0	0.0	0	0.0
discontinued due to a serious drug-related adverse event	0	0.0	0	0.0	0	0.0

Subjects in Population (N1) = Subjects treated with MK-3222

ADA Evaluable (N2) = Subjects evaluable for immunogenicity (ADA=anti-drug antibody) analysis are those with one or more samples obtained after MK-3222 administration.

Treatment emergent positive (n1) = subjects who had a negative pre-treatment (baseline) sample and at least 1 (treatment induced) positive post-dose sample and subjects who had a positive pre-treatment and post-dose samples in which the titer increased post-dose by >= 2-fold (treatment boosted positive).

Negative = subjects who had negative pre-treatment and post-dose samples with the MK-3222 concentration in the last post-dose sample below the drug tolerance limit for the ADA assay

Inconclusive = subjects who had negative pre-treatment and post-dose samples with the MK-3222 concentration in the last post-dose sample equal to or above the drug tolerance limit for the ADA assay.

Negative and inconclusive subjects combined= n2.

Non-treatment emergent positive subjects are not reported.

Source: [ISSV01: analysis-adsl; adpada01] [ISSV01: tabulations-aeplus] SourceはSASシステム中の電子的データのため5章に含めなかった。

付録 2.7.4-24
ADA 発現有無別の有害事象の要約 第 I 相試験 - 乾癬患者集団
MK-3222 の投与を 1 回以上受けた被験者

	Subjects in Population (N1=75)		ADA Evaluable (N2=75)			
			Treatment Emergent Positive		Negative or Inconclusive	
	(n)	n/N1(%)	n1	n1/N2 (%)	n2	n2/N2(%)
Subjects in population	75	100.0	10	13.3	59	78.7
Adverse Event Category			n	n/n1 (%)	n	n/n2 (%)
with one or more adverse events	58	77.3	8	80.0	45	76.3
with no adverse event	17	22.7	2	20.0	14	23.7
with drug-related adverse events	17	22.7	3	30.0	13	22.0
with serious adverse events	9	12.0	1	10.0	7	11.9
with serious drug-related adverse events	2	2.7	0	0.0	2	3.4
who died	0	0.0	0	0.0	0	0.0
discontinued due to an adverse event	2	2.7	0	0.0	2	3.4
discontinued due to a drug-related adverse event	2	2.7	0	0.0	2	3.4
discontinued due to a serious adverse event	2	2.7	0	0.0	2	3.4
discontinued due to a serious drug-related adverse event	2	2.7	0	0.0	2	3.4

Subjects in Population (N1) = Subjects treated with MK-3222

ADA Evaluable (N2) = Subjects evaluable for immunogenicity (ADA=anti-drug antibody) analysis are those with one or more samples obtained after MK-3222 administration.

Treatment emergent positive (n1) = subjects who had a negative pre-treatment (baseline) sample and at least 1 (treatment induced) positive post-dose sample and subjects who had a positive pre-treatment and post-dose samples in which the titer increased post-dose by >= 2-fold (treatment boosted positive).

Negative = subjects who had negative pre-treatment and post-dose samples with the MK-3222 concentration in the last post-dose sample below the drug tolerance limit for the ADA assay

Inconclusive = subjects who had negative pre-treatment and post-dose samples with the MK-3222 concentration in the last post-dose sample equal to or above the drug tolerance limit for the ADA assay.

Negative and inconclusive subjects combined= n2.

Non-treatment emergent positive subjects are not reported.

MK-3222 includes subjects who received CYP probe on top of MK-3222 in P009.

Source: [ISSV01: analysis-adsl; adpada01] [ISSV01: tabulations-aeplus] SourceはSASシステム中の電子的データのため5章に含めなかった。

付録 2.7.4-25
有害事象の要約
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 100mg		MK-3222 200mg		MK-3222 100 / 200 mg		Etanercept 50mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	310		616		622		1,238		313	
with one or more adverse events	160	(51.6)	282	(45.8)	285	(45.8)	567	(45.8)	169	(54.0)
with no adverse event	150	(48.4)	334	(54.2)	337	(54.2)	671	(54.2)	144	(46.0)
with drug-related† adverse events	37	(11.9)	82	(13.3)	82	(13.2)	164	(13.2)	92	(29.4)
with serious adverse events	5	(1.6)	9	(1.5)	14	(2.3)	23	(1.9)	7	(2.2)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	2	(0.3)	2	(0.2)	2	(0.6)
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)	3	(0.5)	8	(1.3)	11	(0.9)	6	(1.9)
discontinued due to a drug-related adverse event	1	(0.3)	1	(0.2)	2	(0.3)	3	(0.2)	4	(1.3)
discontinued due to a serious adverse event	0	(0.0)	1	(0.2)	4	(0.6)	5	(0.4)	2	(0.6)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)

† Determined by the investigator to be related to the drug.
‡ Study medication withdrawn.
[Source: 5.3.5.3-10]

付録 2.7.4-26
有害事象発現被験者 (1 投与群以上で発現率 ≥ 1%)
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 100mg		MK-3222 200mg		MK-3222 100 / 200 mg		Etanercept 50mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	355		705		708		1,413		313	
with one or more adverse events	191	(53.8)	340	(48.2)	339	(47.9)	679	(48.1)	169	(54.0)
with no adverse events	164	(46.2)	365	(51.8)	369	(52.1)	734	(51.9)	144	(46.0)
Cardiac disorders	**7**	**(2.0)**	**9**	**(1.3)**	**4**	**(0.6)**	**13**	**(0.9)**	**6**	**(1.9)**
Ear and labyrinth disorders	**5**	**(1.4)**	**3**	**(0.4)**	**4**	**(0.6)**	**7**	**(0.5)**	**2**	**(0.6)**
Eye disorders	**2**	**(0.6)**	**8**	**(1.1)**	**9**	**(1.3)**	**17**	**(1.2)**	**2**	**(0.6)**
Gastrointestinal disorders	**19**	**(5.4)**	**45**	**(6.4)**	**50**	**(7.1)**	**95**	**(6.7)**	**21**	**(6.7)**
Diarrhoea	5	(1.4)	13	(1.8)	10	(1.4)	23	(1.6)	4	(1.3)
Nausea	3	(0.8)	7	(1.0)	11	(1.6)	18	(1.3)	1	(0.3)
General disorders and administration site conditions	**30**	**(8.5)**	**61**	**(8.7)**	**48**	**(6.8)**	**109**	**(7.7)**	**65**	**(20.8)**
Fatigue	6	(1.7)	17	(2.4)	7	(1.0)	24	(1.7)	4	(1.3)
Injection site bruising	0	(0.0)	3	(0.4)	3	(0.4)	6	(0.4)	3	(1.0)
Injection site erythema	1	(0.3)	4	(0.6)	3	(0.4)	7	(0.5)	27	(8.6)
Injection site haematoma	1	(0.3)	2	(0.3)	5	(0.7)	7	(0.5)	4	(1.3)
Injection site pain	3	(0.8)	10	(1.4)	9	(1.3)	19	(1.3)	10	(3.2)
Injection site pruritus	0	(0.0)	1	(0.1)	4	(0.6)	5	(0.4)	4	(1.3)
Injection site reaction	1	(0.3)	2	(0.3)	2	(0.3)	4	(0.3)	14	(4.5)
Injection site swelling	2	(0.6)	3	(0.4)	3	(0.4)	6	(0.4)	7	(2.2)

Subjects With Adverse Events (Incidence ≥ 1% in One or More Treatment Groups)
Phase 2 and 3: Placebo-Controlled Safety Pool
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100 / 200 mg		Etanercept 50mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
General disorders and administration site conditions	**30**	**(8.5)**	**61**	**(8.7)**	**48**	**(6.8)**	**109**	**(7.7)**	**65**	**(20.8)**
Oedema peripheral	4	(1.1)	0	(0.0)	2	(0.3)	2	(0.1)	1	(0.3)
Pyrexia	5	(1.4)	5	(0.7)	3	(0.4)	8	(0.6)	2	(0.6)
Infections and infestations	**80**	**(22.5)**	**160**	**(22.7)**	**155**	**(21.9)**	**315**	**(22.3)**	**74**	**(23.6)**
Bronchitis	4	(1.1)	5	(0.7)	5	(0.7)	10	(0.7)	0	(0.0)
Gastroenteritis	4	(1.1)	8	(1.1)	13	(1.8)	21	(1.5)	6	(1.9)
Hordeolum	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)	5	(1.6)
Influenza	7	(2.0)	6	(0.9)	6	(0.8)	12	(0.8)	0	(0.0)
Nasopharyngitis	29	(8.2)	78	(11.1)	66	(9.3)	144	(10.2)	36	(11.5)
Oral herpes	1	(0.3)	4	(0.6)	1	(0.1)	5	(0.4)	3	(1.0)
Rhinitis	2	(0.6)	5	(0.7)	4	(0.6)	9	(0.6)	3	(1.0)
Sinusitis	5	(1.4)	11	(1.6)	12	(1.7)	23	(1.6)	1	(0.3)
Tooth infection	1	(0.3)	2	(0.3)	1	(0.1)	3	(0.2)	4	(1.3)
Upper respiratory tract infection	10	(2.8)	13	(1.8)	21	(3.0)	34	(2.4)	5	(1.6)
Urinary tract infection	5	(1.4)	7	(1.0)	4	(0.6)	11	(0.8)	5	(1.6)
Injury, poisoning and procedural complications	**18**	**(5.1)**	**30**	**(4.3)**	**35**	**(4.9)**	**65**	**(4.6)**	**10**	**(3.2)**
Accidental overdose	2	(0.6)	4	(0.6)	6	(0.8)	10	(0.7)	3	(1.0)
Investigations	**13**	**(3.7)**	**25**	**(3.5)**	**17**	**(2.4)**	**42**	**(3.0)**	**7**	**(2.2)**

Subjects With Adverse Events (Incidence ≥ 1% in One or More Treatment Groups)
Phase 2 and 3: Placebo-Controlled Safety Pool
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100 / 200 mg		Etanercept 50mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Metabolism and nutrition disorders	**4**	**(1.1)**	**10**	**(1.4)**	**9**	**(1.3)**	**19**	**(1.3)**	**2**	**(0.6)**
Musculoskeletal and connective tissue disorders	**23**	**(6.5)**	**44**	**(6.2)**	**58**	**(8.2)**	**102**	**(7.2)**	**18**	**(5.8)**
Arthralgia	7	(2.0)	15	(2.1)	9	(1.3)	24	(1.7)	6	(1.9)
Back pain	4	(1.1)	9	(1.3)	12	(1.7)	21	(1.5)	4	(1.3)
Pain in extremity	2	(0.6)	7	(1.0)	6	(0.8)	13	(0.9)	2	(0.6)
Psoriatic arthropathy	4	(1.1)	3	(0.4)	3	(0.4)	6	(0.4)	0	(0.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**1**	**(0.3)**	**7**	**(1.0)**	**3**	**(0.4)**	**10**	**(0.7)**	**3**	**(1.0)**
Nervous system disorders	**21**	**(5.9)**	**47**	**(6.7)**	**57**	**(8.1)**	**104**	**(7.4)**	**27**	**(8.6)**
Dizziness	0	(0.0)	5	(0.7)	10	(1.4)	15	(1.1)	6	(1.9)
Headache	13	(3.7)	26	(3.7)	30	(4.2)	56	(4.0)	15	(4.8)
Psychiatric disorders	**3**	**(0.8)**	**13**	**(1.8)**	**14**	**(2.0)**	**27**	**(1.9)**	**5**	**(1.6)**
Insomnia	2	(0.6)	4	(0.6)	7	(1.0)	11	(0.8)	2	(0.6)
Renal and urinary disorders	**5**	**(1.4)**	**10**	**(1.4)**	**7**	**(1.0)**	**17**	**(1.2)**	**1**	**(0.3)**
Reproductive system and breast disorders	**2**	**(0.6)**	**8**	**(1.1)**	**7**	**(1.0)**	**15**	**(1.1)**	**1**	**(0.3)**

Subjects With Adverse Events (Incidence ≥ 1% in One or More Treatment Groups)
Phase 2 and 3: Placebo-Controlled Safety Pool
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100 / 200 mg		Etanercept 50mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Respiratory, thoracic and mediastinal disorders	**18**	**(5.1)**	**34**	**(4.8)**	**40**	**(5.6)**	**74**	**(5.2)**	**19**	**(6.1)**
Cough	8	(2.3)	13	(1.8)	18	(2.5)	31	(2.2)	5	(1.6)
Nasal congestion	2	(0.6)	2	(0.3)	2	(0.3)	4	(0.3)	3	(1.0)
Oropharyngeal pain	5	(1.4)	7	(1.0)	7	(1.0)	14	(1.0)	5	(1.6)
Skin and subcutaneous tissue disorders	**42**	**(11.8)**	**40**	**(5.7)**	**44**	**(6.2)**	**84**	**(5.9)**	**17**	**(5.4)**
Pruritus	13	(3.7)	12	(1.7)	13	(1.8)	25	(1.8)	9	(2.9)
Psoriasis	14	(3.9)	4	(0.6)	1	(0.1)	5	(0.4)	2	(0.6)
Vascular disorders	**9**	**(2.5)**	**11**	**(1.6)**	**13**	**(1.8)**	**24**	**(1.7)**	**9**	**(2.9)**
Haematoma	2	(0.6)	1	(0.1)	2	(0.3)	3	(0.2)	4	(1.3)
Hypertension	5	(1.4)	6	(0.9)	8	(1.1)	14	(1.0)	3	(1.0)

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: 5.3.5.3-10]

付録 2.7.4-27
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 投与群以上で発現率 > 0%）
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 100mg		MK-3222 200mg		MK-3222 100 / 200 mg		Etanercept 50mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	310		616		622		1,238		313	
with one or more drug-related adverse events	37	(11.9)	82	(13.3)	82	(13.2)	164	(13.2)	92	(29.4)
with no drug-related adverse events	273	(88.1)	534	(86.7)	540	(86.8)	1,074	(86.8)	221	(70.6)
Blood and lymphatic system disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.3)**
Leukopenia	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)
Cardiac disorders	**2**	**(0.6)**	**2**	**(0.3)**	**0**	**(0.0)**	**2**	**(0.2)**	**1**	**(0.3)**
Palpitations	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Sinus arrhythmia	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
Tachycardia	1	(0.3)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
Ventricular extrasystoles	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)
Ear and labyrinth disorders	**1**	**(0.3)**	**0**	**(0.0)**	**1**	**(0.2)**	**1**	**(0.1)**	**0**	**(0.0)**
Vertigo	1	(0.3)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Eye disorders	**0**	**(0.0)**	**2**	**(0.3)**	**1**	**(0.2)**	**3**	**(0.2)**	**1**	**(0.3)**
Eczema eyelids	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Eye pain	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)
Eye swelling	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
Xerophthalmia	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
Gastrointestinal disorders	**1**	**(0.3)**	**9**	**(1.5)**	**7**	**(1.1)**	**16**	**(1.3)**	**5**	**(1.6)**
Abdominal distension	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)
Abdominal pain	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)

Subjects With Drug-Related Adverse Events (Incidence > 0% in One or More Treatment Groups)
Phase 3: Placebo-Controlled Safety Pool
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100 / 200 mg		Etanercept 50mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Gastrointestinal disorders	**1**	**(0.3)**	**9**	**(1.5)**	**7**	**(1.1)**	**16**	**(1.3)**	**5**	**(1.6)**
Abdominal pain upper	0	(0.0)	1	(0.2)	2	(0.3)	3	(0.2)	1	(0.3)
Constipation	1	(0.3)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
Diarrhoea	0	(0.0)	3	(0.5)	2	(0.3)	5	(0.4)	3	(1.0)
Dry mouth	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Dyspepsia	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Faeces soft	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
Gingival pain	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)
Lip dry	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
Nausea	0	(0.0)	2	(0.3)	3	(0.5)	5	(0.4)	1	(0.3)
Toothache	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
Vomiting	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
General disorders and administration site conditions	**15**	**(4.8)**	**28**	**(4.5)**	**27**	**(4.3)**	**55**	**(4.4)**	**57**	**(18.2)**
Asthenia	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Chest pain	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Chills	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)
Fatigue	3	(1.0)	7	(1.1)	2	(0.3)	9	(0.7)	2	(0.6)
Feeling cold	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Feeling hot	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Impaired healing	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
Injection site bruising	0	(0.0)	2	(0.3)	2	(0.3)	4	(0.3)	2	(0.6)
Injection site discomfort	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)
Injection site erythema	1	(0.3)	3	(0.5)	3	(0.5)	6	(0.5)	26	(8.3)
Injection site haematoma	1	(0.3)	2	(0.3)	5	(0.8)	7	(0.6)	3	(1.0)

Subjects With Drug-Related Adverse Events (Incidence > 0% in One or More Treatment Groups)
Phase 3: Placebo-Controlled Safety Pool
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100 / 200 mg		Etanercept 50mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
General disorders and administration site conditions	**15**	**(4.8)**	**28**	**(4.5)**	**27**	**(4.3)**	**55**	**(4.4)**	**57**	**(18.2)**
Injection site haemorrhage	0	(0.0)	1	(0.2)	2	(0.3)	3	(0.2)	1	(0.3)
Injection site inflammation	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Injection site oedema	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)
Injection site pain	3	(1.0)	10	(1.6)	5	(0.8)	15	(1.2)	10	(3.2)
Injection site papule	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)
Injection site pruritus	0	(0.0)	1	(0.2)	3	(0.5)	4	(0.3)	4	(1.3)
Injection site reaction	1	(0.3)	2	(0.3)	2	(0.3)	4	(0.3)	14	(4.5)
Injection site swelling	2	(0.6)	1	(0.2)	3	(0.5)	4	(0.3)	7	(2.2)
Injection site urticaria	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
Malaise	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
Oedema peripheral	1	(0.3)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Peripheral swelling	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Pyrexia	1	(0.3)	1	(0.2)	1	(0.2)	2	(0.2)	0	(0.0)
Hepatobiliary disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.3)**
Bile duct stone	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)
Infections and infestations	**14**	**(4.5)**	**32**	**(5.2)**	**34**	**(5.5)**	**66**	**(5.3)**	**29**	**(9.3)**
Abscess neck	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Bronchitis	0	(0.0)	1	(0.2)	1	(0.2)	2	(0.2)	0	(0.0)
Cellulitis	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
Cervicitis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)
Conjunctivitis	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
Diarrhoea infectious	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

Subjects With Drug-Related Adverse Events (Incidence > 0% in One or More Treatment Groups)
Phase 3: Placebo-Controlled Safety Pool
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100 / 200 mg		Etanercept 50mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Infections and infestations	**14**	**(4.5)**	**32**	**(5.2)**	**34**	**(5.5)**	**66**	**(5.3)**	**29**	**(9.3)**
Epiglottitis	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Folliculitis	0	(0.0)	1	(0.2)	1	(0.2)	2	(0.2)	0	(0.0)
Furuncle	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)
Gangrene	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Gastroenteritis	1	(0.3)	1	(0.2)	1	(0.2)	2	(0.2)	3	(1.0)
Gastrointestinal infection	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)
Gingival abscess	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
Gingivitis	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	1	(0.3)
Herpes simplex	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Hordeolum	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)
Influenza	1	(0.3)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
Myringitis	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Nasopharyngitis	4	(1.3)	20	(3.2)	12	(1.9)	32	(2.6)	15	(4.8)
Oral herpes	1	(0.3)	1	(0.2)	1	(0.2)	2	(0.2)	1	(0.3)
Papilloma viral infection	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
Pharyngitis	1	(0.3)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
Pulpitis dental	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Rash pustular	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Rhinitis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.6)
Sialoadenitis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)
Sinusitis	2	(0.6)	1	(0.2)	5	(0.8)	6	(0.5)	0	(0.0)
Skin candida	0	(0.0)	1	(0.2)	1	(0.2)	2	(0.2)	0	(0.0)
Skin infection	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Tinea pedis	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Tooth abscess	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)

Subjects With Drug-Related Adverse Events (Incidence > 0% in One or More Treatment Groups)
Phase 3: Placebo-Controlled Safety Pool
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100 / 200 mg		Etanercept 50mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Infections and infestations	**14**	**(4.5)**	**32**	**(5.2)**	**34**	**(5.5)**	**66**	**(5.3)**	**29**	**(9.3)**
Tooth infection	0	(0.0)	1	(0.2)	1	(0.2)	2	(0.2)	2	(0.6)
Upper respiratory tract infection	3	(1.0)	1	(0.2)	5	(0.8)	6	(0.5)	2	(0.6)
Urinary tract infection	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	1	(0.3)
Wound infection	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Injury, poisoning and procedural complications	**0**	**(0.0)**	**0**	**(0.0)**	**2**	**(0.3)**	**2**	**(0.2)**	**0**	**(0.0)**
Contusion	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Injection related reaction	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Investigations	**1**	**(0.3)**	**8**	**(1.3)**	**3**	**(0.5)**	**11**	**(0.9)**	**2**	**(0.6)**
Alanine aminotransferase increased	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.2)	1	(0.3)
Aspartate aminotransferase increased	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.2)	0	(0.0)
Blood triglycerides increased	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
Blood urine present	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
C-reactive protein increased	0	(0.0)	1	(0.2)	1	(0.2)	2	(0.2)	0	(0.0)
ECG signs of myocardial ischaemia	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Electrocardiogram abnormal	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Gamma-glutamyltransferase increased	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.2)	0	(0.0)
Hepatic enzyme increased	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
Liver function test increased	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Weight increased	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)
Metabolism and nutrition disorders	**0**	**(0.0)**	**0**	**(0.0)**	**2**	**(0.3)**	**2**	**(0.2)**	**0**	**(0.0)**
Decreased appetite	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)

Subjects With Drug-Related Adverse Events (Incidence > 0% in One or More Treatment Groups)
Phase 3: Placebo-Controlled Safety Pool
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100 / 200 mg		Etanercept 50mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Metabolism and nutrition disorders	**0**	**(0.0)**	**0**	**(0.0)**	**2**	**(0.3)**	**2**	**(0.2)**	**0**	**(0.0)**
Diabetes mellitus	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Musculoskeletal and connective tissue disorders	**3**	**(1.0)**	**5**	**(0.8)**	**3**	**(0.5)**	**8**	**(0.6)**	**1**	**(0.3)**
Arthralgia	2	(0.6)	2	(0.3)	1	(0.2)	3	(0.2)	1	(0.3)
Back pain	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	1	(0.3)
Joint swelling	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
Pain in extremity	1	(0.3)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
Psoriatic arthropathy	0	(0.0)	1	(0.2)	1	(0.2)	2	(0.2)	0	(0.0)
Nervous system disorders	**2**	**(0.6)**	**9**	**(1.5)**	**13**	**(2.1)**	**22**	**(1.8)**	**11**	**(3.5)**
Dizziness	0	(0.0)	1	(0.2)	2	(0.3)	3	(0.2)	4	(1.3)
Dysgeusia	0	(0.0)	1	(0.2)	2	(0.3)	3	(0.2)	0	(0.0)
Headache	1	(0.3)	7	(1.1)	8	(1.3)	15	(1.2)	5	(1.6)
Hyperaesthesia	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Lethargy	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)
Paraesthesia	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Presyncope	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)
Psychiatric disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**3**	**(1.0)**
Depression	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)
Insomnia	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)
Sleep disorder	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)
Renal and urinary disorders	**0**	**(0.0)**	**2**	**(0.3)**	**0**	**(0.0)**	**2**	**(0.2)**	**0**	**(0.0)**

Subjects With Drug-Related Adverse Events (Incidence > 0% in One or More Treatment Groups)
Phase 3: Placebo-Controlled Safety Pool
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100 / 200 mg		Etanercept 50mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Renal and urinary disorders	**0**	**(0.0)**	**2**	**(0.3)**	**0**	**(0.0)**	**2**	**(0.2)**	**0**	**(0.0)**
Proteinuria	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.2)	0	(0.0)
Reproductive system and breast disorders	**0**	**(0.0)**	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**	**0**	**(0.0)**
Erection increased	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
Respiratory, thoracic and mediastinal disorders	**3**	**(1.0)**	**4**	**(0.6)**	**5**	**(0.8)**	**9**	**(0.7)**	**6**	**(1.9)**
Cough	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	2	(0.6)
Dysphonia	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
Dyspnoea exertional	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Epistaxis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)
Nasal congestion	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)
Oropharyngeal pain	1	(0.3)	2	(0.3)	3	(0.5)	5	(0.4)	0	(0.0)
Paranasal sinus hypersecretion	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Respiratory disorder	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Rhinitis allergic	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)
Rhinorrhoea	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)
Skin and subcutaneous tissue disorders	**2**	**(0.6)**	**10**	**(1.6)**	**13**	**(2.1)**	**23**	**(1.9)**	**10**	**(3.2)**
Acne	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	2	(0.6)
Alopecia	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
Angioedema	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Dermatitis	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Ecchymosis	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
Eczema	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.2)	0	(0.0)

Subjects With Drug-Related Adverse Events (Incidence > 0% in One or More Treatment Groups)
Phase 3: Placebo-Controlled Safety Pool
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100 / 200 mg		Etanercept 50mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Skin and subcutaneous tissue disorders	**2**	**(0.6)**	**10**	**(1.6)**	**13**	**(2.1)**	**23**	**(1.9)**	**10**	**(3.2)**
Erythema	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	2	(0.6)
Hyperhidrosis	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.2)	1	(0.3)
Neurodermatitis	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Night sweats	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	1	(0.3)
Pruritus	0	(0.0)	1	(0.2)	5	(0.8)	6	(0.5)	7	(2.2)
Pruritus generalised	0	(0.0)	1	(0.2)	1	(0.2)	2	(0.2)	0	(0.0)
Psoriasis	1	(0.3)	1	(0.2)	1	(0.2)	2	(0.2)	0	(0.0)
Rash	0	(0.0)	2	(0.3)	1	(0.2)	3	(0.2)	0	(0.0)
Rash papulosquamous	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Skin atrophy	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
Skin burning sensation	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Skin swelling	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Skin tightness	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Urticaria	1	(0.3)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Vascular disorders	**3**	**(1.0)**	**2**	**(0.3)**	**1**	**(0.2)**	**3**	**(0.2)**	**1**	**(0.3)**
Flushing	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
Haematoma	1	(0.3)	1	(0.2)	0	(0.0)	1	(0.1)	1	(0.3)
Hot flush	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Hypertension	1	(0.3)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)

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: 5.3.5.3-10]

付録 2.7.4-28
重篤な有害事象発現被験者（1 投与群以上で発現率 > 0%）
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 100mg		MK-3222 200mg		MK-3222 100 / 200 mg		Etanercept 50mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	310		616		622		1,238		313	
with one or more serious adverse events	5	(1.6)	9	(1.5)	14	(2.3)	23	(1.9)	7	(2.2)
with no serious adverse events	305	(98.4)	607	(98.5)	608	(97.7)	1,215	(98.1)	306	(97.8)
Cardiac disorders	**1**	**(0.3)**	**2**	**(0.3)**	**3**	**(0.5)**	**5**	**(0.4)**	**2**	**(0.6)**
Acute myocardial infarction	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
Atrial fibrillation	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Cardiac failure congestive	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)
Cardiomyopathy alcoholic	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
Coronary artery disease	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Coronary artery stenosis	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)
Pericarditis	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Tachycardia	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Gastrointestinal disorders	**0**	**(0.0)**	**1**	**(0.2)**	**3**	**(0.5)**	**4**	**(0.3)**	**0**	**(0.0)**
Abdominal hernia	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Oesophageal polyp	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
Pancreatitis acute	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Salivary gland enlargement	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Hepatobiliary disorders	**0**	**(0.0)**	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**	**1**	**(0.3)**
Bile duct stone	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)
Steatohepatitis	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
Infections and infestations	**1**	**(0.3)**	**1**	**(0.2)**	**2**	**(0.3)**	**3**	**(0.2)**	**0**	**(0.0)**
Cellulitis	1	(0.3)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)

Subjects With Serious Adverse Events (Incidence > 0% in One or More Treatment Groups)
Phase 3: Placebo-Controlled Safety Pool
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100 / 200 mg		Etanercept 50mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Infections and infestations	**1**	**(0.3)**	**1**	**(0.2)**	**2**	**(0.3)**	**3**	**(0.2)**	**0**	**(0.0)**
Epiglottitis	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Wound infection	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Musculoskeletal and connective tissue disorders	**1**	**(0.3)**	**0**	**(0.0)**	**1**	**(0.2)**	**1**	**(0.1)**	**1**	**(0.3)**
Intervertebral disc protrusion	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Osteoarthritis	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Rotator cuff syndrome	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**0**	**(0.0)**	**1**	**(0.2)**	**1**	**(0.2)**	**2**	**(0.2)**	**1**	**(0.3)**
Basal cell carcinoma	0	(0.0)	1	(0.2)	1	(0.2)	2	(0.2)	1	(0.3)
Nervous system disorders	**1**	**(0.3)**	**0**	**(0.0)**	**1**	**(0.2)**	**1**	**(0.1)**	**2**	**(0.6)**
Carotid artery stenosis	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Headache	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)
Presyncope	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Seizure	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)
Pregnancy, puerperium and perinatal conditions	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.2)**	**1**	**(0.1)**	**0**	**(0.0)**
Abortion spontaneous	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Psychiatric disorders	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.2)**	**1**	**(0.1)**	**0**	**(0.0)**
Suicide attempt	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)

Subjects With Serious Adverse Events (Incidence > 0% in One or More Treatment Groups)
Phase 3: Placebo-Controlled Safety Pool
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100 / 200 mg		Etanercept 50mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Renal and urinary disorders	**1**	**(0.3)**	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**	**0**	**(0.0)**
Nephrolithiasis	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
Ureterolithiasis	1	(0.3)	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
Respiratory, thoracic and mediastinal disorders	**0**	**(0.0)**	**1**	**(0.2)**	**1**	**(0.2)**	**2**	**(0.2)**	**0**	**(0.0)**
Chronic obstructive pulmonary disease	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Pneumothorax	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
Skin and subcutaneous tissue disorders	**0**	**(0.0)**	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**	**0**	**(0.0)**
Psoriasis	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
Vascular disorders	**0**	**(0.0)**	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**	**0**	**(0.0)**
Peripheral arterial occlusive disease	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)

Every subject is counted a single time for each applicable row and column.
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[Source: 5.3.5.3-10]

付録 2.7.4-29
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 投与群以上で発現率 > 0%）
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 100mg		MK-3222 200mg		MK-3222 100 / 200 mg		Etanercept 50mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	310		616		622		1,238		313	
with one or more serious and drug-related adverse events	0	(0.0)	0	(0.0)	2	(0.3)	2	(0.2)	2	(0.6)
with no serious and drug-related adverse events	310	(100.0)	616	(100.0)	620	(99.7)	1,236	(99.8)	311	(99.4)
Hepatobiliary disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.3)**
Bile duct stone	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)
Infections and infestations	**0**	**(0.0)**	**0**	**(0.0)**	**2**	**(0.3)**	**2**	**(0.2)**	**0**	**(0.0)**
Epiglottitis	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Wound infection	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Nervous system disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.3)**
Headache	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(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: 5.3.5.3-10]

付録 2.7.4-30
治験中止に至った重篤な有害事象発現被験者（1 投与群以上で発現率 > 0%）
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 100mg		MK-3222 200mg		MK-3222 100 / 200 mg		Etanercept 50mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	310		616		622		1,238		313	
with one or more serious adverse events leading to discontinuation	0	(0.0)	1	(0.2)	4	(0.6)	5	(0.4)	2	(0.6)
with no serious adverse events leading to discontinuation	310	(100.0)	615	(99.8)	618	(99.4)	1,233	(99.6)	311	(99.4)
Cardiac disorders	**0**	**(0.0)**	**1**	**(0.2)**	**2**	**(0.3)**	**3**	**(0.2)**	**0**	**(0.0)**
Atrial fibrillation	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Cardiomyopathy alcoholic	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
Coronary artery disease	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Hepatobiliary disorders	**0**	**(0.0)**	**1**	**(0.2)**	**0**	**(0.0)**	**1**	**(0.1)**	**0**	**(0.0)**
Steatohepatitis	0	(0.0)	1	(0.2)	0	(0.0)	1	(0.1)	0	(0.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.3)**
Basal cell carcinoma	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)
Nervous system disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.3)**
Headache	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)	1	(0.3)
Psychiatric disorders	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.2)**	**1**	**(0.1)**	**0**	**(0.0)**
Suicide attempt	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)
Respiratory, thoracic and mediastinal disorders	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.2)**	**1**	**(0.1)**	**0**	**(0.0)**

Subjects With Serious Adverse Events Leading to Discontinuation (Incidence > 0% in One or More Treatment Groups)
Phase 3: Placebo-Controlled Safety Pool
All Subjects as Treated

	Placebo		MK-3222 100mg		MK-3222 200mg		MK-3222 100 / 200 mg		Etanercept 50mg	
	n	(%)	n	(%)	n	(%)	n	(%)	n	(%)
Respiratory, thoracic and mediastinal disorders	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.2)**	**1**	**(0.1)**	**0**	**(0.0)**
Chronic obstructive pulmonary disease	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)	0	(0.0)

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:5.3.5.3-10]

付録 2.7.4-31
有害事象発現被験者（1 投与群以上で 100 人年当たり被験者 > 0 例で発現）
曝露期間で調整済み（12 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

	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†)
Subjects in population	588		1083		1041		1911		313		381		363		933	
with one or more adverse events	334	152.61	764	76.53	732	78.81	1392	72.23	228	148.61	298	60.54	295	61.97	739	61.30
with no adverse events	254	116.06	319	31.95	309	33.27	519	26.93	85	55.40	83	16.86	68	14.28	194	16.09
Blood and lymphatic system disorders	**5**	**2.28**	**19**	**1.90**	**11**	**1.18**	**30**	**1.56**	**5**	**3.26**	**9**	**1.83**	**9**	**1.89**	**21**	**1.74**
Anaemia	2	0.91	5	0.50	4	0.43	9	0.47	1	0.65	2	0.41	4	0.84	7	0.58
Febrile neutropenia	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Iron deficiency anaemia	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	0	0.00	1	0.21	1	0.08
Leukocytosis	0	0.00	2	0.20	0	0.00	2	0.10	2	1.30	1	0.20	0	0.00	1	0.08
Leukopenia	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Lymphadenopathy	3	1.37	6	0.60	2	0.22	8	0.42	1	0.65	3	0.61	0	0.00	4	0.33
Lymphopenia	0	0.00	2	0.20	1	0.11	3	0.16	0	0.00	2	0.41	1	0.21	3	0.25
Neutropenia	0	0.00	2	0.20	2	0.22	4	0.21	0	0.00	1	0.20	2	0.42	4	0.33
Polycythaemia	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Splenomegaly	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Thrombocytopenia	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Cardiac disorders	**9**	**4.11**	**30**	**3.01**	**19**	**2.05**	**49**	**2.54**	**8**	**5.21**	**11**	**2.23**	**5**	**1.05**	**20**	**1.66**
Acute myocardial infarction	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Angina pectoris	0	0.00	3	0.30	3	0.32	6	0.31	1	0.65	1	0.20	1	0.21	2	0.17
Aortic valve incompetence	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Aortic valve stenosis	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Arrhythmia	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Atrial fibrillation	0	0.00	4	0.40	2	0.22	6	0.31	1	0.65	1	0.20	1	0.21	2	0.17
Atrioventricular block first degree	0	0.00	6	0.60	0	0.00	6	0.31	0	0.00	2	0.41	0	0.00	3	0.25

Subjects with Adverse Events (Occurring in > 0 Subjects per 100 Subject Years in One or More Treatment Groups)
Exposure Adjusted (Based on 12-Week Follow-up)
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

	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†)
Bradycardia	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Bundle branch block right	2	0.91	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Cardiac disorder	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Cardiac failure congestive	0	0.00	0	0.00	1	0.11	1	0.05	1	0.65	0	0.00	0	0.00	0	0.00
Cardiac hypertrophy	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Cardiomegaly	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Cardiomyopathy alcoholic	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Coronary artery disease	0	0.00	1	0.10	4	0.43	5	0.26	0	0.00	0	0.00	0	0.00	0	0.00
Coronary artery stenosis	0	0.00	1	0.10	0	0.00	1	0.05	1	0.65	1	0.20	0	0.00	1	0.08
Diastolic dysfunction	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Left ventricular hypertrophy	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Mitral valve calcification	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Mitral valve incompetence	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	0	0.00	1	0.21	1	0.08
Myocardial infarction	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Myocardial ischaemia	0	0.00	0	0.00	1	0.11	1	0.05	1	0.65	0	0.00	1	0.21	1	0.08
Palpitations	2	0.91	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Pericarditis	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Sinus arrhythmia	0	0.00	1	0.10	0	0.00	1	0.05	1	0.65	1	0.20	0	0.00	1	0.08
Sinus bradycardia	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	0	0.00	1	0.21	2	0.17
Sinus tachycardia	1	0.46	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Supraventricular tachycardia	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Tachyarrhythmia	0	0.00	2	0.20	0	0.00	2	0.10	0	0.00	1	0.20	0	0.00	1	0.08
Tachycardia	2	0.91	5	0.50	2	0.22	7	0.36	2	1.30	0	0.00	0	0.00	3	0.25

Subjects with Adverse Events (Occurring in > 0 Subjects per 100 Subject Years in One or More Treatment Groups)
Exposure Adjusted (Based on 12-Week Follow-up)
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

	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†)
Tricuspid valve incompetence	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Ventricular extrasystoles	1	0.46	2	0.20	1	0.11	3	0.16	1	0.65	1	0.20	0	0.00	1	0.08
Ventricular tachycardia	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Congenital, familial and genetic disorders	**0**	**0.00**	**1**	**0.10**	**0**	**0.00**	**1**	**0.05**	**0**	**0.00**	**0**	**0.00**	**0**	**0.00**	**0**	**0.00**
Malformation venous	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Ear and labyrinth disorders	**8**	**3.66**	**20**	**2.00**	**12**	**1.29**	**32**	**1.66**	**5**	**3.26**	**7**	**1.42**	**8**	**1.68**	**21**	**1.74**
Auricular pseudocyst	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Cerumen impaction	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Deafness unilateral	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Ear canal erythema	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Ear discomfort	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Ear pain	2	0.91	2	0.20	3	0.32	5	0.26	3	1.96	2	0.41	1	0.21	4	0.33
Eustachian tube dysfunction	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Excessive cerumen production	2	0.91	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
External ear inflammation	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	1	0.20	1	0.21	2	0.17
Hypoacusis	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Meniere's disease	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Otorrhoea	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Tinnitus	1	0.46	4	0.40	0	0.00	4	0.21	1	0.65	0	0.00	0	0.00	1	0.08
Vertigo	3	1.37	9	0.90	5	0.54	14	0.73	1	0.65	4	0.81	3	0.63	11	0.91
Endocrine disorders	**0**	**0.00**	**6**	**0.60**	**5**	**0.54**	**11**	**0.57**	**0**	**0.00**	**4**	**0.81**	**3**	**0.63**	**7**	**0.58**
Adrenomegaly	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Autoimmune thyroiditis	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00

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Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

	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†)
Hyperthyroidism	0	0.00	2	0.20	0	0.00	2	0.10	0	0.00	2	0.41	0	0.00	2	0.17
Hypothyroidism	0	0.00	3	0.30	4	0.43	7	0.36	0	0.00	2	0.41	2	0.42	4	0.33
Eye disorders	**4**	**1.83**	**20**	**2.00**	**20**	**2.15**	**40**	**2.08**	**7**	**4.56**	**11**	**2.23**	**7**	**1.47**	**25**	**2.07**
Accommodation disorder	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Blepharitis	0	0.00	2	0.20	0	0.00	2	0.10	0	0.00	2	0.41	0	0.00	2	0.17
Blepharospasm	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Cataract	0	0.00	3	0.30	2	0.22	5	0.26	0	0.00	2	0.41	0	0.00	2	0.17
Conjunctivitis allergic	0	0.00	0	0.00	6	0.65	6	0.31	0	0.00	0	0.00	2	0.42	2	0.17
Corneal bleeding	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Dry eye	1	0.46	4	0.40	1	0.11	5	0.26	1	0.65	2	0.41	1	0.21	4	0.33
Eczema eyelids	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Episcleritis	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Eye discharge	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Eye inflammation	1	0.46	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Eye irritation	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Eye pain	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Eye pruritus	0	0.00	1	0.10	2	0.22	3	0.16	0	0.00	1	0.20	1	0.21	2	0.17
Eye swelling	1	0.46	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Eye ulcer	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Eyelid oedema	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Macular degeneration	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Macular fibrosis	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Ocular discomfort	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00

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	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)
Ocular hyperaemia	1	0.46	0	0.00	1	0.11	1	0.05	1	0.65	0	0.00	0	0.00	1	0.08
Optic ischaemic neuropathy	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Scleritis	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Ulcerative keratitis	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Vision blurred	0	0.00	2	0.20	1	0.11	3	0.16	0	0.00	2	0.41	1	0.21	3	0.25
Visual acuity reduced	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Visual impairment	0	0.00	1	0.10	0	0.00	1	0.05	2	1.30	0	0.00	0	0.00	1	0.08
Xerophthalmia	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Gastrointestinal disorders	**27**	**12.34**	**153**	**15.33**	**121**	**13.03**	**268**	**13.91**	**37**	**24.12**	**66**	**13.41**	**58**	**12.18**	**161**	**13.35**
Abdominal discomfort	0	0.00	4	0.40	3	0.32	7	0.36	2	1.30	2	0.41	1	0.21	4	0.33
Abdominal distension	0	0.00	1	0.10	1	0.11	2	0.10	2	1.30	1	0.20	0	0.00	1	0.08
Abdominal hernia	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Abdominal pain	2	0.91	15	1.50	14	1.51	29	1.50	5	3.26	7	1.42	10	2.10	21	1.74
Abdominal pain lower	0	0.00	2	0.20	2	0.22	4	0.21	1	0.65	1	0.20	1	0.21	2	0.17
Abdominal pain upper	0	0.00	9	0.90	10	1.08	19	0.99	1	0.65	4	0.81	6	1.26	15	1.24
Abdominal rigidity	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Abdominal tenderness	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Anal erosion	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Anal fissure	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Anal pruritus	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Aphthous ulcer	0	0.00	1	0.10	0	0.00	1	0.05	1	0.65	0	0.00	0	0.00	0	0.00
Cheilitis	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Chronic gastritis	0	0.00	3	0.30	0	0.00	3	0.16	0	0.00	0	0.00	0	0.00	0	0.00

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	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)
Colitis	0	0.00	1	0.10	0	0.00	1	0.05	1	0.65	1	0.20	0	0.00	1	0.08
Constipation	3	1.37	6	0.60	8	0.86	14	0.73	3	1.96	3	0.61	3	0.63	8	0.66
Dental caries	2	0.91	10	1.00	6	0.65	16	0.83	1	0.65	5	1.02	3	0.63	11	0.91
Dental necrosis	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Diaphragmatic hernia	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Diarrhoea	7	3.20	42	4.21	36	3.88	77	4.00	8	5.21	19	3.86	18	3.78	47	3.90
Diverticulum	1	0.46	3	0.30	1	0.11	3	0.16	0	0.00	1	0.20	0	0.00	2	0.17
Diverticulum intestinal	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Diverticulum intestinal haemorrhagic	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Dry mouth	0	0.00	2	0.20	2	0.22	4	0.21	2	1.30	2	0.41	1	0.21	4	0.33
Dyschezia	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Dyspepsia	2	0.91	5	0.50	5	0.54	10	0.52	2	1.30	1	0.20	2	0.42	7	0.58
Dysphagia	0	0.00	0	0.00	1	0.11	1	0.05	1	0.65	0	0.00	1	0.21	1	0.08
Enlarged uvula	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Enteritis	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	0	0.00	1	0.21	1	0.08
Faeces soft	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Flatulence	0	0.00	2	0.20	1	0.11	3	0.16	0	0.00	1	0.20	0	0.00	1	0.08
Food poisoning	1	0.46	3	0.30	1	0.11	4	0.21	0	0.00	1	0.20	0	0.00	1	0.08
Gastric disorder	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Gastric polyps	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	0	0.00	0	0.00	1	0.08
Gastritis	1	0.46	4	0.40	1	0.11	5	0.26	3	1.96	3	0.61	1	0.21	4	0.33
Gastrointestinal disorder	0	0.00	2	0.20	0	0.00	2	0.10	1	0.65	2	0.41	0	0.00	2	0.17
Gastrointestinal pain	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08

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	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)
Gastrointestinal sounds abnormal	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Gastrooesophageal reflux disease	1	0.46	8	0.80	5	0.54	13	0.67	1	0.65	2	0.41	3	0.63	9	0.75
Gingival hypertrophy	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Gingival pain	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Haemorrhoids	0	0.00	1	0.10	2	0.22	3	0.16	0	0.00	1	0.20	1	0.21	2	0.17
Haemorrhoids thrombosed	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	1	0.20	0	0.00	2	0.17
Hiatus hernia	1	0.46	2	0.20	0	0.00	2	0.10	0	0.00	0	0.00	0	0.00	1	0.08
Hyperchlorhydria	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Inguinal hernia	0	0.00	0	0.00	1	0.11	1	0.05	1	0.65	0	0.00	1	0.21	1	0.08
Intestinal polyp	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Intra-abdominal haematoma	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Irritable bowel syndrome	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Large intestine polyp	1	0.46	2	0.20	3	0.32	5	0.26	1	0.65	2	0.41	1	0.21	4	0.33
Lip dry	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Lip swelling	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Malpositioned teeth	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Mouth ulceration	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Nausea	3	1.37	25	2.50	22	2.37	47	2.44	3	1.96	13	2.64	13	2.73	32	2.65
Oesophageal polyp	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Oral pruritus	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Pancreatic steatosis	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Pancreatitis	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Pancreatitis acute	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00

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	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)
Peptic ulcer	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	1	0.20	1	0.21	2	0.17
Periodontal disease	0	0.00	2	0.20	0	0.00	2	0.10	0	0.00	1	0.20	0	0.00	1	0.08
Plicated tongue	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Rectal haemorrhage	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	0	0.00	0	0.00	0	0.00
Retching	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Salivary gland enlargement	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Stomatitis	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Swollen tongue	0	0.00	2	0.20	0	0.00	2	0.10	0	0.00	0	0.00	0	0.00	0	0.00
Tongue discolouration	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Tongue ulceration	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Tooth loss	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Toothache	4	1.83	22	2.20	14	1.51	36	1.87	4	2.61	7	1.42	6	1.26	19	1.58
Umbilical hernia	0	0.00	2	0.20	1	0.11	3	0.16	0	0.00	1	0.20	1	0.21	3	0.25
Vomiting	1	0.46	19	1.90	8	0.86	27	1.40	1	0.65	7	1.42	4	0.84	15	1.24
General disorders and administration site conditions	**40**	**18.28**	**118**	**11.82**	**98**	**10.55**	**213**	**11.05**	**74**	**48.23**	**54**	**10.97**	**51**	**10.71**	**139**	**11.53**
Asthenia	1	0.46	5	0.50	1	0.11	6	0.31	1	0.65	2	0.41	0	0.00	2	0.17
Chest discomfort	1	0.46	1	0.10	1	0.11	2	0.10	0	0.00	0	0.00	0	0.00	1	0.08
Chest pain	1	0.46	5	0.50	2	0.22	7	0.36	1	0.65	2	0.41	2	0.42	4	0.33
Chills	0	0.00	1	0.10	1	0.11	2	0.10	1	0.65	0	0.00	0	0.00	1	0.08
Cyst	0	0.00	2	0.20	3	0.32	5	0.26	0	0.00	1	0.20	2	0.42	3	0.25
Death	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Fatigue	8	3.66	28	2.80	22	2.37	50	2.59	4	2.61	10	2.03	11	2.31	29	2.41
Feeling cold	0	0.00	2	0.20	1	0.11	3	0.16	0	0.00	1	0.20	0	0.00	2	0.17

Subjects with Adverse Events (Occurring in > 0 Subjects per 100 Subject Years in One or More Treatment Groups)
Exposure Adjusted (Based on 12-Week Follow-up)
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

	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†)
Feeling hot	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Impaired healing	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Influenza like illness	2	0.91	7	0.70	4	0.43	11	0.57	0	0.00	4	0.81	0	0.00	4	0.33
Injection site bruising	0	0.00	5	0.50	4	0.43	9	0.47	3	1.96	3	0.61	1	0.21	6	0.50
Injection site discomfort	1	0.46	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Injection site dryness	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Injection site erythema	2	0.91	8	0.80	8	0.86	16	0.83	28	18.25	6	1.22	5	1.05	12	1.00
Injection site haematoma	1	0.46	6	0.60	7	0.75	13	0.67	4	2.61	5	1.02	3	0.63	12	1.00
Injection site haemorrhage	0	0.00	2	0.20	2	0.22	4	0.21	2	1.30	1	0.20	2	0.42	4	0.33
Injection site hypoaesthesia	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Injection site induration	0	0.00	1	0.10	0	0.00	1	0.05	1	0.65	0	0.00	0	0.00	0	0.00
Injection site inflammation	0	0.00	0	0.00	2	0.22	2	0.10	0	0.00	0	0.00	2	0.42	2	0.17
Injection site oedema	0	0.00	1	0.10	0	0.00	1	0.05	1	0.65	1	0.20	0	0.00	1	0.08
Injection site pain	4	1.83	12	1.20	13	1.40	25	1.30	11	7.17	8	1.63	8	1.68	20	1.66
Injection site papule	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Injection site paraesthesia	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Injection site pruritus	0	0.00	3	0.30	7	0.75	10	0.52	5	3.26	2	0.41	4	0.84	8	0.66
Injection site reaction	2	0.91	4	0.40	5	0.54	9	0.47	17	11.08	3	0.61	2	0.42	6	0.50
Injection site swelling	3	1.37	4	0.40	5	0.54	9	0.47	7	4.56	3	0.61	3	0.63	7	0.58
Injection site urticaria	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Injury associated with device	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Local swelling	0	0.00	1	0.10	0	0.00	1	0.05	1	0.65	1	0.20	0	0.00	1	0.08
Malaise	0	0.00	4	0.40	2	0.22	6	0.31	0	0.00	2	0.41	2	0.42	5	0.41

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Phase 2 and 3: Base Period Safety Pool
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	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†)
Nodule	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Non-cardiac chest pain	3	1.37	1	0.10	5	0.54	6	0.31	0	0.00	1	0.20	5	1.05	6	0.50
Oedema peripheral	4	1.83	8	0.80	7	0.75	15	0.78	2	1.30	5	1.02	4	0.84	12	1.00
Pain	0	0.00	6	0.60	3	0.32	9	0.47	0	0.00	3	0.61	1	0.21	4	0.33
Peripheral swelling	2	0.91	8	0.80	5	0.54	13	0.67	0	0.00	3	0.61	4	0.84	9	0.75
Pyrexia	8	3.66	19	1.90	9	0.97	28	1.45	5	3.26	6	1.22	3	0.63	17	1.41
Sensation of foreign body	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Strangulated hernia	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Thirst	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Vaccination site reaction	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Hepatobiliary disorders	**1**	**0.46**	**15**	**1.50**	**7**	**0.75**	**21**	**1.09**	**7**	**4.56**	**4**	**0.81**	**5**	**1.05**	**15**	**1.24**
Alcoholic liver disease	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Bile duct stone	0	0.00	0	0.00	1	0.11	1	0.05	1	0.65	0	0.00	1	0.21	1	0.08
Cholecystitis	1	0.46	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Cholelithiasis	1	0.46	2	0.20	1	0.11	3	0.16	2	1.30	1	0.20	1	0.21	3	0.25
Drug-induced liver injury	0	0.00	2	0.20	0	0.00	2	0.10	0	0.00	0	0.00	0	0.00	0	0.00
Hepatic fibrosis	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Hepatic function abnormal	0	0.00	2	0.20	0	0.00	2	0.10	1	0.65	1	0.20	0	0.00	1	0.08
Hepatic steatosis	0	0.00	5	0.50	3	0.32	8	0.42	2	1.30	2	0.41	3	0.63	6	0.50
Hepatitis	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Hepatomegaly	0	0.00	1	0.10	1	0.11	2	0.10	1	0.65	0	0.00	1	0.21	2	0.17
Hyperbilirubinaemia	0	0.00	1	0.10	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Steatohepatitis	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00

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	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†)
Immune system disorders	**3**	**1.37**	**14**	**1.40**	**10**	**1.08**	**24**	**1.25**	**1**	**0.65**	**7**	**1.42**	**5**	**1.05**	**14**	**1.16**
Allergic oedema	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Allergy to animal	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Allergy to arthropod bite	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Allergy to arthropod sting	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Anaphylactic reaction	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Drug hypersensitivity	0	0.00	3	0.30	2	0.22	5	0.26	0	0.00	2	0.41	1	0.21	3	0.25
Food allergy	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Hypersensitivity	1	0.46	3	0.30	0	0.00	3	0.16	0	0.00	1	0.20	0	0.00	1	0.08
Seasonal allergy	2	0.91	5	0.50	6	0.65	11	0.57	1	0.65	3	0.61	4	0.84	8	0.66
Infections and infestations	**171**	**78.13**	**483**	**48.38**	**485**	**52.21**	**925**	**48.00**	**130**	**84.73**	**210**	**42.66**	**207**	**43.48**	**527**	**43.71**
Abscess	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Abscess limb	0	0.00	3	0.30	1	0.11	4	0.21	0	0.00	0	0.00	1	0.21	2	0.17
Abscess neck	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Abscess oral	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Acarodermatitis	0	0.00	1	0.10	1	0.11	2	0.10	1	0.65	0	0.00	1	0.21	1	0.08
Acne pustular	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Acute sinusitis	3	1.37	3	0.30	2	0.22	5	0.26	0	0.00	1	0.20	1	0.21	2	0.17
Anal abscess	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Anal fungal infection	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Appendicitis	0	0.00	2	0.20	0	0.00	2	0.10	0	0.00	1	0.20	0	0.00	1	0.08
Asymptomatic bacteriuria	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Atypical pneumonia	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08

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	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)
Bacterial disease carrier	1	0.46	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Bacterial pyelonephritis	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Bacterial rhinitis	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Bacterial vaginosis	0	0.00	0	0.00	3	0.32	3	0.16	0	0.00	0	0.00	3	0.63	3	0.25
Bacteriuria	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Balanitis candida	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Body tinea	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	0	0.00	1	0.21	1	0.08
Bone tuberculosis	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Breast abscess	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Bronchitis	6	2.74	28	2.80	31	3.34	59	3.06	5	3.26	12	2.44	17	3.57	36	2.99
Bronchitis viral	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Carbuncle	1	0.46	2	0.20	1	0.11	3	0.16	0	0.00	1	0.20	0	0.00	2	0.17
Cellulitis	2	0.91	8	0.80	8	0.86	16	0.83	1	0.65	4	0.81	4	0.84	9	0.75
Cellulitis of male external genital organ	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Cellulitis orbital	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Cervicitis	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Chlamydial infection	0	0.00	2	0.20	0	0.00	2	0.10	0	0.00	0	0.00	0	0.00	1	0.08
Chronic sinusitis	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Conjunctivitis	1	0.46	12	1.20	3	0.32	15	0.78	1	0.65	6	1.22	1	0.21	11	0.91
Conjunctivitis viral	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Cystitis	1	0.46	9	0.90	6	0.65	15	0.78	0	0.00	4	0.81	3	0.63	11	0.91
Cytomegalovirus infection	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Diarrhoea infectious	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00

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	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)
Diverticulitis	0	0.00	3	0.30	6	0.65	9	0.47	0	0.00	1	0.20	2	0.42	3	0.25
Ear infection	1	0.46	3	0.30	5	0.54	8	0.42	1	0.65	2	0.41	0	0.00	4	0.33
Eczema impetiginous	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Eczema infected	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Epiglottitis	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	0	0.00	0	0.00	1	0.08
Erysipelas	1	0.46	1	0.10	0	0.00	1	0.05	1	0.65	1	0.20	0	0.00	1	0.08
Erythema migrans	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Erythrasma	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
External ear cellulitis	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Eye infection	0	0.00	3	0.30	2	0.22	5	0.26	0	0.00	1	0.20	0	0.00	3	0.25
Folliculitis	4	1.83	5	0.50	10	1.08	15	0.78	2	1.30	2	0.41	5	1.05	10	0.83
Fungal infection	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Fungal paronychia	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Fungal skin infection	1	0.46	5	0.50	1	0.11	6	0.31	0	0.00	3	0.61	0	0.00	3	0.25
Furuncle	3	1.37	3	0.30	4	0.43	7	0.36	1	0.65	0	0.00	1	0.21	3	0.25
Gangrene	1	0.46	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Gastroenteritis	7	3.20	25	2.50	29	3.12	54	2.80	8	5.21	9	1.83	14	2.94	31	2.57
Gastroenteritis bacterial	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Gastroenteritis norovirus	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Gastroenteritis salmonella	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Gastroenteritis viral	3	1.37	5	0.50	5	0.54	10	0.52	0	0.00	2	0.41	2	0.42	5	0.41
Gastrointestinal infection	0	0.00	6	0.60	6	0.65	12	0.62	1	0.65	3	0.61	4	0.84	10	0.83
Genital herpes	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	1	0.20	1	0.21	2	0.17

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Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

	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†)
Genital infection fungal	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Gingival abscess	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Gingivitis	0	0.00	4	0.40	4	0.43	8	0.42	2	1.30	3	0.61	3	0.63	6	0.50
Hand-foot-and-mouth disease	0	0.00	1	0.10	2	0.22	3	0.16	0	0.00	1	0.20	2	0.42	3	0.25
Herpes simplex	0	0.00	0	0.00	3	0.32	3	0.16	0	0.00	0	0.00	2	0.42	2	0.17
Herpes virus infection	1	0.46	2	0.20	1	0.11	3	0.16	0	0.00	0	0.00	0	0.00	1	0.08
Herpes zoster	0	0.00	3	0.30	2	0.22	5	0.26	2	1.30	2	0.41	1	0.21	3	0.25
Hordeolum	1	0.46	3	0.30	2	0.22	5	0.26	5	3.26	2	0.41	1	0.21	4	0.33
Impetigo	1	0.46	3	0.30	1	0.11	4	0.21	0	0.00	1	0.20	0	0.00	1	0.08
Infected bite	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	1	0.20	0	0.00	2	0.17
Infected cyst	1	0.46	1	0.10	1	0.11	2	0.10	0	0.00	0	0.00	1	0.21	1	0.08
Influenza	18	8.22	31	3.11	39	4.20	70	3.63	4	2.61	14	2.84	16	3.36	38	3.15
Kidney infection	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Labyrinthitis	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Laryngitis	0	0.00	0	0.00	1	0.11	1	0.05	1	0.65	0	0.00	0	0.00	0	0.00
Lice infestation	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Localised infection	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	1	0.20	0	0.00	1	0.08
Lower respiratory tract infection	1	0.46	2	0.20	4	0.43	6	0.31	0	0.00	1	0.20	3	0.63	4	0.33
Molluscum contagiosum	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Mumps	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Myringitis	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Nasal vestibulitis	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Nasopharyngitis	55	25.13	231	23.14	205	22.07	425	22.05	61	39.76	111	22.55	98	20.59	275	22.81

Subjects with Adverse Events (Occurring in > 0 Subjects per 100 Subject Years in One or More Treatment Groups)
Exposure Adjusted (Based on 12-Week Follow-up)
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

	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†)
Onychomycosis	1	0.46	1	0.10	0	0.00	1	0.05	1	0.65	1	0.20	0	0.00	1	0.08
Ophthalmic herpes zoster	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Oral candidiasis	0	0.00	2	0.20	6	0.65	8	0.42	0	0.00	1	0.20	5	1.05	6	0.50
Oral herpes	1	0.46	12	1.20	10	1.08	22	1.14	4	2.61	2	0.41	4	0.84	10	0.83
Orchitis	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Osteomyelitis	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Otitis externa	0	0.00	3	0.30	1	0.11	4	0.21	0	0.00	1	0.20	1	0.21	2	0.17
Otitis media	1	0.46	4	0.40	2	0.22	6	0.31	1	0.65	2	0.41	2	0.42	5	0.41
Otitis media acute	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Otosalpingitis	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Papilloma viral infection	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Paronychia	1	0.46	3	0.30	3	0.32	6	0.31	0	0.00	2	0.41	0	0.00	2	0.17
Parvovirus infection	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Periodontitis	0	0.00	3	0.30	1	0.11	4	0.21	1	0.65	1	0.20	1	0.21	3	0.25
Pharyngitis	3	1.37	19	1.90	8	0.86	26	1.35	4	2.61	5	1.02	3	0.63	13	1.08
Pharyngitis streptococcal	5	2.28	8	0.80	0	0.00	8	0.42	0	0.00	4	0.81	0	0.00	5	0.41
Pilonidal cyst	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Pneumonia	0	0.00	1	0.10	4	0.43	5	0.26	1	0.65	0	0.00	2	0.42	2	0.17
Pneumonia mycoplasmal	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Post procedural infection	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Postoperative wound infection	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Pseudomonas infection	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Pulpitis dental	1	0.46	2	0.20	7	0.75	9	0.47	1	0.65	2	0.41	3	0.63	6	0.50

Subjects with Adverse Events (Occurring in > 0 Subjects per 100 Subject Years in One or More Treatment Groups)
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Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

	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†)
Pyelonephritis	1	0.46	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Rash pustular	1	0.46	1	0.10	1	0.11	2	0.10	0	0.00	1	0.20	0	0.00	1	0.08
Respiratory syncytial virus infection	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Respiratory tract infection	1	0.46	2	0.20	1	0.11	3	0.16	1	0.65	0	0.00	0	0.00	1	0.08
Respiratory tract infection viral	0	0.00	1	0.10	0	0.00	1	0.05	1	0.65	1	0.20	0	0.00	1	0.08
Rhinitis	3	1.37	17	1.70	18	1.94	34	1.76	5	3.26	6	1.22	12	2.52	22	1.82
Rhinovirus infection	0	0.00	0	0.00	1	0.11	1	0.05	2	1.30	0	0.00	1	0.21	1	0.08
Septic shock	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Sialoadenitis	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Sinusitis	10	4.57	39	3.91	28	3.01	67	3.48	3	1.96	24	4.88	13	2.73	48	3.98
Skin bacterial infection	0	0.00	4	0.40	1	0.11	5	0.26	0	0.00	1	0.20	1	0.21	2	0.17
Skin candida	0	0.00	2	0.20	6	0.65	8	0.42	0	0.00	2	0.41	2	0.42	4	0.33
Skin infection	3	1.37	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Streptococcal infection	0	0.00	0	0.00	1	0.11	1	0.05	1	0.65	0	0.00	1	0.21	1	0.08
Subcutaneous abscess	0	0.00	2	0.20	4	0.43	6	0.31	0	0.00	1	0.20	3	0.63	5	0.41
Sweat gland infection	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Syphilis	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Tinea cruris	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Tinea infection	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Tinea pedis	2	0.91	4	0.40	5	0.54	9	0.47	0	0.00	4	0.81	3	0.63	7	0.58
Tinea versicolour	2	0.91	1	0.10	5	0.54	6	0.31	2	1.30	0	0.00	1	0.21	2	0.17
Tonsillitis	1	0.46	7	0.70	12	1.29	19	0.99	3	1.96	2	0.41	6	1.26	10	0.83
Tooth abscess	1	0.46	7	0.70	10	1.08	17	0.88	2	1.30	5	1.02	5	1.05	11	0.91

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Phase 2 and 3: Base Period Safety Pool
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	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†)
Tooth infection	2	0.91	7	0.70	5	0.54	12	0.62	6	3.91	3	0.61	4	0.84	8	0.66
Tracheitis	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Trichophytosis	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	0	0.00	0	0.00	0	0.00
Upper respiratory tract infection	32	14.62	63	6.31	86	9.26	147	7.63	10	6.52	21	4.27	41	8.61	75	6.22
Urethritis	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Urinary tract infection	10	4.57	24	2.40	19	2.05	43	2.23	12	7.82	9	1.83	10	2.10	24	1.99
Urinary tract infection fungal	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	1	0.20	1	0.21	2	0.17
Urosepsis	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Vaginal infection	0	0.00	2	0.20	3	0.32	5	0.26	0	0.00	1	0.20	2	0.42	3	0.25
Viral infection	3	1.37	5	0.50	8	0.86	13	0.67	0	0.00	0	0.00	3	0.63	5	0.41
Viral pharyngitis	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Viral rhinitis	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Viral upper respiratory tract infection	3	1.37	6	0.60	4	0.43	10	0.52	2	1.30	2	0.41	1	0.21	3	0.25
Vulvovaginal candidiasis	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Vulvovaginal mycotic infection	0	0.00	1	0.10	3	0.32	4	0.21	1	0.65	0	0.00	0	0.00	1	0.08
Wound infection	0	0.00	3	0.30	1	0.11	4	0.21	1	0.65	0	0.00	0	0.00	1	0.08
Yersinia infection	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Injury, poisoning and procedural complications	**35**	**15.99**	**113**	**11.32**	**120**	**12.92**	**228**	**11.83**	**30**	**19.55**	**48**	**9.75**	**66**	**13.86**	**141**	**11.70**
Accidental overdose	2	0.91	6	0.60	14	1.51	20	1.04	5	3.26	5	1.02	9	1.89	17	1.41
Anaemia postoperative	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Animal bite	0	0.00	1	0.10	2	0.22	3	0.16	0	0.00	0	0.00	1	0.21	2	0.17
Animal scratch	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Ankle fracture	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00

Subjects with Adverse Events (Occurring in > 0 Subjects per 100 Subject Years in One or More Treatment Groups)
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Phase 2 and 3: Base Period Safety Pool
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	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†)
Arthropod bite	3	1.37	3	0.30	2	0.22	5	0.26	2	1.30	2	0.41	2	0.42	4	0.33
Arthropod sting	1	0.46	4	0.40	4	0.43	8	0.42	0	0.00	0	0.00	1	0.21	1	0.08
Back injury	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	0	0.00	0	0.00	1	0.08
Bone contusion	0	0.00	3	0.30	2	0.22	5	0.26	1	0.65	1	0.20	2	0.42	4	0.33
Burns first degree	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	1	0.20	1	0.21	2	0.17
Burns second degree	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Cartilage injury	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Chemical injury	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Chest injury	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Chillblains	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Comminuted fracture	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Concussion	0	0.00	0	0.00	2	0.22	2	0.10	0	0.00	0	0.00	2	0.42	2	0.17
Contusion	2	0.91	11	1.10	12	1.29	23	1.19	4	2.61	7	1.42	5	1.05	14	1.16
Corneal abrasion	0	0.00	2	0.20	0	0.00	2	0.10	1	0.65	1	0.20	0	0.00	1	0.08
Epicondylitis	0	0.00	4	0.40	2	0.22	6	0.31	1	0.65	1	0.20	2	0.42	4	0.33
Excoriation	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Eye injury	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Facial bones fracture	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Fall	1	0.46	6	0.60	4	0.43	9	0.47	1	0.65	3	0.61	1	0.21	7	0.58
Foot fracture	0	0.00	5	0.50	6	0.65	11	0.57	1	0.65	3	0.61	4	0.84	9	0.75
Forearm fracture	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Foreign body	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Foreign body in eye	0	0.00	0	0.00	1	0.11	1	0.05	1	0.65	0	0.00	1	0.21	1	0.08

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All Subjects as Treated

	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†)
Fracture	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Fractured coccyx	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Hand fracture	1	0.46	4	0.40	3	0.32	7	0.36	0	0.00	2	0.41	2	0.42	4	0.33
Head injury	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Heat illness	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Humerus fracture	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Hypobarism	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Injection related reaction	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Injury	0	0.00	2	0.20	0	0.00	2	0.10	0	0.00	1	0.20	0	0.00	2	0.17
Joint dislocation	2	0.91	1	0.10	1	0.11	2	0.10	0	0.00	1	0.20	1	0.21	2	0.17
Joint injury	1	0.46	4	0.40	1	0.11	5	0.26	0	0.00	2	0.41	0	0.00	4	0.33
Laceration	4	1.83	8	0.80	6	0.65	14	0.73	0	0.00	4	0.81	3	0.63	8	0.66
Ligament injury	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Ligament rupture	1	0.46	1	0.10	2	0.22	3	0.16	0	0.00	0	0.00	1	0.21	1	0.08
Ligament sprain	3	1.37	11	1.10	5	0.54	15	0.78	1	0.65	8	1.63	2	0.42	11	0.91
Limb injury	3	1.37	3	0.30	2	0.22	5	0.26	1	0.65	3	0.61	1	0.21	5	0.41
Limb traumatic amputation	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Lower limb fracture	0	0.00	2	0.20	2	0.22	4	0.21	0	0.00	1	0.20	1	0.21	2	0.17
Meniscus injury	1	0.46	1	0.10	2	0.22	3	0.16	2	1.30	1	0.20	2	0.42	3	0.25
Muscle rupture	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Muscle strain	7	3.20	17	1.70	12	1.29	28	1.45	0	0.00	6	1.22	7	1.47	18	1.49
Penis injury	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Post procedural haematoma	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08

Subjects with Adverse Events (Occurring in > 0 Subjects per 100 Subject Years in One or More Treatment Groups)
Exposure Adjusted (Based on 12-Week Follow-up)
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

	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†)
Post procedural swelling	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Post-traumatic neck syndrome	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	0	0.00	1	0.21	1	0.08
Procedural nausea	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Procedural pain	2	0.91	1	0.10	6	0.65	7	0.36	2	1.30	0	0.00	2	0.42	3	0.25
Procedural vomiting	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Radius fracture	0	0.00	3	0.30	0	0.00	3	0.16	0	0.00	1	0.20	0	0.00	1	0.08
Rib fracture	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Road traffic accident	0	0.00	2	0.20	2	0.22	4	0.21	0	0.00	0	0.00	2	0.42	2	0.17
Skin abrasion	1	0.46	8	0.80	2	0.22	10	0.52	0	0.00	4	0.81	1	0.21	5	0.41
Skin injury	0	0.00	0	0.00	2	0.22	2	0.10	0	0.00	0	0.00	1	0.21	1	0.08
Skin wound	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Soft tissue injury	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	0	0.00	0	0.00	0	0.00
Splinter	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Subcutaneous haematoma	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Sunburn	0	0.00	1	0.10	4	0.43	5	0.26	0	0.00	0	0.00	3	0.63	4	0.33
Synovial rupture	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Tendon rupture	0	0.00	2	0.20	6	0.65	8	0.42	0	0.00	1	0.20	3	0.63	5	0.41
Thermal burn	1	0.46	3	0.30	3	0.32	6	0.31	3	1.96	2	0.41	2	0.42	4	0.33
Tibia fracture	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Tooth fracture	1	0.46	2	0.20	3	0.32	5	0.26	1	0.65	1	0.20	2	0.42	3	0.25
Traumatic haematoma	0	0.00	1	0.10	1	0.11	2	0.10	1	0.65	0	0.00	1	0.21	1	0.08
Traumatic haemorrhage	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Upper limb fracture	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00

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Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

	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†)
Wound	0	0.00	1	0.10	3	0.32	4	0.21	0	0.00	0	0.00	1	0.21	2	0.17
Wrist fracture	1	0.46	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Investigations	**16**	**7.31**	**80**	**8.01**	**70**	**7.54**	**149**	**7.73**	**14**	**9.13**	**30**	**6.09**	**36**	**7.56**	**80**	**6.64**
Alanine aminotransferase increased	3	1.37	13	1.30	12	1.29	25	1.30	3	1.96	7	1.42	7	1.47	16	1.33
Aspartate aminotransferase increased	0	0.00	12	1.20	8	0.86	20	1.04	2	1.30	6	1.22	3	0.63	12	1.00
Blood alkaline phosphatase decreased	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Blood alkaline phosphatase increased	0	0.00	0	0.00	2	0.22	2	0.10	0	0.00	0	0.00	1	0.21	1	0.08
Blood bilirubin increased	0	0.00	3	0.30	0	0.00	3	0.16	1	0.65	0	0.00	0	0.00	1	0.08
Blood chloride decreased	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Blood cholesterol increased	0	0.00	2	0.20	3	0.32	5	0.26	0	0.00	2	0.41	3	0.63	5	0.41
Blood creatine phosphokinase increased	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Blood creatinine decreased	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Blood creatinine increased	0	0.00	3	0.30	2	0.22	5	0.26	0	0.00	1	0.20	1	0.21	3	0.25
Blood glucose abnormal	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Blood glucose increased	2	0.91	4	0.40	2	0.22	6	0.31	1	0.65	1	0.20	0	0.00	1	0.08
Blood iron decreased	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Blood lactate dehydrogenase increased	0	0.00	2	0.20	1	0.11	3	0.16	0	0.00	1	0.20	1	0.21	2	0.17
Blood potassium increased	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Blood pressure increased	1	0.46	5	0.50	5	0.54	10	0.52	1	0.65	2	0.41	4	0.84	7	0.58
Blood sodium decreased	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Blood testosterone decreased	1	0.46	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Blood thyroid stimulating hormone increased	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Blood triglycerides increased	0	0.00	6	0.60	2	0.22	8	0.42	0	0.00	1	0.20	1	0.21	2	0.17

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Phase 2 and 3: Base Period Safety Pool
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	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†)
Blood urine present	0	0.00	4	0.40	2	0.22	6	0.31	0	0.00	0	0.00	1	0.21	1	0.08
Breath sounds abnormal	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
C-reactive protein increased	2	0.91	10	1.00	6	0.65	16	0.83	1	0.65	5	1.02	3	0.63	9	0.75
Cardiac murmur	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Drug screen positive	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
ECG signs of myocardial ischaemia	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Electrocardiogram PR shortened	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Electrocardiogram Q wave abnormal	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Electrocardiogram QRS complex abnormal	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Electrocardiogram QT interval abnormal	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Electrocardiogram QT prolonged	0	0.00	3	0.30	2	0.22	5	0.26	0	0.00	0	0.00	1	0.21	1	0.08
Electrocardiogram ST segment elevation	1	0.46	2	0.20	1	0.11	3	0.16	0	0.00	1	0.20	0	0.00	2	0.17
Electrocardiogram T wave peaked	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Electrocardiogram abnormal	0	0.00	1	0.10	1	0.11	2	0.10	1	0.65	0	0.00	0	0.00	1	0.08
Eosinophil count increased	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Gamma-glutamyltransferase increased	3	1.37	16	1.60	13	1.40	29	1.50	3	1.96	5	1.02	6	1.26	15	1.24
Glucose urine	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Glucose urine present	0	0.00	2	0.20	1	0.11	3	0.16	0	0.00	1	0.20	0	0.00	1	0.08
Haematocrit decreased	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Heart rate increased	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Hepatic enzyme increased	0	0.00	2	0.20	4	0.43	6	0.31	1	0.65	1	0.20	1	0.21	2	0.17
High density lipoprotein increased	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Intraocular pressure increased	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00

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	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†)
Lipoprotein (a) increased	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Liver function test increased	1	0.46	0	0.00	3	0.32	3	0.16	1	0.65	0	0.00	2	0.42	2	0.17
Neutrophil count increased	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Protein urine	0	0.00	0	0.00	2	0.22	2	0.10	0	0.00	0	0.00	1	0.21	1	0.08
Protein urine present	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Red blood cells urine	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Red blood cells urine positive	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Serum ferritin abnormal	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Streptococcus test positive	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Transaminases increased	1	0.46	3	0.30	3	0.32	6	0.31	0	0.00	1	0.20	2	0.42	3	0.25
Urinary sediment present	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	1	0.20	0	0.00	1	0.08
Urine analysis abnormal	0	0.00	2	0.20	2	0.22	4	0.21	0	0.00	0	0.00	2	0.42	2	0.17
Urine barbiturates	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Vitamin B12 decreased	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Weight decreased	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	1	0.20	1	0.21	2	0.17
Weight increased	0	0.00	2	0.20	2	0.22	4	0.21	2	1.30	1	0.20	0	0.00	2	0.17
White blood cell count decreased	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
White blood cell count increased	0	0.00	3	0.30	1	0.11	4	0.21	0	0.00	2	0.41	0	0.00	2	0.17
White blood cells urine	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
White blood cells urine positive	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Metabolism and nutrition disorders	**10**	**4.57**	**44**	**4.41**	**40**	**4.31**	**84**	**4.36**	**3**	**1.96**	**17**	**3.45**	**16**	**3.36**	**40**	**3.32**
Decreased appetite	1	0.46	3	0.30	3	0.32	6	0.31	0	0.00	0	0.00	0	0.00	3	0.25
Dehydration	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00

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	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†)
Diabetes mellitus	4	1.83	2	0.20	9	0.97	11	0.57	0	0.00	0	0.00	4	0.84	4	0.33
Dyslipidaemia	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Glucose tolerance impaired	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Gout	1	0.46	9	0.90	3	0.32	12	0.62	0	0.00	2	0.41	1	0.21	3	0.25
Hypercholesterolaemia	0	0.00	5	0.50	3	0.32	8	0.42	0	0.00	4	0.81	1	0.21	6	0.50
Hyperglycaemia	0	0.00	3	0.30	3	0.32	6	0.31	0	0.00	2	0.41	1	0.21	5	0.41
Hyperkalaemia	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Hyperlipidaemia	0	0.00	7	0.70	4	0.43	11	0.57	0	0.00	2	0.41	2	0.42	4	0.33
Hyperphagia	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Hypertriglyceridaemia	0	0.00	6	0.60	2	0.22	8	0.42	1	0.65	5	1.02	0	0.00	5	0.41
Hyperuricaemia	1	0.46	4	0.40	1	0.11	5	0.26	0	0.00	1	0.20	1	0.21	2	0.17
Hypokalaemia	1	0.46	3	0.30	2	0.22	5	0.26	0	0.00	1	0.20	1	0.21	2	0.17
Hypovolaemia	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Impaired fasting glucose	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Iron deficiency	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	1	0.20	1	0.21	2	0.17
Malnutrition	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Obesity	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Type 2 diabetes mellitus	2	0.91	4	0.40	6	0.65	10	0.52	1	0.65	3	0.61	3	0.63	7	0.58
Vitamin D deficiency	0	0.00	2	0.20	3	0.32	5	0.26	0	0.00	0	0.00	2	0.42	2	0.17
Musculoskeletal and connective tissue disorders	**43**	**19.65**	**180**	**18.03**	**168**	**18.09**	**341**	**17.69**	**42**	**27.38**	**74**	**15.03**	**86**	**18.06**	**197**	**16.34**
Ankle deformity	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Arthralgia	8	3.66	50	5.01	33	3.55	83	4.31	10	6.52	20	4.06	16	3.36	45	3.73
Arthritis	4	1.83	4	0.40	4	0.43	8	0.42	1	0.65	2	0.41	1	0.21	3	0.25

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	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)
Arthritis reactive	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Arthropathy	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	0	0.00	0	0.00	2	0.17
Back disorder	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Back pain	7	3.20	45	4.51	41	4.41	86	4.46	8	5.21	17	3.45	23	4.83	50	4.15
Bone pain	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Bone swelling	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Bursitis	1	0.46	6	0.60	3	0.32	9	0.47	1	0.65	1	0.20	0	0.00	5	0.41
Cervical spinal stenosis	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Dactylitis	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	1	0.20	1	0.21	2	0.17
Dupuytren's contracture	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Exostosis	0	0.00	3	0.30	1	0.11	4	0.21	0	0.00	1	0.20	1	0.21	2	0.17
Fibromyalgia	0	0.00	0	0.00	2	0.22	2	0.10	0	0.00	0	0.00	1	0.21	1	0.08
Flank pain	1	0.46	1	0.10	0	0.00	1	0.05	2	1.30	0	0.00	0	0.00	0	0.00
Foot deformity	0	0.00	0	0.00	2	0.22	2	0.10	0	0.00	0	0.00	2	0.42	2	0.17
Groin pain	0	0.00	0	0.00	1	0.11	1	0.05	1	0.65	0	0.00	0	0.00	0	0.00
Haemarthrosis	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Inguinal mass	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Intervertebral disc degeneration	0	0.00	2	0.20	1	0.11	3	0.16	0	0.00	1	0.20	0	0.00	1	0.08
Intervertebral disc disorder	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Intervertebral disc displacement	0	0.00	2	0.20	0	0.00	2	0.10	0	0.00	0	0.00	0	0.00	1	0.08
Intervertebral disc protrusion	1	0.46	1	0.10	2	0.22	3	0.16	1	0.65	0	0.00	1	0.21	1	0.08
Joint crepitation	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Joint effusion	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08

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Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

	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†)
Joint stiffness	0	0.00	0	0.00	1	0.11	1	0.05	1	0.65	0	0.00	1	0.21	1	0.08
Joint swelling	1	0.46	4	0.40	4	0.43	8	0.42	0	0.00	3	0.61	0	0.00	5	0.41
Limb discomfort	0	0.00	0	0.00	2	0.22	2	0.10	0	0.00	0	0.00	1	0.21	2	0.17
Medial tibial stress syndrome	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Muscle disorder	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Muscle fatigue	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	0	0.00	0	0.00	1	0.08
Muscle spasms	2	0.91	4	0.40	7	0.75	11	0.57	2	1.30	4	0.81	5	1.05	10	0.83
Muscle tightness	0	0.00	3	0.30	0	0.00	3	0.16	0	0.00	3	0.61	0	0.00	3	0.25
Muscular weakness	0	0.00	1	0.10	3	0.32	4	0.21	0	0.00	1	0.20	1	0.21	2	0.17
Musculoskeletal chest pain	0	0.00	2	0.20	2	0.22	4	0.21	0	0.00	0	0.00	1	0.21	2	0.17
Musculoskeletal discomfort	1	0.46	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Musculoskeletal pain	1	0.46	10	1.00	10	1.08	20	1.04	4	2.61	5	1.02	6	1.26	14	1.16
Musculoskeletal stiffness	2	0.91	2	0.20	0	0.00	2	0.10	2	1.30	0	0.00	0	0.00	0	0.00
Myalgia	2	0.91	13	1.30	10	1.08	23	1.19	3	1.96	7	1.42	8	1.68	17	1.41
Myalgia intercostal	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Neck pain	1	0.46	3	0.30	4	0.43	7	0.36	1	0.65	0	0.00	2	0.42	3	0.25
Osteitis	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Osteoarthritis	0	0.00	1	0.10	8	0.86	9	0.47	1	0.65	1	0.20	5	1.05	6	0.50
Osteochondrosis	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Osteonecrosis	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Pain in extremity	3	1.37	25	2.50	16	1.72	41	2.13	3	1.96	12	2.44	8	1.68	24	1.99
Pain in jaw	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Periarthritis	0	0.00	2	0.20	3	0.32	5	0.26	0	0.00	0	0.00	3	0.63	4	0.33

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Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

	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†)
Peripheral arthritis	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Plantar fasciitis	0	0.00	3	0.30	1	0.11	4	0.21	0	0.00	1	0.20	0	0.00	1	0.08
Psoriatic arthropathy	7	3.20	10	1.00	9	0.97	19	0.99	2	1.30	3	0.61	5	1.05	10	0.83
Rheumatic disorder	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Rheumatoid arthritis	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Rotator cuff syndrome	0	0.00	1	0.10	5	0.54	6	0.31	1	0.65	1	0.20	3	0.63	4	0.33
Sacroiliitis	0	0.00	2	0.20	0	0.00	2	0.10	0	0.00	0	0.00	0	0.00	1	0.08
Spinal column stenosis	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Spinal deformity	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Spinal osteoarthritis	1	0.46	1	0.10	3	0.32	4	0.21	1	0.65	0	0.00	2	0.42	3	0.25
Spinal pain	0	0.00	2	0.20	2	0.22	4	0.21	1	0.65	2	0.41	1	0.21	3	0.25
Spondylitis	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Spondyloarthropathy	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Spondylolisthesis	1	0.46	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Synovial cyst	0	0.00	2	0.20	1	0.11	3	0.16	1	0.65	2	0.41	1	0.21	3	0.25
Temporomandibular joint syndrome	0	0.00	0	0.00	1	0.11	1	0.05	1	0.65	0	0.00	1	0.21	1	0.08
Tendon disorder	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	1	0.20	1	0.21	2	0.17
Tendon pain	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	0	0.00	1	0.21	1	0.08
Tendonitis	2	0.91	2	0.20	4	0.43	6	0.31	3	1.96	0	0.00	1	0.21	4	0.33
Tenosynovitis	2	0.91	3	0.30	3	0.32	6	0.31	1	0.65	1	0.20	0	0.00	2	0.17
Tenosynovitis stenosans	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Trigger finger	0	0.00	3	0.30	2	0.22	5	0.26	0	0.00	1	0.20	1	0.21	2	0.17
Wrist deformity	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08

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Phase 2 and 3: Base Period Safety Pool
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	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†)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**5**	**2.28**	**40**	**4.01**	**26**	**2.80**	**66**	**3.42**	**9**	**5.87**	**15**	**3.05**	**12**	**2.52**	**30**	**2.49**
Acrochordon	0	0.00	0	0.00	3	0.32	3	0.16	0	0.00	0	0.00	1	0.21	1	0.08
Acute myeloid leukaemia	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Adrenal adenoma	1	0.46	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Anogenital warts	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Basal cell carcinoma	1	0.46	7	0.70	5	0.54	12	0.62	2	1.30	1	0.20	2	0.42	3	0.25
Benign biliary neoplasm	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Benign breast neoplasm	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Benign hepatic neoplasm	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Benign renal neoplasm	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Benign uterine neoplasm	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Bladder transitional cell carcinoma	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Bowen's disease	0	0.00	2	0.20	1	0.11	3	0.16	0	0.00	0	0.00	1	0.21	1	0.08
Breast cancer	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Carcinoma in situ of skin	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Colon adenoma	0	0.00	0	0.00	0	0.00	0	0.00	2	1.30	0	0.00	0	0.00	0	0.00
Dysplastic naevus	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	0	0.00	0	0.00	1	0.08
Fibroma	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Haemangioma	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Haemangioma of liver	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Leiomyoma	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Lipoma	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	0	0.00	0	0.00	0	0.00
Lung adenocarcinoma	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00

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	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)
Malignant melanoma in situ	0	0.00	2	0.20	0	0.00	2	0.10	0	0.00	1	0.20	0	0.00	1	0.08
Melanocytic naevus	2	0.91	1	0.10	5	0.54	6	0.31	2	1.30	1	0.20	2	0.42	3	0.25
Neuroma	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Oral fibroma	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Pancreatic carcinoma	0	0.00	0	0.00	2	0.22	2	0.10	0	0.00	0	0.00	0	0.00	0	0.00
Penile wart	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Rectal cancer	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Renal oncocytoma	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Seborrhoeic keratosis	0	0.00	3	0.30	2	0.22	5	0.26	1	0.65	1	0.20	1	0.21	3	0.25
Skin papilloma	1	0.46	13	1.30	1	0.11	14	0.73	0	0.00	8	1.63	1	0.21	9	0.75
Squamous cell carcinoma of skin	1	0.46	3	0.30	2	0.22	5	0.26	0	0.00	0	0.00	2	0.42	2	0.17
Thyroid cancer	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Uterine leiomyoma	0	0.00	0	0.00	2	0.22	2	0.10	1	0.65	0	0.00	1	0.21	1	0.08
Nervous system disorders	**33**	**15.08**	**120**	**12.02**	**109**	**11.73**	**224**	**11.62**	**40**	**26.07**	**43**	**8.74**	**54**	**11.34**	**131**	**10.87**
Alcoholic seizure	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Amputation stump pain	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Anaesthesia	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Aphonia	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Balance disorder	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Burning sensation	0	0.00	0	0.00	2	0.22	2	0.10	1	0.65	0	0.00	1	0.21	1	0.08
Carotid arteriosclerosis	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Carotid artery stenosis	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Carpal tunnel syndrome	1	0.46	6	0.60	2	0.22	8	0.42	0	0.00	1	0.20	2	0.42	6	0.50

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	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)
Cerebellar infarction	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Cervicobrachial syndrome	0	0.00	1	0.10	2	0.22	3	0.16	0	0.00	1	0.20	1	0.21	2	0.17
Dizziness	2	0.91	13	1.30	19	2.05	32	1.66	7	4.56	4	0.81	9	1.89	16	1.33
Dysgeusia	0	0.00	2	0.20	2	0.22	4	0.21	0	0.00	1	0.20	1	0.21	3	0.25
Formication	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Headache	16	7.31	62	6.21	57	6.14	115	5.97	18	11.73	27	5.49	28	5.88	73	6.06
Hyperaesthesia	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Hypertonia	0	0.00	2	0.20	1	0.11	3	0.16	0	0.00	1	0.20	0	0.00	2	0.17
Hypoaesthesia	4	1.83	4	0.40	3	0.32	7	0.36	1	0.65	1	0.20	2	0.42	3	0.25
Hypotonia	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Intercostal neuralgia	0	0.00	1	0.10	0	0.00	1	0.05	1	0.65	0	0.00	0	0.00	0	0.00
Lacunar infarction	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Lethargy	1	0.46	1	0.10	2	0.22	3	0.16	1	0.65	0	0.00	0	0.00	0	0.00
Loss of consciousness	0	0.00	2	0.20	1	0.11	3	0.16	0	0.00	1	0.20	0	0.00	1	0.08
Memory impairment	0	0.00	2	0.20	0	0.00	2	0.10	0	0.00	1	0.20	0	0.00	1	0.08
Migraine	2	0.91	8	0.80	6	0.65	14	0.73	1	0.65	2	0.41	6	1.26	11	0.91
Migraine with aura	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Morton's neuralgia	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Motor neurone disease	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Muscle contractions involuntary	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	0	0.00	0	0.00	0	0.00
Nerve compression	1	0.46	0	0.00	2	0.22	2	0.10	0	0.00	0	0.00	1	0.21	1	0.08
Nervous system disorder	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Neuralgia	0	0.00	2	0.20	0	0.00	2	0.10	2	1.30	0	0.00	0	0.00	0	0.00

Subjects with Adverse Events (Occurring in > 0 Subjects per 100 Subject Years in One or More Treatment Groups)
Exposure Adjusted (Based on 12-Week Follow-up)
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

	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†)
Neuritis	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Neuropathy peripheral	1	0.46	2	0.20	1	0.11	3	0.16	0	0.00	0	0.00	1	0.21	1	0.08
Orthostatic intolerance	0	0.00	0	0.00	1	0.11	1	0.05	1	0.65	0	0.00	1	0.21	1	0.08
Paraesthesia	3	1.37	4	0.40	5	0.54	9	0.47	2	1.30	1	0.20	3	0.63	5	0.41
Paralysis	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Parosmia	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Post herpetic neuralgia	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Presyncope	1	0.46	0	0.00	2	0.22	2	0.10	2	1.30	0	0.00	1	0.21	2	0.17
Radiculopathy	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Restless legs syndrome	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Sciatica	0	0.00	3	0.30	7	0.75	10	0.52	1	0.65	1	0.20	3	0.63	7	0.58
Seizure	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Somnolence	1	0.46	3	0.30	2	0.22	5	0.26	1	0.65	0	0.00	1	0.21	4	0.33
Syncope	0	0.00	4	0.40	1	0.11	5	0.26	0	0.00	2	0.41	0	0.00	2	0.17
Tension headache	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	1	0.20	0	0.00	2	0.17
Transient ischaemic attack	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	1	0.20	0	0.00	1	0.08
Tremor	0	0.00	1	0.10	2	0.22	3	0.16	1	0.65	0	0.00	1	0.21	1	0.08
Vertebrobasilar insufficiency	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Visual field defect	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Pregnancy, puerperium and perinatal conditions	**0**	**0.00**	**1**	**0.10**	**2**	**0.22**	**3**	**0.16**	**0**	**0.00**	**0**	**0.00**	**0**	**0.00**	**0**	**0.00**
Abortion	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Abortion spontaneous	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Pregnancy	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00

Subjects with Adverse Events (Occurring in > 0 Subjects per 100 Subject Years in One or More Treatment Groups)
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Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

	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†)
Product issues	**0**	**0.00**	**2**	**0.20**	**1**	**0.11**	**3**	**0.16**	**0**	**0.00**	**2**	**0.41**	**0**	**0.00**	**3**	**0.25**
Device dislocation	0	0.00	2	0.20	0	0.00	2	0.10	0	0.00	2	0.41	0	0.00	2	0.17
Device occlusion	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Psychiatric disorders	**4**	**1.83**	**32**	**3.21**	**38**	**4.09**	**70**	**3.63**	**8**	**5.21**	**20**	**4.06**	**15**	**3.15**	**45**	**3.73**
Adjustment disorder	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Agitation	1	0.46	1	0.10	1	0.11	2	0.10	0	0.00	1	0.20	1	0.21	2	0.17
Alcohol abuse	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Alcoholism	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Anxiety	1	0.46	6	0.60	5	0.54	11	0.57	0	0.00	5	1.02	2	0.42	8	0.66
Apathy	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Attention deficit/hyperactivity disorder	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Bipolar disorder	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Borderline personality disorder	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Depressed mood	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Depression	0	0.00	10	1.00	8	0.86	18	0.93	2	1.30	6	1.22	1	0.21	10	0.83
Drug abuse	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Emotional disorder	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Initial insomnia	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Insomnia	2	0.91	6	0.60	14	1.51	20	1.04	2	1.30	3	0.61	6	1.26	12	1.00
Irritability	0	0.00	3	0.30	0	0.00	3	0.16	0	0.00	2	0.41	0	0.00	3	0.25
Libido decreased	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Major depression	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Mental disorder	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08

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	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†)
Mood swings	0	0.00	0	0.00	2	0.22	2	0.10	0	0.00	0	0.00	1	0.21	1	0.08
Panic attack	1	0.46	1	0.10	1	0.11	2	0.10	0	0.00	1	0.20	0	0.00	1	0.08
Sleep disorder	0	0.00	1	0.10	4	0.43	5	0.26	1	0.65	1	0.20	1	0.21	3	0.25
Somnambulism	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Stress	0	0.00	2	0.20	1	0.11	3	0.16	0	0.00	1	0.20	1	0.21	2	0.17
Suicide attempt	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Renal and urinary disorders	**9**	**4.11**	**40**	**4.01**	**33**	**3.55**	**72**	**3.74**	**7**	**4.56**	**16**	**3.25**	**12**	**2.52**	**37**	**3.07**
Azotaemia	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Bladder mass	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Bladder pain	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Bladder spasm	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Calculus urinary	0	0.00	1	0.10	0	0.00	1	0.05	1	0.65	0	0.00	0	0.00	0	0.00
Calyceal diverticulum	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Cystitis noninfective	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
End stage renal disease	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Glycosuria	1	0.46	2	0.20	8	0.86	10	0.52	1	0.65	1	0.20	2	0.42	4	0.33
Haematuria	1	0.46	12	1.20	8	0.86	20	1.04	2	1.30	4	0.81	2	0.42	8	0.66
Hydronephrosis	1	0.46	1	0.10	1	0.11	2	0.10	0	0.00	0	0.00	1	0.21	1	0.08
Hypertonic bladder	2	0.91	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Ketonuria	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Leukocyturia	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	1	0.20	1	0.21	2	0.17
Micturition urgency	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Nephrolithiasis	0	0.00	9	0.90	3	0.32	12	0.62	0	0.00	3	0.61	1	0.21	5	0.41

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	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)
Nitrituria	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Nocturia	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Obstructive uropathy	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Oliguria	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Perinephric effusion	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Pollakiuria	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Proteinuria	3	1.37	11	1.10	8	0.86	18	0.93	2	1.30	5	1.02	4	0.84	13	1.08
Renal atrophy	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Renal colic	0	0.00	2	0.20	1	0.11	3	0.16	0	0.00	1	0.20	1	0.21	2	0.17
Renal cyst	1	0.46	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Renal failure	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Renal pain	1	0.46	1	0.10	1	0.11	2	0.10	0	0.00	1	0.20	0	0.00	2	0.17
Ureterolithiasis	1	0.46	3	0.30	1	0.11	4	0.21	0	0.00	2	0.41	1	0.21	4	0.33
Urinary bladder polyp	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Vesical fistula	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Reproductive system and breast disorders	**5**	**2.28**	**20**	**2.00**	**14**	**1.51**	**34**	**1.76**	**3**	**1.96**	**8**	**1.63**	**9**	**1.89**	**23**	**1.91**
Balanoposthitis	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	0	0.00	1	0.21	1	0.08
Bartholin's cyst	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Benign prostatic hyperplasia	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Breast cyst	0	0.00	1	0.10	2	0.22	3	0.16	0	0.00	0	0.00	2	0.42	2	0.17
Breast inflammation	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Breast pain	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	0	0.00	0	0.00	1	0.08
Cervical dysplasia	1	0.46	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00

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	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)
Dysmenorrhoea	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Dyspareunia	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Endometrial hyperplasia	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Endometrial thickening	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Erectile dysfunction	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Erection increased	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Galactorrhoea	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Genital discomfort	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Gynaecomastia	0	0.00	1	0.10	2	0.22	3	0.16	0	0.00	1	0.20	1	0.21	2	0.17
Haematospermia	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Menometrorrhagia	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Menstruation delayed	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	1	0.20	1	0.21	2	0.17
Menstruation irregular	0	0.00	2	0.20	0	0.00	2	0.10	0	0.00	1	0.20	0	0.00	2	0.17
Metrorrhagia	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Ovarian cyst	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	0	0.00	1	0.21	2	0.17
Postmenopausal haemorrhage	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Prostatomegaly	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Pruritus genital	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Testicular cyst	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Testicular pain	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	0	0.00	0	0.00	2	0.17
Uterine haemorrhage	1	0.46	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Vaginal lesion	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Vaginal perforation	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00

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	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)
Vaginal polyp	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Vulvovaginal dryness	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Vulvovaginal pruritus	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Respiratory, thoracic and mediastinal disorders	**33**	**15.08**	**107**	**10.72**	**112**	**12.06**	**216**	**11.21**	**29**	**18.90**	**33**	**6.70**	**57**	**11.97**	**123**	**10.20**
Asthma	0	0.00	5	0.50	6	0.65	11	0.57	1	0.65	2	0.41	3	0.63	5	0.41
Atelectasis	0	0.00	1	0.10	2	0.22	3	0.16	0	0.00	0	0.00	1	0.21	1	0.08
Bronchitis chronic	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Catarrh	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Chronic obstructive pulmonary disease	0	0.00	0	0.00	3	0.32	3	0.16	0	0.00	0	0.00	0	0.00	0	0.00
Cough	16	7.31	42	4.21	40	4.31	81	4.20	8	5.21	11	2.23	23	4.83	44	3.65
Dry throat	0	0.00	0	0.00	4	0.43	4	0.21	0	0.00	0	0.00	1	0.21	2	0.17
Dysphonia	0	0.00	3	0.30	2	0.22	5	0.26	0	0.00	1	0.20	2	0.42	4	0.33
Dyspnoea	0	0.00	2	0.20	5	0.54	7	0.36	1	0.65	0	0.00	3	0.63	4	0.33
Dyspnoea exertional	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	0	0.00	0	0.00	2	0.17
Emphysema	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Epistaxis	1	0.46	4	0.40	2	0.22	6	0.31	2	1.30	2	0.41	0	0.00	3	0.25
Haemoptysis	0	0.00	2	0.20	0	0.00	2	0.10	0	0.00	0	0.00	0	0.00	1	0.08
Hyperventilation	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Interstitial lung disease	0	0.00	1	0.10	0	0.00	1	0.05	1	0.65	1	0.20	0	0.00	1	0.08
Laryngeal pain	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Larynx irritation	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Nasal congestion	3	1.37	5	0.50	8	0.86	13	0.67	3	1.96	3	0.61	2	0.42	5	0.41
Nasal dryness	0	0.00	0	0.00	1	0.11	1	0.05	1	0.65	0	0.00	1	0.21	1	0.08

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Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

	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†)
Nasal inflammation	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Nasal oedema	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Nasal polyps	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Oropharyngeal discomfort	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Oropharyngeal pain	7	3.20	23	2.30	32	3.45	53	2.75	8	5.21	9	1.83	14	2.94	35	2.90
Paranasal sinus hypersecretion	0	0.00	0	0.00	2	0.22	2	0.10	0	0.00	0	0.00	2	0.42	2	0.17
Pharyngeal disorder	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Pharyngeal erythema	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Pharyngeal oedema	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Pleural effusion	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Pneumothorax	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Productive cough	0	0.00	0	0.00	1	0.11	1	0.05	1	0.65	0	0.00	1	0.21	1	0.08
Pulmonary embolism	0	0.00	0	0.00	2	0.22	2	0.10	0	0.00	0	0.00	0	0.00	0	0.00
Pulmonary oedema	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Pulmonary sarcoidosis	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Respiratory arrest	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Respiratory disorder	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Respiratory distress	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Respiratory failure	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Respiratory tract congestion	0	0.00	3	0.30	3	0.32	6	0.31	0	0.00	1	0.20	0	0.00	1	0.08
Rhinitis allergic	1	0.46	6	0.60	6	0.65	12	0.62	2	1.30	1	0.20	2	0.42	6	0.50
Rhinorrhoea	2	0.91	5	0.50	5	0.54	10	0.52	1	0.65	3	0.61	3	0.63	6	0.50
Rhonchi	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00

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	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)
Sinus congestion	3	1.37	3	0.30	6	0.65	8	0.42	1	0.65	0	0.00	1	0.21	3	0.25
Sinus pain	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Sleep apnoea syndrome	0	0.00	4	0.40	1	0.11	5	0.26	1	0.65	1	0.20	0	0.00	3	0.25
Sneezing	0	0.00	0	0.00	2	0.22	2	0.10	0	0.00	0	0.00	1	0.21	1	0.08
Stridor	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Throat irritation	0	0.00	0	0.00	3	0.32	3	0.16	0	0.00	0	0.00	2	0.42	2	0.17
Tonsillar hypertrophy	0	0.00	0	0.00	2	0.22	2	0.10	0	0.00	0	0.00	1	0.21	2	0.17
Upper respiratory tract congestion	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Upper-airway cough syndrome	0	0.00	3	0.30	3	0.32	6	0.31	0	0.00	2	0.41	3	0.63	5	0.41
Wheezing	0	0.00	1	0.10	2	0.22	3	0.16	0	0.00	0	0.00	2	0.42	2	0.17
Skin and subcutaneous tissue disorders	**68**	**31.07**	**135**	**13.52**	**118**	**12.70**	**250**	**12.97**	**40**	**26.07**	**66**	**13.41**	**66**	**13.86**	**163**	**13.52**
Acne	1	0.46	7	0.70	5	0.54	12	0.62	4	2.61	6	1.22	4	0.84	10	0.83
Acne cystic	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Actinic keratosis	1	0.46	4	0.40	3	0.32	7	0.36	1	0.65	1	0.20	2	0.42	3	0.25
Alopecia	2	0.91	6	0.60	7	0.75	13	0.67	0	0.00	3	0.61	3	0.63	8	0.66
Alopecia areata	1	0.46	2	0.20	0	0.00	2	0.10	0	0.00	2	0.41	0	0.00	2	0.17
Angioedema	1	0.46	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Asteatosis	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Blister	0	0.00	3	0.30	0	0.00	3	0.16	0	0.00	1	0.20	0	0.00	2	0.17
Cold sweat	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Dermal cyst	1	0.46	3	0.30	4	0.43	7	0.36	1	0.65	2	0.41	3	0.63	6	0.50
Dermatitis	0	0.00	3	0.30	4	0.43	7	0.36	1	0.65	2	0.41	1	0.21	5	0.41
Dermatitis allergic	0	0.00	2	0.20	0	0.00	2	0.10	1	0.65	1	0.20	0	0.00	1	0.08

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	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)
Dermatitis atopic	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Dermatitis contact	3	1.37	11	1.10	7	0.75	18	0.93	2	1.30	6	1.22	4	0.84	13	1.08
Diffuse alopecia	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Dry skin	0	0.00	4	0.40	1	0.11	5	0.26	0	0.00	2	0.41	1	0.21	3	0.25
Dyshidrotic eczema	0	0.00	1	0.10	3	0.32	4	0.21	0	0.00	0	0.00	2	0.42	4	0.33
Ecchymosis	0	0.00	2	0.20	1	0.11	3	0.16	1	0.65	2	0.41	1	0.21	3	0.25
Eczema	2	0.91	13	1.30	6	0.65	19	0.99	3	1.96	7	1.42	4	0.84	11	0.91
Eczema asteatotic	1	0.46	2	0.20	1	0.11	3	0.16	0	0.00	1	0.20	0	0.00	1	0.08
Erythema	2	0.91	3	0.30	9	0.97	12	0.62	3	1.96	1	0.20	5	1.05	8	0.66
Generalised erythema	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Guttate psoriasis	2	0.91	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Hand dermatitis	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Hyperhidrosis	0	0.00	5	0.50	4	0.43	9	0.47	2	1.30	3	0.61	1	0.21	4	0.33
Hyperkeratosis	2	0.91	1	0.10	1	0.11	2	0.10	0	0.00	0	0.00	0	0.00	0	0.00
Ingrowing nail	3	1.37	4	0.40	3	0.32	7	0.36	0	0.00	3	0.61	1	0.21	4	0.33
Intertrigo	2	0.91	2	0.20	5	0.54	7	0.36	1	0.65	2	0.41	4	0.84	6	0.50
Keloid scar	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Keratosis pilaris	0	0.00	1	0.10	0	0.00	1	0.05	1	0.65	1	0.20	0	0.00	1	0.08
Lentigo	1	0.46	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Macule	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Miliaria	1	0.46	2	0.20	2	0.22	4	0.21	0	0.00	2	0.41	2	0.42	4	0.33
Myxoid cyst	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Neurodermatitis	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	1	0.20	1	0.21	2	0.17

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	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)
Night sweats	1	0.46	6	0.60	2	0.22	8	0.42	1	0.65	2	0.41	1	0.21	4	0.33
Onychoclasis	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Pain of skin	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Palmar erythema	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Papule	0	0.00	2	0.20	1	0.11	3	0.16	2	1.30	1	0.20	1	0.21	3	0.25
Photosensitivity reaction	0	0.00	1	0.10	2	0.22	3	0.16	1	0.65	1	0.20	2	0.42	3	0.25
Pigmentation disorder	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Polymorphic light eruption	1	0.46	0	0.00	2	0.22	2	0.10	0	0.00	0	0.00	1	0.21	1	0.08
Prurigo	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	1	0.20	0	0.00	1	0.08
Pruritus	15	6.85	25	2.50	32	3.45	56	2.91	11	7.17	11	2.23	20	4.20	39	3.24
Pruritus generalised	0	0.00	1	0.10	2	0.22	3	0.16	5	3.26	0	0.00	2	0.42	2	0.17
Pseudofolliculitis barbae	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Psoriasis	24	10.97	9	0.90	13	1.40	22	1.14	10	6.52	4	0.81	9	1.89	16	1.33
Pustular psoriasis	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Rash	1	0.46	11	1.10	3	0.32	14	0.73	0	0.00	5	1.02	3	0.63	11	0.91
Rash macular	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Rash papular	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Rash papulosquamous	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Rash pruritic	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Rosacea	0	0.00	0	0.00	2	0.22	2	0.10	1	0.65	0	0.00	1	0.21	1	0.08
Scar pain	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Sebaceous hyperplasia	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Seborrhoeic dermatitis	0	0.00	5	0.50	4	0.43	9	0.47	0	0.00	2	0.41	1	0.21	7	0.58

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	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)
Skin atrophy	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Skin burning sensation	1	0.46	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Skin erosion	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Skin exfoliation	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Skin fissures	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	1	0.20	1	0.21	2	0.17
Skin fragility	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Skin irritation	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Skin mass	0	0.00	1	0.10	0	0.00	1	0.05	1	0.65	1	0.20	0	0.00	1	0.08
Skin odour abnormal	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Skin swelling	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Skin tightness	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Skin ulcer	2	0.91	2	0.20	1	0.11	3	0.16	0	0.00	0	0.00	0	0.00	0	0.00
Skin warm	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Solar dermatitis	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Solar lentigo	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Stasis dermatitis	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	1	0.20	0	0.00	1	0.08
Swelling face	0	0.00	2	0.20	1	0.11	3	0.16	0	0.00	1	0.20	0	0.00	1	0.08
Telangiectasia	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Urticaria	3	1.37	9	0.90	8	0.86	17	0.88	1	0.65	3	0.61	5	1.05	11	0.91
Urticaria chronic	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Social circumstances	**0**	**0.00**	**1**	**0.10**	**1**	**0.11**	**2**	**0.10**	**0**	**0.00**	**1**	**0.20**	**0**	**0.00**	**2**	**0.17**
Menarche	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Menopause	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08

Subjects with Adverse Events (Occurring in > 0 Subjects per 100 Subject Years in One or More Treatment Groups)
Exposure Adjusted (Based on 12-Week Follow-up)
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

	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†)
Surgical and medical procedures	**0**	**0.00**	**3**	**0.30**	**0**	**0.00**	**3**	**0.16**	**0**	**0.00**	**0**	**0.00**	**0**	**0.00**	**1**	**0.08**
Renal stone removal	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Tooth extraction	0	0.00	2	0.20	0	0.00	2	0.10	0	0.00	0	0.00	0	0.00	0	0.00
Vascular disorders	**12**	**5.48**	**50**	**5.01**	**49**	**5.28**	**98**	**5.09**	**16**	**10.43**	**27**	**5.49**	**23**	**4.83**	**60**	**4.98**
Aneurysm	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Arteriosclerosis	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Blood pressure fluctuation	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Deep vein thrombosis	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Flushing	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Haematoma	2	0.91	2	0.20	4	0.43	6	0.31	5	3.26	1	0.20	2	0.42	5	0.41
Hot flush	2	0.91	4	0.40	2	0.22	6	0.31	1	0.65	1	0.20	1	0.21	3	0.25
Hypertension	8	3.66	36	3.61	30	3.23	66	3.42	9	5.87	22	4.47	12	2.52	40	3.32
Hypotension	0	0.00	4	0.40	5	0.54	9	0.47	0	0.00	1	0.20	2	0.42	4	0.33
Hypovolaemic shock	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Lymphoedema	0	0.00	0	0.00	2	0.22	2	0.10	0	0.00	0	0.00	1	0.21	1	0.08
Orthostatic hypotension	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Pallor	0	0.00	0	0.00	1	0.11	1	0.05	1	0.65	0	0.00	1	0.21	1	0.08
Peripheral arterial occlusive disease	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	0	0.00	1	0.21	1	0.08
Peripheral artery thrombosis	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Peripheral coldness	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Phlebitis	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Raynaud's phenomenon	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Shock haemorrhagic	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00

Subjects with Adverse Events (Occurring in > 0 Subjects per 100 Subject Years in One or More Treatment Groups)
Exposure Adjusted (Based on 12-Week Follow-up)
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

	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†)
Thrombophlebitis superficial	0	0.00	2	0.20	0	0.00	2	0.10	0	0.00	1	0.20	0	0.00	1	0.08
Venous occlusion	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Venous thrombosis limb	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00

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

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

[Source: 5.3.5.3-10]

付録 2.7.4-32
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 投与群以上で 100 人年当たり被験者 ≥ 1 例で発現）
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

	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†)
Subjects in population	588		1083		1041		1911		313		381		363		933	
with one or more drug-related adverse events	83	37.92	233	23.34	234	25.19	451	23.40	112	73.00	110	22.35	106	22.27	274	22.73
with no drug-related adverse events	505	230.74	850	85.14	807	86.88	1460	75.76	201	131.01	271	55.06	257	53.98	659	54.66
Blood and lymphatic system disorders	**0**	**0.00**	**7**	**0.70**	**3**	**0.32**	**10**	**0.52**	**2**	**1.30**	**6**	**1.22**	**2**	**0.42**	**8**	**0.66**
Gastrointestinal disorders	**2**	**0.91**	**25**	**2.50**	**20**	**2.15**	**45**	**2.34**	**8**	**5.21**	**13**	**2.64**	**9**	**1.89**	**32**	**2.65**
Diarrhoea	0	0.00	9	0.90	7	0.75	16	0.83	4	2.61	4	0.81	4	0.84	10	0.83
Nausea	0	0.00	5	0.50	4	0.43	9	0.47	2	1.30	2	0.41	3	0.63	7	0.58
General disorders and administration site conditions	**19**	**8.68**	**51**	**5.11**	**47**	**5.06**	**98**	**5.09**	**62**	**40.41**	**32**	**6.50**	**25**	**5.25**	**72**	**5.97**
Fatigue	4	1.83	11	1.10	6	0.65	17	0.88	2	1.30	4	0.81	4	0.84	10	0.83
Injection site bruising	0	0.00	4	0.40	3	0.32	7	0.36	2	1.30	3	0.61	1	0.21	6	0.50
Injection site erythema	2	0.91	7	0.70	6	0.65	13	0.67	27	17.60	5	1.02	3	0.63	9	0.75
Injection site haematoma	1	0.46	5	0.50	7	0.75	12	0.62	3	1.96	5	1.02	3	0.63	12	1.00
Injection site pain	4	1.83	12	1.20	11	1.18	23	1.19	10	6.52	8	1.63	7	1.47	18	1.49
Injection site pruritus	0	0.00	3	0.30	6	0.65	9	0.47	5	3.26	2	0.41	4	0.84	7	0.58
Injection site reaction	2	0.91	4	0.40	5	0.54	9	0.47	17	11.08	3	0.61	2	0.42	6	0.50
Injection site swelling	3	1.37	2	0.20	3	0.32	5	0.26	7	4.56	2	0.41	1	0.21	4	0.33
Hepatobiliary disorders	**1**	**0.46**	**2**	**0.20**	**2**	**0.22**	**3**	**0.16**	**2**	**1.30**	**1**	**0.20**	**1**	**0.21**	**3**	**0.25**
Infections and infestations	**41**	**18.73**	**121**	**12.12**	**145**	**15.61**	**260**	**13.49**	**45**	**29.33**	**55**	**11.17**	**70**	**14.70**	**159**	**13.19**
Bronchitis	0	0.00	3	0.30	11	1.18	14	0.73	2	1.30	2	0.41	9	1.89	11	0.91
Gastroenteritis	2	0.91	4	0.40	4	0.43	8	0.42	4	2.61	1	0.20	3	0.63	4	0.33
Gingivitis	0	0.00	1	0.10	0	0.00	1	0.05	2	1.30	1	0.20	0	0.00	1	0.08
Influenza	4	1.83	7	0.70	4	0.43	11	0.57	1	0.65	1	0.20	3	0.63	7	0.58
Nasopharyngitis	7	3.20	50	5.01	60	6.46	107	5.55	21	13.69	27	5.49	30	6.30	76	6.30

Subjects with Drug-Related Adverse Events (Occurring in >= 1 Subjects per 100 Subject Years in One or More Treatment Groups)
Exposure Adjusted (Based on 20-Week Follow-up)
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

	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†)
Oral herpes	1	0.46	4	0.40	4	0.43	8	0.42	2	1.30	1	0.20	2	0.42	4	0.33
Pharyngitis	1	0.46	6	0.60	3	0.32	9	0.47	2	1.30	2	0.41	1	0.21	5	0.41
Rhinitis	0	0.00	4	0.40	5	0.54	9	0.47	3	1.96	2	0.41	4	0.84	7	0.58
Sinusitis	3	1.37	9	0.90	11	1.18	20	1.04	1	0.65	7	1.42	6	1.26	14	1.16
Tooth infection	0	0.00	2	0.20	2	0.22	4	0.21	4	2.61	1	0.20	2	0.42	3	0.25
Upper respiratory tract infection	12	5.48	14	1.40	31	3.34	45	2.34	3	1.96	6	1.22	18	3.78	26	2.16
Urinary tract infection	1	0.46	3	0.30	6	0.65	9	0.47	1	0.65	2	0.41	5	1.05	8	0.66
Investigations	**5**	**2.28**	**22**	**2.20**	**13**	**1.40**	**35**	**1.82**	**4**	**2.61**	**8**	**1.63**	**8**	**1.68**	**19**	**1.58**
Alanine aminotransferase increased	2	0.91	6	0.60	3	0.32	9	0.47	2	1.30	4	0.81	2	0.42	6	0.50
Musculoskeletal and connective tissue disorders	**6**	**2.74**	**16**	**1.60**	**16**	**1.72**	**32**	**1.66**	**3**	**1.96**	**7**	**1.42**	**8**	**1.68**	**18**	**1.49**
Arthralgia	2	0.91	5	0.50	7	0.75	12	0.62	2	1.30	2	0.41	3	0.63	6	0.50
Nervous system disorders	**4**	**1.83**	**23**	**2.30**	**21**	**2.26**	**44**	**2.28**	**15**	**9.78**	**11**	**2.23**	**9**	**1.89**	**26**	**2.16**
Dizziness	1	0.46	3	0.30	4	0.43	7	0.36	4	2.61	1	0.20	3	0.63	5	0.41
Headache	1	0.46	12	1.20	15	1.61	27	1.40	6	3.91	9	1.83	4	0.84	17	1.41
Psychiatric disorders	**0**	**0.00**	**4**	**0.40**	**3**	**0.32**	**7**	**0.36**	**3**	**1.96**	**4**	**0.81**	**0**	**0.00**	**4**	**0.33**
Renal and urinary disorders	**0**	**0.00**	**8**	**0.80**	**4**	**0.43**	**12**	**0.62**	**0**	**0.00**	**6**	**1.22**	**1**	**0.21**	**8**	**0.66**
Respiratory, thoracic and mediastinal disorders	**7**	**3.20**	**12**	**1.20**	**15**	**1.61**	**27**	**1.40**	**7**	**4.56**	**7**	**1.42**	**10**	**2.10**	**22**	**1.82**
Cough	1	0.46	4	0.40	4	0.43	8	0.42	3	1.96	3	0.61	3	0.63	6	0.50
Oropharyngeal pain	3	1.37	5	0.50	5	0.54	10	0.52	0	0.00	2	0.41	3	0.63	9	0.75
Skin and subcutaneous tissue disorders	**14**	**6.40**	**27**	**2.70**	**39**	**4.20**	**66**	**3.42**	**13**	**8.47**	**12**	**2.44**	**21**	**4.41**	**44**	**3.65**
Acne	0	0.00	1	0.10	1	0.11	2	0.10	2	1.30	1	0.20	1	0.21	2	0.17
Erythema	0	0.00	1	0.10	5	0.54	6	0.31	2	1.30	1	0.20	2	0.42	4	0.33
Hyperhidrosis	0	0.00	3	0.30	2	0.22	5	0.26	2	1.30	2	0.41	0	0.00	2	0.17

Subjects with Drug-Related Adverse Events (Occurring in >= 1 Subjects per 100 Subject Years in One or More Treatment Groups)
Exposure Adjusted (Based on 20-Week Follow-up)
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

	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†)
Pruritus	1	0.46	3	0.30	13	1.40	16	0.83	8	5.21	1	0.20	6	1.26	11	0.91
Psoriasis	7	3.20	3	0.30	4	0.43	7	0.36	1	0.65	2	0.41	1	0.21	5	0.41
Vascular disorders	**4**	**1.83**	**8**	**0.80**	**8**	**0.86**	**16**	**0.83**	**4**	**2.61**	**5**	**1.02**	**5**	**1.05**	**10**	**0.83**
Haematoma	1	0.46	1	0.10	0	0.00	1	0.05	2	1.30	1	0.20	0	0.00	1	0.08
Hypertension	1	0.46	4	0.40	4	0.43	8	0.42	2	1.30	3	0.61	3	0.63	6	0.50

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

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

A system organ class or adverse event appears on this report only if it occurred in >=1 subjects per 100 subject years in one or more treatment groups of Placebo, MK-3222 100mg, MK-3222 200mg, and Etanercept 50mg.

[Source: 5.3.5.3-10]

付録 2.7.4-33
死亡例における有害事象の一覧表
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

Subject ID	Epoch	Onset Date [Relative Day]	Adverse Event MedDRA Preferred Term [Adverse Event Verbatim]	Duration	Intensity [Toxicity Grade]	Serious	Related	Action Taken	Outcome	Death Date [Relative Day]
MK-3222 100mg										
Trial Number=3222-003, Site Number=0808, Subject ID=[redacted], Gender=M, Age=6[redacted] Years, Race=White										
[redacted]			Alcohol abuse [ALCOHOL ABUSE]	Unknown	Severe [3]		N	N/A	Resolved	
	Screening	[redacted]	Urine ketone body present	Continuing	Moderate		N	N/A	Not Resolved	
	Screening	[-1]	[KETONE IN URINALYSIS]		[2]					
	Treatment	[redacted]	Blood glucose increased	2.14 Weeks	Mild		N	N/A	Resolved	
	Treatment	[1]	[HIGH VALUE OF BLOOD GLUCOSE]		[1]					
	Treatment	[redacted]	Glucose urine present	2.14 Weeks	Mild		N	N/A	Resolved	
	Treatment	[1]	[GLUCOSE IN URINALYSIS]		[1]					
	Treatment	[redacted]	Gamma-glutamyltransferase increased	2.29 Weeks	Moderate		Y	N/A	Resolved	
	Treatment	[15]	[HIGH GAMMA GLUTAMYL TRANSFERASE IN LABORATORY]		[2]					
	Treatment	[redacted]	Death	1 Days	Severe	Y	N	Discontinued	Fatal	
	Treatment	[46]	[UNKNOWN CAUSE OF DEATH]		[5]					
Trial Number=3222-011, Site Number=0168, Subject ID=[redacted], Gender=F, Age=5[redacted] Years, Race=White										
[redacted]	Part 1	[redacted]	Gamma-glutamyltransferase increased	Continuing	Moderate	N	N	None	Not Resolved	[redacted]
	Part 1	[85]	[Elevated GGT]							[96]
	Part 1	[redacted]	Transaminases increased	Continuing	Moderate	N	N	None	Not Resolved	[redacted]
	Part 1	[85]	[Transaminitis]							[96]
	Part 1	[redacted]	Alcoholic seizure	Continuing	Moderate	N	N	None	Not Resolved	[redacted]
	Part 1	[96]	[Alcohol-related seizure disorder]							[96]
	Part 1	[redacted]	Anaemia	Continuing	Moderate	N	N	None	Not Resolved	[redacted]

Listing of Adverse Events in Subjects Who Died
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

Subject ID	Epoch	Onset Date [Relative Day]	Adverse Event MedDRA Preferred Term [Adverse Event Verbatim]	Duration	Intensity [Toxicity Grade]	Serious	Related	Action Taken	Outcome	Death Date [Relative Day]
MK-3222 100mg										
Trial Number=3222-011, Site Number=0168, Subject ID=[redacted], Gender=F, Age=5[redacted] Years, Race=White										
[redacted]	Part 1	[96]	[Alcohol-related anemia]							[96]
	Part 1	[redacted]	Asthenia	Continuing	Moderate	N	N	None	Not Resolved	[redacted]
	Part 1	[96]	[asthenia]							[96]
	Part 1	[redacted]	Cardiomyopathy alcoholic	1 Days	Severe	Y	N	Discontinued	Fatal	[redacted]
	Part 1	[96]	[Cardiomyopathy alcoholic]							[96]
	Part 1	[redacted]	Steatohepatitis	1 Days	Severe	Y	N	Discontinued	Fatal	[redacted]
	Part 1	[96]	[Severe Alcoholic steatohepatitis]							[96]
Trial Number=3222-011, Site Number=0177, Subject ID=[redacted], Gender=M, Age=4[redacted] Years, Race=White										
[redacted]	Part 1	[redacted]	Abdominal pain upper	2.73 Months	Mild	N	N	None	Resolved	[redacted]
	Part 1	[1]	[STOMACH ACHE FOLLOWING INJECTION]							[356]
	Part 1	[redacted]	Decreased appetite	9.17 Months	Mild	N	N	None	Resolved	[redacted]
	Part 1	[1]	[Decrease of Appetite Following Injection]							[356]
	Part 1	[redacted]	Arthralgia	Continuing	Moderate	N	N	None	Not Resolved	[redacted]
	Part 1	[78]	[Right Knee Pain]							[356]
	Part 2	[redacted]	Arthralgia	Continuing	Moderate	N	N	None	Not Resolved	[redacted]
	Part 2	[134]	[Achy Joints (feet, wrisits, ankles)]							[356]
	Part 3	[redacted]	Headache	Continuing	Mild	N	N	None	Not Resolved	[redacted]
	Part 3	[234]	[Headaches (intermittent)]							[356]
	Part 3	[redacted]	Night sweats	Continuing	Mild	N	N	None	Not Resolved	[redacted]
	Part 3	[234]	[night sweats(intermittent)]							[356]

Listing of Adverse Events in Subjects Who Died
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

Subject ID	Epoch	Onset Date [Relative Day]	Adverse Event MedDRA Preferred Term [Adverse Event Verbatim]	Duration	Intensity [Toxicity Grade]	Serious	Related	Action Taken	Outcome	Death Date [Relative Day]
MK-3222 100mg										
Trial Number=3222-011, Site Number=0177, Subject ID=[redacted], Gender=M, Age=4[redacted] Years, Race=White										
[redacted]	Part 3	[redacted]	Arthralgia	Continuing	Moderate	N	N	None	Not Resolved	[redacted]
	Part 3	[236]	[Knee Pain (Due to Fall)]							[356]
	Part 3	[redacted]	Upper respiratory tract infection	1 Weeks	Moderate	N	N	None	Resolved	[redacted]
	Part 3	[238]	[Upper Respitory Infection]							[356]
	Part 3	[redacted]	Abscess oral	Continuing	Moderate	N	N	None	Not Resolved	[redacted]
	Part 3	[300]	[Oral Abcess]							[356]
	Part 3	[redacted]	Acute sinusitis	Continuing	Moderate	N	N	None	Not Resolved	[redacted]
	Part 3	[300]	[Right Maxillary Sinusitis Acute]							[356]
	Part 3	[redacted]	Nausea	Continuing	Severe	N	N	None	Not Resolved	[redacted]
	Part 3	[312]	[Nausea with vomiting]							[356]
	Part 3	[redacted]	Acute myeloid leukaemia	37 Days	Moderate	Y	N	Discontinued	Fatal	[redacted]
	Part 3	[320]	[Acute Myelogenous Leukemia]							[356]
	Part 3	[redacted]	Azotaemia	Continuing		N	N	None	Not Resolved	[redacted]
	Part 3	[320]	[Uremia]							[356]
	Part 3	[redacted]	Gingival hypertrophy	Continuing	Severe	N	N	None	Not Resolved	[redacted]
	Part 3	[320]	[gingival hyperplasia]							[356]
	Part 3	[redacted]	Hypovolaemia	Continuing		N	N	None	Not Resolved	[redacted]
	Part 3	[320]	[Hypovolemia]							[356]
	Part 3	[redacted]	Malnutrition	Continuing		N	N	None	Not Resolved	[redacted]
	Part 3	[320]	[Severe protein-calorie malnutrition]							[356]
	Part 3	[redacted]	Oedema peripheral	Continuing	Mild	N	N	None	Not Resolved	[redacted]
	Part 3	[320]	[Lower extremity Edema]							[356]

Listing of Adverse Events in Subjects Who Died
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

Subject ID	Epoch	Onset Date [Relative Day]	Adverse Event MedDRA Preferred Term [Adverse Event Verbatim]	Duration	Intensity [Toxicity Grade]	Serious	Related	Action Taken	Outcome	Death Date [Relative Day]
MK-3222 100mg										
Trial Number=3222-011, Site Number=0177, Subject ID=[redacted], Gender=M, Age=4[redacted] Years, Race=White										
[redacted]	Part 3	[redacted]	Oedema peripheral	Continuing		N	N	None	Not Resolved	[redacted]
	Part 3	[320]	[Periphreal Edema]							[356]
	Part 3	[redacted]	Oliguria	Continuing		N	N	None	Not Resolved	[redacted]
	Part 3	[320]	[Oliguria]							[356]
	Part 3	[redacted]	Pain	Continuing		N	N	None	Not Resolved	[redacted]
	Part 3	[320]	[Chronic Pain]							[356]
	Part 3	[redacted]	Respiratory distress	Continuing		N	N	None	Not Resolved	[redacted]
	Part 3	[320]	[Dyspnea-Acute respiratory distress]							[356]
	Part 3	[redacted]	Retching	Continuing		N	N	None	Not Resolved	[redacted]
	Part 3	[320]	[Gagging]							[356]
	Part 3	[redacted]	Shock haemorrhagic	Continuing		N	N	None	Not Resolved	[redacted]
	Part 3	[320]	[Hemorrhagic Shock]							[356]
	Part 3	[redacted]	Ventricular tachycardia	Continuing		N	N	None	Not Resolved	[redacted]
	Part 3	[320]	[Non-Sustained Ventricular Tachycardia]							[356]
	Part 3	[redacted]	Atelectasis	Continuing	Mild	N	N	None	Not Resolved	[redacted]
	Part 3	[324]	[Bibasilar Atelectasis]							[356]
	Part 3	[redacted]	Peripheral swelling	Continuing	Moderate	N	N	None	Not Resolved	[redacted]
	Part 3	[326]	[Left Leg Swelling]							[356]
	Part 3	[redacted]	Thrombophlebitis superficial	Continuing	Moderate	N	N	None	Not Resolved	[redacted]
	Part 3	[328]	[superficial venous thrombosis involving the cephalic vein]							[356]
	Part 3	[redacted]	Inguinal mass	Continuing	Moderate	N	N	None	Not Resolved	[redacted]

Listing of Adverse Events in Subjects Who Died
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

Subject ID	Epoch	Onset Date [Relative Day]	Adverse Event MedDRA Preferred Term [Adverse Event Verbatim]	Duration	Intensity [Toxicity Grade]	Serious	Related	Action Taken	Outcome	Death Date [Relative Day]
MK-3222 100mg										
Trial Number=3222-011, Site Number=0177, Subject ID=[redacted], Gender=M, Age=4[redacted] Years, Race=White										
[redacted]	Part 3	[329]	[Left groin hypoechoic mass]							[356]
	Part 3	[redacted]	Oral candidiasis	Continuing	Mild	N	N	None	Not Resolved	[redacted]
	Part 3	[329]	[Thrush (oral)]							[356]
	Part 3	[redacted]	Atelectasis	Continuing		N	N	None	Not Resolved	[redacted]
	Part 3	[332]	[Atelectasis]							[356]
	Part 3	[redacted]	Febrile neutropenia	Continuing		N	N	None	Not Resolved	[redacted]
	Part 3	[332]	[Neutropenic Fever]							[356]
	Part 3	[redacted]	Thrombocytopenia	Continuing		N	N	None	Not Resolved	[redacted]
	Part 3	[332]	[Thrombocytopenia]							[356]
	Part 3	[redacted]	Pulmonary oedema	Continuing		N	N	None	Not Resolved	[redacted]
	Part 3	[340]	[Pulmonary edema and bilateral effusions]							[356]
	Part 3	[redacted]	End stage renal disease	Continuing	Severe	N	N	None	Not Resolved	[redacted]
	Part 3	[341]	[Renal Failure-end stage]							[356]
	Part 3	[redacted]	Hypotension	Continuing		N	N	None	Not Resolved	[redacted]
	Part 3	[341]	[Hypotension]							[356]
	Part 3	[redacted]	Respiratory failure	2.29 Weeks		N	N	None	Resolved	[redacted]
	Part 3	[341]	[Hypoxemic respiratory failure]							[356]
	Part 3	[redacted]	Septic shock	Continuing	Severe	N	N	None	Not Resolved	[redacted]
	Part 3	[341]	[Septic shock-Stenotrophomonas maltophia]							[356]
	Part 3	[redacted]	Atrial fibrillation	Continuing		N	N	None	Not Resolved	[redacted]
	Part 3	[342]	[A-fib with RVR]							[356]
	Part 3	[redacted]	Bone marrow failure	Continuing		N	N	None	Not Resolved	[redacted]

Listing of Adverse Events in Subjects Who Died
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

Subject ID	Epoch	Onset Date [Relative Day]	Adverse Event MedDRA Preferred Term [Adverse Event Verbatim]	Duration	Intensity [Toxicity Grade]	Serious	Related	Action Taken	Outcome	Death Date [Relative Day]
MK-3222 100mg										
Trial Number=3222-011, Site Number=0177, Subject ID=[redacted], Gender=M, Age=4[redacted] Years, Race=White										
[redacted]	Part 3	[342]	[Bone marrow suppression]							[356]
	Part 3	[redacted]	Coagulopathy	Continuing		N	N	None	Not Resolved	[redacted]
	Part 3	[342]	[Coagulopathy]							[356]
	Part 3	[redacted]	Encephalopathy	Continuing		N	N	None	Not Resolved	[redacted]
	Part 3	[342]	[Encephalopathy]							[356]
	Part 3	[redacted]	Gastric ileus	Continuing	Severe	N	N	None	Not Resolved	[redacted]
	Part 3	[342]	[Ileus with high gastric residual volumes]							[356]
	Part 3	[redacted]	Generalised oedema	Continuing		N	N	None	Not Resolved	[redacted]
	Part 3	[342]	[Anasarca]							[356]
	Part 3	[redacted]	Hyperbilirubinaemia	Continuing	Severe	N	N	None	Not Resolved	[redacted]
	Part 3	[342]	[Hyperbilirubinemia]							[356]
	Part 3	[redacted]	Metabolic acidosis	Continuing		N	N	None	Not Resolved	[redacted]
	Part 3	[342]	[Uncompensated metabolic acidosis]							[356]
	Part 3	[redacted]	Pancytopenia	Continuing		N	N	None	Not Resolved	[redacted]
	Part 3	[342]	[Pancytopenia]							[356]
	Part 3	[redacted]	Panniculitis	Continuing		N	N	None	Not Resolved	[redacted]
	Part 3	[342]	[Panniculitis]							[356]
	Part 3	[redacted]	Pneumonia bacterial	Continuing		N	N	None	Not Resolved	[redacted]
	Part 3	[342]	[Stenotrophomonas pneumonia and bacteremia]							[356]
	Part 3	[redacted]	Upper gastrointestinal haemorrhage	Continuing		N	N	None	Not Resolved	[redacted]
	Part 3	[348]	[Upper gastrointestinal bleeding]							[356]
	Part 3	[redacted]	Hypoalbuminaemia	Continuing	Severe	N	N	None	Not Resolved	[redacted]

Listing of Adverse Events in Subjects Who Died
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

Subject ID	Epoch	Onset Date [Relative Day]	Adverse Event MedDRA Preferred Term [Adverse Event Verbatim]	Duration	Intensity [Toxicity Grade]	Serious	Related	Action Taken	Outcome	Death Date [Relative Day]
MK-3222 100mg										
Trial Number=3222-011, Site Number=0177, Subject ID=[redacted], Gender=M, Age=4[redacted] Years, Race=White										
[redacted]	Part 3	[349]	[Hypoalbuminemia]							[356]
	Part 3	[redacted]	Ischaemic ulcer	Continuing		N	N	None	Not Resolved	[redacted]
	Part 3	[349]	[ISCHEMIC ULCER]							[356]
	Part 3	[redacted]	Complications of bone marrow transplant	Continuing		N	N	None	Not Resolved	[redacted]
	Part 3	[353]	[Complication of bone marrow transplant]							[356]
Trial Number=3222-011, Site Number=1169, Subject ID=[redacted], Gender=M, Age=7[redacted] Years, Race=Asian										
[redacted]	Part 1	[redacted]	Skin abrasion	1.14 Weeks	Mild	N	N	None	Resolved	[redacted]
	Part 1	[53]	[Abrasions on left upper lip and left forearm - healing, no infection]							[290]
	Part 2	[redacted]	Plantar fasciitis	4 Weeks	Moderate	N	N	None	Resolved	[redacted]
	Part 2	[200]	[Bilateral Plantar Facitis]							[290]
	Part 3	[redacted]	Psoriatic arthropathy	Continuing	Moderate	N	N	None	Not Resolved	[redacted]
	Part 3	[245]	[Psoriatic Arthritis]							[290]
	Part 3	[redacted]	Joint swelling	Continuing	Moderate	N	N	None	Not Resolved	[redacted]
	Part 3	[261]	[Right hand D3 PIP joint edema]							[290]
	Part 3	[redacted]	Respiratory arrest	1 Days	Severe	Y	N	Discontinued	Fatal	[redacted]
	Part 3	[290]	[Respiratory Arrest]							[290]
Trial Number=3222-011, Site Number=4908, Subject ID=[redacted], Gender=M, Age=4[redacted] Years, Race=White										
[redacted]	Part 1	[redacted]	Nasopharyngitis	4 Days	Moderate	N	Y	None	Resolved	[redacted]
	Part 1	[58]	[common cold]							[376]

Listing of Adverse Events in Subjects Who Died
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

Subject ID	Epoch	Onset Date [Relative Day]	Adverse Event MedDRA Preferred Term [Adverse Event Verbatim]	Duration	Intensity [Toxicity Grade]	Serious	Related	Action Taken	Outcome	Death Date [Relative Day]
MK-3222 100mg										
Trial Number=3222-011, Site Number=4908, Subject ID=[redacted], Gender=M, Age=4[redacted] Years, Race=White										
[redacted]	Part 2	[redacted]	Device dislocation	2 Days	Moderate	N	N	None	Resolved	[redacted]
	Part 2	[149]	[Gastric band migration]							[376]
	Part 3	[redacted]	Renal colic	1.29 Weeks	Moderate	N	N	None	Resolved	[redacted]
	Part 3	[208]	[renal colic]							[376]
	Part 3	[redacted]	Myocardial infarction	1 Days	Severe	Y	N	None	Fatal	[redacted]
	Part 3	[376]	[cardiac infarction]							[376]
MK-3222 200mg										
Trial Number=3222-010, Site Number=0114, Subject ID=[redacted], Gender=M, Age=5[redacted] Years, Race=Multi-Racial										
[redacted]	Part 1	[redacted]	Cough	Continuing	Mild	N	N	None	Not Resolved	[redacted]
	Part 1	[10]	[Cough in a.m.]		[1]					[411]
	Part 1	[redacted]	Arthralgia	1.05 Months	Mild	N	N	None	Resolved	[redacted]
	Part 1	[89]	[Right Knee Pain]							[411]
	Part 3	[redacted]	Nasopharyngitis	2 Days	Mild	N	N	None	Resolved	[redacted]
	Part 3	[220]	[Common Cold]							[411]
	Part 3	[redacted]	Arthralgia	Continuing	Mild	N	N	None	Not Resolved	[redacted]
	Part 3	[284]	[Joint Pain]							[411]
	Part 3	[redacted]	Laceration	Continuing	Moderate	N	N	None	Not Resolved	[redacted]
	Part 3	[359]	[Laceration - Lower Left Leg]							[411]
	Part 3	[redacted]	Aneurysm	8 Days	Severe	Y	N	None	Fatal	[redacted]
	Part 3	[404]	[Type 1 aneurysmosis.]							[411]

Listing of Adverse Events in Subjects Who Died
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

Subject ID	Epoch	Onset Date [Relative Day]	Adverse Event MedDRA Preferred Term [Adverse Event Verbatim]	Duration	Intensity [Toxicity Grade]	Serious	Related	Action Taken	Outcome	Death Date [Relative Day]
MK-3222 200mg										
Trial Number=3222-010, Site Number=0114, Subject ID=[redacted], Gender=M, Age=5[redacted] Years, Race=Multi-Racial										
[redacted]	Part 3	[redacted]	Coronary artery disease	Continuing	Severe	Y	N	None	Not Resolved	[redacted]
	Part 3	[404]	[Coronary Artery Disease]							[411]
Etanercept 50mg										
Trial Number=3222-011, Site Number=3906, Subject ID=[redacted], Gender=M, Age=6[redacted] Years, Race=White										
[redacted]	Part 2	[redacted]	Lung adenocarcinoma	Continuing	Severe	Y	N	Discontinued	Not Resolved	[redacted]
	Part 2	[191]	[adenocarcinoma of lung]							[452]
	Part 3	[redacted]	Cholelithiasis	Continuing	Mild	N	N	None	Not Resolved	[redacted]
	Part 3	[218]	[gallstones]							[452]
	Part 3	[redacted]	Sepsis	12 Days	Severe	Y	N	N/A	Fatal	[redacted]

Listing of Adverse Events in Subjects Who Died
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

Subject ID	Epoch	Onset Date [Relative Day]	Adverse Event MedDRA Preferred Term [Adverse Event Verbatim]	Duration	Intensity [Toxicity Grade]	Serious	Related	Action Taken	Outcome	Death Date [Relative Day]
Etanercept 50mg										
Trial Number=3222-011, Site Number=3906, Subject ID=[redacted], Gender=M, Age=6[redacted] Years, Race=White										
[redacted]	Part 3	[441]	[Septicemia]							[452]

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.

Subject [redacted] completed the Base period on day 360, did not enter the extension or follow-up period and died 16 days after, on day 376. Subject [redacted] discontinued the Base Part 3 period due to an AE on day 286, did not enter the extension or follow-up period and died later, on day 452.

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: 5.3.5.3-10]

付録 2.7.4-34
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

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

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

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

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	Bowen's disease	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

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

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 With Sequelae
6102	[redacted]	MK-3222 100 mg	407	447	Cholelithiasis	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

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	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	Carcinoma in situ 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	Rotator cuff syndrome	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
6107	[redacted]	Placebo	450	456	Squamous cell carcinoma of skin	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

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
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
0172	[redacted]	MK-3222 200 mg	112	364	Basal cell carcinoma	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

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 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
0187	[redacted]	MK-3222 200 mg	30	22	Atrial fibrillation	Severe	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

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
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
3602	[redacted]	MK-3222 200 mg	329	391	Spondylolisthesis	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

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
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
4901	[redacted]	MK-3222 100 mg	278	365	Transient ischaemic attack	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

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
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
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

Listing of Subjects with Serious Adverse Events
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

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
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
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

Listing of Subjects with Serious Adverse Events
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

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
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
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

Listing of Subjects with Serious Adverse Events
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

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
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

Listing of Subjects with Serious Adverse Events
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

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
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
4939	[redacted]	MK-3222 100 mg	307	362	Dyspepsia	Moderate	Not Related	Dose Not Changed	Recovered/Resolved
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.

[Source: 5.3.5.3-10]

付録 2.7.4-35
重篤な有害事象発現被験者（1 投与群以上で 100 人年当たり被験者 > 0 例で発現）
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

	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†)
Subjects in population	588		1083		1041		1911		313		381		363		933	
with one or more serious adverse events	14	6.40	58	5.81	67	7.21	124	6.43	20	13.04	24	4.88	26	5.46	57	4.73
with no serious adverse events	574	262.27	1025	102.67	974	104.86	1787	92.73	293	190.98	357	72.53	337	70.79	876	72.66
Blood and lymphatic system disorders	**1**	**0.46**	**0**	**0.00**	**0**	**0.00**	**0**	**0.00**	**0**	**0.00**	**0**	**0.00**	**0**	**0.00**	**0**	**0.00**
Anaemia	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Cardiac disorders	**1**	**0.46**	**6**	**0.60**	**8**	**0.86**	**14**	**0.73**	**2**	**1.30**	**2**	**0.41**	**1**	**0.21**	**3**	**0.25**
Acute myocardial infarction	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Angina pectoris	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Atrial fibrillation	0	0.00	2	0.20	2	0.22	4	0.21	0	0.00	0	0.00	1	0.21	1	0.08
Atrial flutter	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Cardiac failure	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Cardiac failure congestive	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Cardiomyopathy alcoholic	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Coronary artery disease	0	0.00	0	0.00	4	0.43	4	0.21	0	0.00	0	0.00	0	0.00	0	0.00
Coronary artery stenosis	0	0.00	1	0.10	0	0.00	1	0.05	1	0.65	1	0.20	0	0.00	1	0.08
Mitral valve incompetence	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Myocardial infarction	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Pericarditis	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Tachycardia	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Ear and labyrinth disorders	**0**	**0.00**	**1**	**0.10**	**0**	**0.00**	**1**	**0.05**	**0**	**0.00**	**1**	**0.20**	**0**	**0.00**	**1**	**0.08**
Vertigo	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Endocrine disorders	**0**	**0.00**	**1**	**0.10**	**0**	**0.00**	**1**	**0.05**	**0**	**0.00**	**1**	**0.20**	**0**	**0.00**	**1**	**0.08**
Hyperthyroidism	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08

Subjects with Serious Adverse Events (Occurring in > 0 Subjects per 100 Subject Years in One or More Treatment Groups)
Exposure Adjusted (Based on 20-Week Follow-up)
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

	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†)
Eye disorders	**0**	**0.00**	**0**	**0.00**	**1**	**0.11**	**1**	**0.05**	**0**	**0.00**	**0**	**0.00**	**0**	**0.00**	**0**	**0.00**
Cataract	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Macular fibrosis	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Gastrointestinal disorders	**1**	**0.46**	**8**	**0.80**	**4**	**0.43**	**12**	**0.62**	**0**	**0.00**	**5**	**1.02**	**2**	**0.42**	**7**	**0.58**
Abdominal hernia	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Abdominal pain	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Abdominal pain upper	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Constipation	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Diverticulum	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Dyspepsia	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Food poisoning	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Gastritis	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Haemorrhoids thrombosed	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Oesophageal polyp	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Pancreatitis	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Pancreatitis acute	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Salivary gland enlargement	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
General disorders and administration site conditions	**0**	**0.00**	**2**	**0.20**	**2**	**0.22**	**4**	**0.21**	**0**	**0.00**	**1**	**0.20**	**2**	**0.42**	**3**	**0.25**
Death	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Non-cardiac chest pain	0	0.00	1	0.10	2	0.22	3	0.16	0	0.00	1	0.20	2	0.42	3	0.25
Hepatobiliary disorders	**0**	**0.00**	**3**	**0.30**	**1**	**0.11**	**4**	**0.21**	**1**	**0.65**	**1**	**0.20**	**1**	**0.21**	**3**	**0.25**
Bile duct stone	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Cholecystitis	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08

Subjects with Serious Adverse Events (Occurring in > 0 Subjects per 100 Subject Years in One or More Treatment Groups)
Exposure Adjusted (Based on 20-Week Follow-up)
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

	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†)
Cholelithiasis	0	0.00	2	0.20	0	0.00	2	0.10	0	0.00	1	0.20	0	0.00	2	0.17
Steatohepatitis	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Immune system disorders	**0**	**0.00**	**0**	**0.00**	**1**	**0.11**	**1**	**0.05**	**0**	**0.00**	**0**	**0.00**	**0**	**0.00**	**0**	**0.00**
Anaphylactic reaction	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Infections and infestations	**2**	**0.91**	**10**	**1.00**	**15**	**1.61**	**25**	**1.30**	**2**	**1.30**	**4**	**0.81**	**4**	**0.84**	**12**	**1.00**
Appendicitis	0	0.00	2	0.20	0	0.00	2	0.10	0	0.00	1	0.20	0	0.00	1	0.08
Bone tuberculosis	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Cellulitis	2	0.91	1	0.10	3	0.32	4	0.21	0	0.00	0	0.00	1	0.21	2	0.17
Diverticulitis	0	0.00	1	0.10	3	0.32	4	0.21	0	0.00	0	0.00	1	0.21	1	0.08
Epiglottitis	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	0	0.00	0	0.00	1	0.08
Erysipelas	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Gastroenteritis	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	0	0.00	0	0.00	0	0.00
Gastroenteritis salmonella	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Herpes zoster	0	0.00	0	0.00	1	0.11	1	0.05	1	0.65	0	0.00	0	0.00	0	0.00
Pneumonia	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Pyelonephritis	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Sepsis	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Sinusitis	0	0.00	3	0.30	0	0.00	3	0.16	0	0.00	2	0.41	0	0.00	3	0.25
Soft tissue infection	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Urosepsis	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Wound infection	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	0	0.00	0	0.00	1	0.08
Injury, poisoning and procedural complications	**0**	**0.00**	**6**	**0.60**	**4**	**0.43**	**10**	**0.52**	**2**	**1.30**	**3**	**0.61**	**4**	**0.84**	**8**	**0.66**
Ankle fracture	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00

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Exposure Adjusted (Based on 20-Week Follow-up)
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

	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†)
Concussion	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Contusion	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Hand fracture	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Humerus fracture	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Lower limb fracture	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	0	0.00	1	0.21	1	0.08
Meniscus injury	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Tendon rupture	0	0.00	2	0.20	2	0.22	4	0.21	0	0.00	1	0.20	2	0.42	3	0.25
Investigations	**0**	**0.00**	**0**	**0.00**	**0**	**0.00**	**0**	**0.00**	**1**	**0.65**	**0**	**0.00**	**0**	**0.00**	**0**	**0.00**
Blood glucose increased	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Metabolism and nutrition disorders	**0**	**0.00**	**0**	**0.00**	**0**	**0.00**	**0**	**0.00**	**1**	**0.65**	**0**	**0.00**	**0**	**0.00**	**0**	**0.00**
Obesity	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Musculoskeletal and connective tissue disorders	**1**	**0.46**	**3**	**0.30**	**8**	**0.86**	**11**	**0.57**	**1**	**0.65**	**2**	**0.41**	**5**	**1.05**	**10**	**0.83**
Arthropathy	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Back pain	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	1	0.20	1	0.21	2	0.17
Bursitis	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Cervical spinal stenosis	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Intervertebral disc disorder	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Intervertebral disc protrusion	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Osteoarthritis	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Osteonecrosis	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Psoriatic arthropathy	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Rotator cuff syndrome	0	0.00	0	0.00	1	0.11	1	0.05	1	0.65	0	0.00	1	0.21	1	0.08
Spondylolisthesis	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08

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	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†)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**3**	**1.37**	**15**	**1.50**	**10**	**1.08**	**25**	**1.30**	**5**	**3.26**	**4**	**0.81**	**4**	**0.84**	**8**	**0.66**
Acute myeloid leukaemia	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Basal cell carcinoma	1	0.46	5	0.50	4	0.43	9	0.47	2	1.30	1	0.20	1	0.21	2	0.17
Benign biliary neoplasm	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Bladder transitional cell carcinoma	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Bowen's disease	0	0.00	2	0.20	1	0.11	3	0.16	0	0.00	0	0.00	1	0.21	1	0.08
Breast cancer	0	0.00	0	0.00	1	0.11	1	0.05	1	0.65	0	0.00	0	0.00	0	0.00
Carcinoma in situ of skin	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Lung adenocarcinoma	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Malignant melanoma in situ	0	0.00	2	0.20	0	0.00	2	0.10	0	0.00	1	0.20	0	0.00	1	0.08
Pancreatic carcinoma	0	0.00	0	0.00	2	0.22	2	0.10	0	0.00	0	0.00	0	0.00	0	0.00
Rectal cancer	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Renal oncocytoma	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Squamous cell carcinoma of skin	1	0.46	3	0.30	2	0.22	5	0.26	0	0.00	0	0.00	2	0.42	2	0.17
Thyroid cancer	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Nervous system disorders	**2**	**0.91**	**2**	**0.20**	**5**	**0.54**	**7**	**0.36**	**2**	**1.30**	**2**	**0.41**	**2**	**0.42**	**4**	**0.33**
Carotid artery stenosis	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Cerebellar infarction	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Headache	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Lacunar infarction	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Presyncope	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Radiculopathy	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Sciatica	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08

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	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)	n	(m†)
Seizure	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Thrombotic cerebral infarction	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Transient ischaemic attack	0	0.00	1	0.10	1	0.11	2	0.10	0	0.00	1	0.20	0	0.00	1	0.08
Pregnancy, puerperium and perinatal conditions	**0**	**0.00**	**0**	**0.00**	**2**	**0.22**	**2**	**0.10**	**0**	**0.00**	**0**	**0.00**	**0**	**0.00**	**0**	**0.00**
Abortion spontaneous	0	0.00	0	0.00	2	0.22	2	0.10	0	0.00	0	0.00	0	0.00	0	0.00
Psychiatric disorders	**0**	**0.00**	**2**	**0.20**	**1**	**0.11**	**3**	**0.16**	**2**	**1.30**	**2**	**0.41**	**0**	**0.00**	**2**	**0.17**
Alcoholism	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Bipolar disorder	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	1	0.20	0	0.00	1	0.08
Borderline personality disorder	0	0.00	0	0.00	0	0.00	0	0.00	1	0.65	0	0.00	0	0.00	0	0.00
Depression	0	0.00	2	0.20	0	0.00	2	0.10	0	0.00	2	0.41	0	0.00	2	0.17
Suicide attempt	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Renal and urinary disorders	**1**	**0.46**	**2**	**0.20**	**1**	**0.11**	**3**	**0.16**	**0**	**0.00**	**0**	**0.00**	**0**	**0.00**	**1**	**0.08**
Nephrolithiasis	0	0.00	2	0.20	0	0.00	2	0.10	0	0.00	0	0.00	0	0.00	0	0.00
Obstructive uropathy	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	1	0.08
Ureterolithiasis	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Reproductive system and breast disorders	**1**	**0.46**	**0**	**0.00**	**2**	**0.22**	**2**	**0.10**	**0**	**0.00**	**0**	**0.00**	**2**	**0.42**	**2**	**0.17**
Breast cyst	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Ovarian cyst	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	1	0.21	1	0.08
Uterine haemorrhage	1	0.46	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00	0	0.00
Respiratory, thoracic and mediastinal disorders	**0**	**0.00**	**3**	**0.30**	**3**	**0.32**	**6**	**0.31**	**1**	**0.65**	**0**	**0.00**	**0**	**0.00**	**0**	**0.00**
Chronic obstructive pulmonary disease	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Pneumothorax	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Pulmonary embolism	0	0.00	0	0.00	2	0.22	2	0.10	0	0.00	0	0.00	0	0.00	0	0.00

Subjects with Serious Adverse Events (Occurring in > 0 Subjects per 100 Subject Years in One or More Treatment Groups)
Exposure Adjusted (Based on 20-Week Follow-up)
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

	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†)
Respiratory arrest	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Sleep apnoea syndrome	0	0.00	1	0.10	0	0.00	1	0.05	1	0.65	0	0.00	0	0.00	0	0.00
Skin and subcutaneous tissue disorders	**1**	**0.46**	**2**	**0.20**	**1**	**0.11**	**3**	**0.16**	**1**	**0.65**	**0**	**0.00**	**0**	**0.00**	**0**	**0.00**
Psoriasis	1	0.46	2	0.20	1	0.11	3	0.16	1	0.65	0	0.00	0	0.00	0	0.00
Vascular disorders	**0**	**0.00**	**1**	**0.10**	**3**	**0.32**	**4**	**0.21**	**0**	**0.00**	**0**	**0.00**	**0**	**0.00**	**0**	**0.00**
Aneurysm	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Deep vein thrombosis	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Lymphoedema	0	0.00	0	0.00	1	0.11	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00
Peripheral arterial occlusive disease	0	0.00	1	0.10	0	0.00	1	0.05	0	0.00	0	0.00	0	0.00	0	0.00

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

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

[Source: 5.3.5.3-10]

付録 2.7.4-36
治験中止に至った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

Site Number	Subject ID	Onset Treatment	Rel Day of Onset	Rel Day of Last Recorded Dose of Study Medication	Adverse Event	Intensity	Serious	Related	Action Taken	Outcome
Trial Number = 3222-003										
0100	[redacted]	MK-3222 25 mg	1	1	Diabetes mellitus	Mild	N	Not Related	Drug Withdrawn	Not Recovered/Not Resolved
0112	[redacted]	MK-3222 25 mg	379	366	Guttate psoriasis	Moderate	N	Not Related	Drug Withdrawn	Not Recovered/Not Resolved
0220	[redacted]	MK-3222 25 mg	190	113	Pregnancy	Mild	N	Not Related	Drug Withdrawn	Not Recovered/Not Resolved
0235	[redacted]	MK-3222 100 mg	170	115	Rectal cancer	Severe	Y	Not Related	Drug Withdrawn	Not Recovered/Not Resolved
0300	[redacted]	MK-3222 5 mg	30	1	Lymphadenopathy	Severe	N	Related	Drug Withdrawn	Recovered/Resolved
0300	[redacted]	MK-3222 100 mg	163	281	Gamma-glutamyltransferase increased	Moderate	N	Not Related	Drug Withdrawn	Not Recovered/Not Resolved
0300	[redacted]	MK-3222 100 mg	323	281	Alanine aminotransferase increased	Moderate	N	Not Related	Drug Withdrawn	Not Recovered/Not Resolved
0300	[redacted]	MK-3222 100 mg	323	281	Aspartate aminotransferase increased	Moderate	N	Not Related	Drug Withdrawn	Not Recovered/Not Resolved
0301	[redacted]	MK-3222 25 mg	366	281	Gamma-glutamyltransferase increased	Moderate	N	Related	Drug Withdrawn	Not Recovered/Not Resolved
0301	[redacted]	MK-3222 100 mg	289	191	Hyperlipidaemia	Moderate	N	Related	Drug Withdrawn	Not Recovered/Not Resolved
0301	[redacted]	MK-3222 100 mg	329	281	Pain in extremity	Moderate	N	Related	Drug Withdrawn	Not Recovered/Not Resolved
0301	[redacted]	MK-3222 100 mg	342	281	Hypertriglyceridaemia	Moderate	N	Related	Drug Withdrawn	Not Recovered/Not Resolved

Listing of Subjects with Adverse Events resulting in Discontinuation
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

Site Number	Subject ID	Onset Treatment	Rel Day of Onset	Rel Day of Last Recorded Dose of Study Medication	Adverse Event	Intensity	Serious	Related	Action Taken	Outcome
0303	[redacted]	MK-3222 25 mg	286	195	Psoriatic arthropathy	Moderate	Y	Not Related	Drug Withdrawn	Recovered/Resolved
0400	[redacted]	MK-3222 200 mg	367	302	Pregnancy	Mild	N	Not Related	Drug Withdrawn	Recovered/Resolved
0400	[redacted]	MK-3222 200 mg	143	113	Depression	Moderate	N	Related	Drug Withdrawn	Recovered/Resolved
0503	[redacted]	MK-3222 25 mg	135	113	Malignant melanoma	Severe	Y	Related	Drug Withdrawn	Not Recovered/Not Resolved
0800	[redacted]	MK-3222 100 mg	197	116	Malignant melanoma in situ		Y	Not Related	Drug Withdrawn	Recovered/Resolved
0800	[redacted]	MK-3222 100 mg	208	116	Malignant melanoma in situ		Y	Not Related	Drug Withdrawn	Recovered/Resolved
0801	[redacted]	MK-3222 200 mg	29	1	Lymphoedema	Moderate	Y	Related	Drug Withdrawn	Recovered/Resolved
0803	[redacted]	MK-3222 25 mg	137	113	Ischaemic stroke	Severe	Y	Related	Drug Withdrawn	Not Recovered/Not Resolved
0805	[redacted]	MK-3222 200 mg	256	196	Motor neurone disease	Moderate	N	Not Related	Drug Withdrawn	Not Recovered/Not Resolved
0808	[redacted]	Placebo	57	31	Alanine aminotransferase increased	Moderate	N	Related	Drug Withdrawn	Not Recovered/Not Resolved
0808	[redacted]	Placebo	57	31	Gamma-glutamyltransferase increased	Moderate	N	Related	Drug Withdrawn	Not Recovered/Not Resolved
0808	[redacted]	MK-3222 100 mg	46	30	Death	Severe	Y	Not Related	Drug Withdrawn	Fatal
1103	[redacted]	MK-3222 25 mg	1	1	Back pain	Severe	N	Not Related	Drug Withdrawn	Not Recovered/Not Resolved

Listing of Subjects with Adverse Events resulting in Discontinuation
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

Site Number	Subject ID	Onset Treatment	Rel Day of Onset	Rel Day of Last Recorded Dose of Study Medication	Adverse Event	Intensity	Serious	Related	Action Taken	Outcome
1302	[redacted]	MK-3222 100 mg	478	365	Thrombotic cerebral infarction	Severe	Y	Not Related	Drug Withdrawn	Not Recovered/Not Resolved
Trial Number = 3222-010										
0101	[redacted]	MK-3222 200 mg	27	27	Headache	Moderate	N	Related	Drug Withdrawn	Recovered/Resolved
0119	[redacted]	MK-3222 200 mg	-3	1	Chronic obstructive pulmonary disease	Moderate	Y	Not Related	Drug Withdrawn	Recovered/Resolved With Sequelae
0132	[redacted]	MK-3222 200 mg	53	31	Coronary artery disease	Severe	Y	Not Related	Drug Withdrawn	Recovered/Resolved
0136	[redacted]	MK-3222 200 mg	428	406	Tremor	Moderate	N	Not Related	Drug Withdrawn	Recovering/Resolving
0136	[redacted]	MK-3222 200 mg	78	29	Rash pustular	Mild	N	Related	Drug Withdrawn	Recovered/Resolved
0141	[redacted]	Placebo	88	88	Liver function test increased	Mild	N	Not Related	Drug Withdrawn	Unknown
0144	[redacted]	MK-3222 200 mg	155	113	Pancreatic carcinoma		Y	Not Related	Drug Withdrawn	Not Recovered/Not Resolved
1102	[redacted]	MK-3222 200 mg	87	81	Psoriasis	Moderate	Y	Related	Drug Withdrawn	Recovered/Resolved
1114	[redacted]	Placebo	397	393	Cerebellar infarction	Severe	Y	Not Related	Drug Withdrawn	Recovered/Resolved With Sequelae
1117	[redacted]	MK-3222 200 mg	178	118	Bone tuberculosis	Moderate	Y	Related	Drug Withdrawn	Recovered/Resolved
4402	[redacted]	MK-3222 100 mg	190	345	Squamous cell carcinoma of skin	Mild	Y	Not Related	Drug Withdrawn	Recovered/Resolved

Listing of Subjects with Adverse Events resulting in Discontinuation
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

Site Number	Subject ID	Onset Treatment	Rel Day of Onset	Rel Day of Last Recorded Dose of Study Medication	Adverse Event	Intensity	Serious	Related	Action Taken	Outcome
6104	[redacted]	MK-3222 200 mg	334	306	Pancreatic carcinoma	Severe	Y	Not Related	Drug Withdrawn	Not Recovered/Not Resolved
8107	[redacted]	MK-3222 100 mg	337	449	Psoriasis	Mild	N	Related	Drug Withdrawn	Recovered/Resolved
8112	[redacted]	MK-3222 200 mg	12	1	Suicide attempt	Severe	Y	Not Related	Drug Withdrawn	Recovered/Resolved
8130	[redacted]	MK-3222 100 mg	446	424	Arthritis	Severe	N	Not Related	Drug Withdrawn	Not Recovered/Not Resolved
Trial Number = 3222-011										
0163	[redacted]	Etanercept 50 mg	57	64	Upper respiratory tract infection	Moderate	N	Related	Drug Withdrawn	Recovered/Resolved
0168	[redacted]	MK-3222 100 mg	96	82	Cardiomyopathy alcoholic	Severe	Y	Not Related	Drug Withdrawn	Fatal
0168	[redacted]	MK-3222 100 mg	96	82	Steatohepatitis	Severe	Y	Not Related	Drug Withdrawn	Fatal
0172	[redacted]	MK-3222 200 mg	363	337	Diverticulitis	Mild	N	Not Related	Drug Withdrawn	Not Recovered/Not Resolved
0172	[redacted]	MK-3222 200 mg	4	39	Hepatic enzyme increased	Moderate	N	Not Related	Drug Withdrawn	Not Recovered/Not Resolved
0176	[redacted]	Etanercept 50 mg	139	197	Alcoholism	Severe	Y	Not Related	Drug Withdrawn	Recovered/Resolved
0177	[redacted]	MK-3222 100 mg	320	257	Acute myeloid leukaemia	Moderate	Y	Not Related	Drug Withdrawn	Fatal
0178	[redacted]	MK-3222 100 mg	116	114	Hypersensitivity	Moderate	N	Related	Drug Withdrawn	Recovered/Resolved

Listing of Subjects with Adverse Events resulting in Discontinuation
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

Site Number	Subject ID	Onset Treatment	Rel Day of Onset	Rel Day of Last Recorded Dose of Study Medication	Adverse Event	Intensity	Serious	Related	Action Taken	Outcome
0178	[redacted]	Placebo	50	56	Psoriasis	Severe	N	Not Related	Drug Withdrawn	Recovered/Resolved
0178	[redacted]	Etanercept 50 mg	71	105	Basal cell carcinoma	Mild	Y	Not Related	Drug Withdrawn	Recovered/Resolved
0182	[redacted]	MK-3222 100 mg	234	255	Optic ischaemic neuropathy	Moderate	N	Related	Drug Withdrawn	Not Recovered/Not Resolved
0186	[redacted]	Placebo	5	4	Angioedema	Severe	N	Related	Drug Withdrawn	Recovered/Resolved With Sequelae
0187	[redacted]	MK-3222 200 mg	30	22	Atrial fibrillation	Severe	Y	Not Related	Drug Withdrawn	Recovered/Resolved
0189	[redacted]	MK-3222 100 mg	84	60	Tachycardia	Mild	N	Related	Drug Withdrawn	Recovered/Resolved
1169	[redacted]	MK-3222 100 mg	290	282	Respiratory arrest	Severe	Y	Not Related	Drug Withdrawn	Fatal
1169	[redacted]	MK-3222 100 mg	105	191	Intraocular pressure increased	Moderate	N	Not Related	Drug Withdrawn	Recovered/Resolved
3304	[redacted]	MK-3222 200 mg	55	109	Psoriatic arthropathy	Moderate	N	Not Related	Drug Withdrawn	Not Recovered/Not Resolved
3307	[redacted]	MK-3222 100 mg	54	5	Abortion	Mild	N	Not Related	Drug Withdrawn	Recovered/Resolved
3906	[redacted]	Etanercept 50 mg	191	222	Lung adenocarcinoma	Severe	Y	Not Related	Drug Withdrawn	Not Recovered/Not Resolved
4305	[redacted]	Etanercept 50 mg	5	36	Injection site erythema	Mild	N	Related	Drug Withdrawn	Recovered/Resolved
4305	[redacted]	Etanercept 50 mg	5	36	Injection site swelling	Mild	N	Related	Drug Withdrawn	Recovered/Resolved

Listing of Subjects with Adverse Events resulting in Discontinuation
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

Site Number	Subject ID	Onset Treatment	Rel Day of Onset	Rel Day of Last Recorded Dose of Study Medication	Adverse Event	Intensity	Serious	Related	Action Taken	Outcome
4804	[redacted]	Etanercept 50 mg	21	1	Erysipelas	Moderate	N	Not Related	Drug Withdrawn	Recovered/Resolved
4904	[redacted]	Etanercept 50 mg	37	37	Injection site reaction	Mild	N	Related	Drug Withdrawn	Recovered/Resolved
4905	[redacted]	MK-3222 100 mg	256	256	Bladder transitional cell carcinoma	Severe	Y	Related	Drug Withdrawn	Recovered/Resolved
4906	[redacted]	MK-3222 200 mg	107	103	Herpes zoster	Moderate	Y	Related	Drug Withdrawn	Recovered/Resolved
4907	[redacted]	MK-3222 100 mg	235	227	Atrial fibrillation	Severe	Y	Not Related	Drug Withdrawn	Recovered/Resolved
4918	[redacted]	Etanercept 50 mg	203	199	Psoriasis	Severe	Y	Not Related	Drug Withdrawn	Not Recovered/Not Resolved
4919	[redacted]	Etanercept 50 mg	37	36	Headache	Severe	Y	Related	Drug Withdrawn	Recovered/Resolved
4923	[redacted]	MK-3222 200 mg	248	222	Breast cancer	Moderate	Y	Related	Drug Withdrawn	Not Recovered/Not Resolved
4933	[redacted]	MK-3222 100 mg	350	333	Transaminases increased	Severe	N	Related	Drug Withdrawn	Not Recovered/Not Resolved
4933	[redacted]	MK-3222 100 mg	199	250	Squamous cell carcinoma of skin	Moderate	Y	Not 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.

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: 5.3.5.3-10]

付録 2.7.4-37
過量投与の有害事象が認められた被験者の一覧表
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

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Intensity	Ser-ious	Related	Action Taken	Outcome
Placebo								
Trial Number=3222-011, Site Number=0178, Subject ID=[redacted], Gender=F, Race=White, Age=5[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=366								
[redacted]	Part 1	1	Accidental overdose	Mild	N	N	None	Resolved
Trial Number=3222-011, Site Number=3207, Subject ID=[redacted], Gender=M, Race=Missing, Age=3[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=361								
[redacted]	Part 1	81	Accidental overdose	Mild	N	N	None	Resolved
Trial Number=3222-011, Site Number=4904, Subject ID=[redacted], Gender=M, Race=White, Age=4[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=366								
[redacted]	Part 2	113	Accidental overdose		N	N	None	Resolved
Trial Number=3222-011, Site Number=4917, Subject ID=[redacted], Gender=M, Race=White, Age=5[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=367								
[redacted]	Part 3	200	Accidental overdose	Mild	N	N	None	Resolved
MK-3222 100mg								
Trial Number=3222-011, Site Number=0178, Subject ID=[redacted], Gender=F, Race=Black Or African American, Age=4[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=371								
[redacted]	Part 1	1	Accidental overdose	Mild	N	N	None	Resolved
Trial Number=3222-011, Site Number=0188, Subject ID=[redacted], Gender=F, Race=White, Age=2[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=366								
[redacted]	Part 1	32	Accidental overdose	Moderate	N	N	None	Resolved
		58	Accidental overdose	Moderate	N	N	None	Resolved
Trial Number=3222-011, Site Number=4901, Subject ID=[redacted], Gender=M, Race=White, Age=4[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=366								
[redacted]	Part 1	60	Accidental overdose	Mild	N	N	None	Resolved

Listing of Subjects With Overdose Adverse Events
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Intensity	Ser-ious	Related	Action Taken	Outcome
MK-3222 100mg								
Trial Number=3222-011, Site Number=4901, Subject ID=[redacted], Gender=M, Race=White, Age=4[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=366								
[redacted]	Part 2	117	Accidental overdose	Mild	N	N	None	Resolved
Trial Number=3222-011, Site Number=4902, Subject ID=[redacted], Gender=F, Race=White, Age=2[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=368								
[redacted]	Part 3	204	Accidental overdose	Mild	N	N	None	Resolved
Trial Number=3222-011, Site Number=4915, Subject ID=[redacted], Gender=F, Race=White, Age=5[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=360								
[redacted]	Part 1	1	Accidental overdose		N	N	None	Resolved
MK-3222 200mg								
Trial Number=3222-010, Site Number=6101, Subject ID=[redacted], Gender=M, Race=White, Age=6[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=447								
[redacted]	Part 3	447	Accidental overdose	Mild	N	N	None	Resolved
Trial Number=3222-011, Site Number=0186, Subject ID=[redacted], Gender=F, Race=White, Age=4[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=365								
[redacted]	Part 1	8	Accidental overdose	Mild	N	N	None	Resolved
Trial Number=3222-011, Site Number=3307, Subject ID=[redacted], Gender=F, Race=White, Age=7[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=365								
[redacted]	Part 2	85	Accidental overdose	Mild	N	N	None	Resolved
Trial Number=3222-011, Site Number=4801, Subject ID=[redacted], Gender=M, Race=White, Age=2[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=364								
[redacted]	Part 1	25	Accidental overdose	Mild	N	N	None	Resolved

Listing of Subjects With Overdose Adverse Events
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Intensity	Ser-ious	Related	Action Taken	Outcome
MK-3222 200mg								
Trial Number=3222-011, Site Number=4804, Subject ID=[redacted], Gender=F, Race=White, Age=3[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=365								
[redacted]	Part 1	58	Accidental overdose	Mild	N	N	None	Resolved
Trial Number=3222-011, Site Number=4901, Subject ID=[redacted], Gender=M, Race=Asian, Age=3[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=360								
[redacted]	Part 1	57	Accidental overdose	Mild	N	N	None	Resolved
Trial Number=3222-011, Site Number=4901, Subject ID=[redacted], Gender=F, Race=White, Age=6[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=363								
[redacted]	Part 2	160	Accidental overdose	Mild	N	N	None	Resolved
Trial Number=3222-011, Site Number=4901, Subject ID=[redacted], Gender=M, Race=White, Age=4[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=365								
[redacted]	Part 1	57	Accidental overdose	Mild	N	N	None	Resolved
Trial Number=3222-011, Site Number=4908, Subject ID=[redacted], Gender=M, Race=White, Age=5[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=363								
[redacted]	Part 1	1	Accidental overdose		N	N	None	Resolved
Trial Number=3222-011, Site Number=4915, Subject ID=[redacted], Gender=M, Race=White, Age=6[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=393								
[redacted]	Part 2	113	Accidental overdose		N	N	None	Resolved
Trial Number=3222-011, Site Number=4918, Subject ID=[redacted], Gender=F, Race=White, Age=4[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=365								
[redacted]	Part 2	150	Accidental overdose		N	N	None	Resolved
Trial Number=3222-011, Site Number=4931, Subject ID=[redacted], Gender=M, Race=White, Age=3[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=338								
[redacted]	Part 2	92	Accidental overdose	Mild	N	N	None	Resolved

Listing of Subjects With Overdose Adverse Events
Phase 2 and 3: Base Period Safety Pool
All Subjects as Treated

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Intensity	Ser-ious	Related	Action Taken	Outcome
MK-3222 200mg								
Trial Number=3222-011, Site Number=4934, Subject ID=[redacted], Gender=M, Race=White, Age=3[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=366								
[redacted]	Part 3	257	Accidental overdose	Moderate	N	N	None	Resolved
Etanercept 50mg								
Trial Number=3222-011, Site Number=3206, Subject ID=[redacted], Gender=M, Race=White, Age=3[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=379								
[redacted]	Part 1	60	Accidental overdose	Mild	N	N	None	Resolved
Trial Number=3222-011, Site Number=3909, Subject ID=[redacted], Gender=F, Race=White, Age=3[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=196								
[redacted]	Part 2	135	Accidental overdose	Mild	N	N	None	Resolved
Trial Number=3222-011, Site Number=4801, Subject ID=[redacted], Gender=M, Race=Multi-Racial, Age=2[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=365								
[redacted]	Part 2	120	Accidental overdose	Mild	N	N	None	Resolved
Trial Number=3222-011, Site Number=4919, Subject ID=[redacted], Gender=M, Race=White, Age=6[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=190								
[redacted]	Part 1	67	Accidental overdose	Mild	N	N	None	Resolved
Trial Number=3222-011, Site Number=4931, Subject ID=[redacted], Gender=M, Race=White, Age=6[redacted] Years, Rel Day of Last Recorded Dose of Study Medication=360								
[redacted]	Part 1	30	Accidental overdose	Mild	N	N	None	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.

[Source: 5.3.5.3-10]

付録 2.7.4-38
重篤な有害事象を発現した被験者の一覧表
第 III 相試験：延長試験の安全性併合解析
1 回以上投与された被験者

Site Number	Subject ID	Onset Treatment	Rel Day of Onset†	Adverse Event	Intensity	Serious	Related	Action Taken	Outcome
Trial Number = 3222-010									
0106	[redacted]	MK-3222 200 mg	824	Cellulitis	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
0115	[redacted]	MK-3222 200 mg	640	Deep vein thrombosis	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
0115	[redacted]	MK-3222 200 mg	641	Pulmonary embolism	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
0117	[redacted]	MK-3222 100 mg	834	Osteoarthritis	Moderate	Y	Not Related	Dose Not Changed	Recovering/Resolving
0119	[redacted]	MK-3222 100 mg	885	Gastrectomy	Moderate	Y	Not 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
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
0137	[redacted]	MK-3222 100 mg	510	Diverticulum	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
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
0144	[redacted]	MK-3222 100 mg	455	Osteoarthritis	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae

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

Site Number	Subject ID	Onset Treatment	Rel Day of Onset†	Adverse Event	Intensity	Serious	Related	Action Taken	Outcome
0144	[redacted]	MK-3222 100 mg	645	Staphylococcal infection	Severe	Y	Related	Drug Withdrawn	Recovered/Resolved With Sequelae
0144	[redacted]	MK-3222 100 mg	799	Arthritis infective	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
0145	[redacted]	MK-3222 200 mg	698	Acetabulum 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 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
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
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
6102	[redacted]	MK-3222 100 mg	407	Cholelithiasis	Moderate	Y	Not Related	Dose Not Changed	Recovered/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
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
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
8141	[redacted]	MK-3222 100 mg	741	Cerebral infarction	Severe	Y	Related	Dose Not Changed	Not Recovered/Not 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 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
0178	[redacted]	MK-3222 100 mg	783	Appendicitis	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
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 200 mg	1031	Back pain	Severe	Y	Not Related	Dose Not Changed	Recovering/Resolving
1163	[redacted]	MK-3222 200 mg	717	Bladder transitional cell carcinoma	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved

Listing of Subjects with Serious Adverse Events
Phase 3: Extension Safety Pool
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	909		Severe	Y	Not Related	Dose Not Changed	Not Recovered/Not Resolved
3101	[redacted]	MK-3222 200 mg	552	Obesity	Moderate	Y	Not Related	Drug Interrupted	Recovered/Resolved
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
3307	[redacted]	MK-3222 200 mg	620	Laceration	Severe	Y	Not Related	Drug Interrupted	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
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	Dose Not Changed	Not Recovered/Not Resolved
3909	[redacted]	MK-3222 100 mg	493	Enterocolitis	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved
4801	[redacted]	MK-3222 200 mg	746	Accidental death	Severe	Y	Not Related	Not Applicable	Fatal
4801	[redacted]	MK-3222 100 mg	627	Psoriatic arthropathy	Moderate	Y	Not Related	Dose Not Changed	Not Recovered/Not Resolved
4802	[redacted]	MK-3222 100 mg	603	Psoriatic arthropathy	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
4804	[redacted]	MK-3222 200 mg	529	Chronic sinusitis	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved With Sequelae
4807	[redacted]	MK-3222 100 mg	797	Varicose vein	Mild	Y	Not Related	Dose Not Changed	Recovered/Resolved

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

Site Number	Subject ID	Onset Treatment	Rel Day of Onset†	Adverse Event	Intensity	Serious	Related	Action Taken	Outcome
4902	[redacted]	MK-3222 200 mg	589	Gastroenteritis bacterial	Severe	Y	Not Related	Dose Not Changed	Recovered/Resolved
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	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
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	688	Appendicitis	Severe	Y	Related	Dose Not Changed	Recovered/Resolved
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
4919	[redacted]	MK-3222 200 mg	404	Atrial fibrillation	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
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	754	Nerve root compression	Severe	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	1011	Myocardial infarction	Severe	Y	Not Related	Dose Not Changed	Recovering/Resolving
4926	[redacted]	MK-3222 200 mg	386	Umbilical hernia	Moderate	Y	Not Related	Dose Not Changed	Recovered/Resolved

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

Site Number	Subject ID	Onset Treatment	Rel Day of Onset†	Adverse Event	Intensity	Serious	Related	Action Taken	Outcome
4926	[redacted]	MK-3222 200 mg	758	Pneumonia	Severe	Y	Related	Drug Interrupted	Not Recovered/Not Resolved
4934	[redacted]	MK-3222 200 mg	709	Malocclusion	Mild	Y	Not Related	Dose Not Changed	Recovered/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
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	Drug Interrupted	Recovered/Resolved
4939	[redacted]	MK-3222 100 mg	470	Mesenteric artery thrombosis	Moderate	Y	Related	Drug Interrupted	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: [ISS-EXT: analysis-adae]　SourceはSASシステム中の電子的データのため5章に含めなかった。

付録 2.7.4-39
治験中止に至った有害事象を発現した被験者の一覧表
第 III 相試験：延長試験の安全性併合解析
1 回以上投与された被験者

Site Number	Subject ID	Onset Treatment	Rel Day of Onset†	Adverse Event	Intensity	Serious	Related	Action Taken	Outcome
Trial Number = 3222-010									
0107	[redacted]	MK-3222 100 mg	802	Arthritis	Moderate	N	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	Staphylococcal infection	Severe	Y	Related	Drug Withdrawn	Recovered/Resolved With Sequelae
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
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
8126	[redacted]	MK-3222 200 mg	873	Pneumonia	Moderate	N	Related	Drug Withdrawn	Not Recovered/Not Resolved
Trial Number = 3222-011									
0172	[redacted]	MK-3222 200 mg	762	Back pain	Moderate	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	Peripheral arthritis	Severe	N	Not Related	Drug Withdrawn	Recovering/Resolving
4501	[redacted]	MK-3222 100 mg	450	Psoriatic arthropathy	Moderate	N	Not Related	Drug Withdrawn	Recovering/Resolving
4915	[redacted]	MK-3222 100 mg	417	Dysphagia	Moderate	N	Related	Drug Withdrawn	Recovered/Resolved
4918	[redacted]	MK-3222 100 mg	629	Hyperthyroidism	Moderate	N	Related	Drug Withdrawn	Not Recovered/Not Resolved
4918	[redacted]	MK-3222 100 mg	629	Thyrotoxic crisis	Severe	Y	Related	Drug Withdrawn	Recovered/Resolved
4918	[redacted]	MK-3222 100 mg	643	Urticaria	Mild	N	Not Related	Drug Withdrawn	Not Recovered/Not Resolved

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

Site Number	Subject ID	Onset Treatment	Rel Day of Onset†	Adverse Event	Intensity	Serious	Related	Action Taken	Outcome
4921	[redacted]	MK-3222 100 mg	532	Psoriatic arthropathy	Severe	N	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: 5.3.5.3-10]

付録 2.7.4-40
事前に規定の基準に該当する肝機能検査値所見を有する被験者
第 III 相試験：延長試験の安全性併合解析
1 回以上投与された被験者

Site Number	Subject ID	Treatment	Relative Day	Analysis Visit	Test	Result	Normal Range		Criteria 1	Criteria 2
							Lower	Upper		
Test Name(s): Aminotransferase (ALT or AST) and Bilirubin and Alkaline Phosphatase										
No subjects were identified that met the predetermined criteria: (ALT >=3 x ULN and BILI >=2 x ULN and ALP <2 x ULN)										

Source: [ISS-EXT: analysis-adsl; addili]　SourceはSASシステム中の電子的データのため5章に含めなかった。

付録 2.7.4-41
有害事象発現被験者
（MK-3222 の両投与群並びに 1 投与群以上で発現率 < 1%，且つプラセボ投与群より高い発現率）
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		Etanercept 50 mg	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	355		705		708		313	
with one or more adverse events	191	(53.8)	340	(48.2)	339	(47.9)	169	(54.0)
with no adverse events	164	(46.2)	365	(51.8)	369	(52.1)	144	(46.0)
Blood and lymphatic system disorders								
Anaemia	0	(0.0)	2	(0.3)	0	(0.0)	0	(0.0)
Leukocytosis	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Neutropenia	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Cardiac disorders								
Acute myocardial infarction	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Angina pectoris	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Atrial fibrillation	0	(0.0)	1	(0.1)	1	(0.1)	1	(0.3)
Atrioventricular block first degree	0	(0.0)	2	(0.3)	0	(0.0)	0	(0.0)
Cardiomegaly	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Cardiomyopathy alcoholic	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Coronary artery disease	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)
Left ventricular hypertrophy	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Sinus arrhythmia	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Sinus bradycardia	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Ear and labyrinth disorders								
Ear canal erythema	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Ear discomfort	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Otorrhoea	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)

Subjects With Adverse Events
(Incidence < 1% in Both MK-3222 Groups and One or More MK-3222 Groups is More Frequently than in the Placebo Group)
Phase 2 and 3: Placebo-Controlled Safety Pool
All Subjects as Treated

	Placebo		MK-3222 100 mg		MK-3222 200 mg		Etanercept 50 mg	
	n	(%)	n	(%)	n	(%)	n	(%)
Tinnitus	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Endocrine disorders	**0**	**(0.0)**	**2**	**(0.3)**	**0**	**(0.0)**	**0**	**(0.0)**
Hypothyroidism	0	(0.0)	2	(0.3)	0	(0.0)	0	(0.0)
Eye disorders								
Accommodation disorder	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Blepharitis	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Blepharospasm	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Cataract	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)
Conjunctivitis allergic	0	(0.0)	0	(0.0)	3	(0.4)	0	(0.0)
Eczema eyelids	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Eye pruritus	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Eyelid oedema	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Ocular hyperaemia	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Scleritis	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Ulcerative keratitis	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Vision blurred	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Xerophthalmia	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Gastrointestinal disorders								
Abdominal discomfort	0	(0.0)	1	(0.1)	0	(0.0)	2	(0.6)
Abdominal hernia	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Abdominal pain	2	(0.6)	5	(0.7)	3	(0.4)	2	(0.6)
Abdominal pain lower	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.3)

Subjects With Adverse Events
(Incidence < 1% in Both MK-3222 Groups and One or More MK-3222 Groups is More Frequently than in the Placebo Group)
Phase 2 and 3: Placebo-Controlled Safety Pool
All Subjects as Treated

	Placebo		MK-3222 100 mg		MK-3222 200 mg		Etanercept 50 mg	
	n	(%)	n	(%)	n	(%)	n	(%)
Abdominal pain upper	0	(0.0)	2	(0.3)	4	(0.6)	1	(0.3)
Abnormal faeces	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Constipation	2	(0.6)	1	(0.1)	4	(0.6)	0	(0.0)
Dental caries	1	(0.3)	2	(0.3)	3	(0.4)	1	(0.3)
Dry mouth	0	(0.0)	1	(0.1)	3	(0.4)	2	(0.6)
Dyspepsia	0	(0.0)	3	(0.4)	1	(0.1)	0	(0.0)
Dysphagia	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Enteritis	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Faeces soft	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Food poisoning	0	(0.0)	2	(0.3)	0	(0.0)	0	(0.0)
Gastrooesophageal reflux disease	0	(0.0)	1	(0.1)	1	(0.1)	1	(0.3)
Irritable bowel syndrome	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Lip dry	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Oesophageal polyp	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Pancreatic steatosis	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Pancreatitis acute	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Periodontal disease	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Salivary gland enlargement	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Toothache	3	(0.8)	6	(0.9)	4	(0.6)	2	(0.6)
Vomiting	0	(0.0)	4	(0.6)	5	(0.7)	0	(0.0)
General disorders and administration site conditions								
Asthenia	1	(0.3)	2	(0.3)	0	(0.0)	1	(0.3)

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

	Placebo		MK-3222 100 mg		MK-3222 200 mg		Etanercept 50 mg	
	n	(%)	n	(%)	n	(%)	n	(%)
Chills	0	(0.0)	1	(0.1)	1	(0.1)	1	(0.3)
Cyst	0	(0.0)	1	(0.1)	2	(0.3)	0	(0.0)
Death	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Feeling cold	0	(0.0)	2	(0.3)	1	(0.1)	0	(0.0)
Feeling hot	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Impaired healing	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Injection site bruising	0	(0.0)	3	(0.4)	3	(0.4)	3	(1.0)
Injection site erythema	1	(0.3)	4	(0.6)	3	(0.4)	27	(8.6)
Injection site haematoma	1	(0.3)	2	(0.3)	5	(0.7)	4	(1.3)
Injection site haemorrhage	0	(0.0)	2	(0.3)	2	(0.3)	1	(0.3)
Injection site inflammation	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Injection site pruritus	0	(0.0)	1	(0.1)	4	(0.6)	4	(1.3)
Injection site reaction	1	(0.3)	2	(0.3)	1	(0.1)	14	(4.5)
Injection site urticaria	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Malaise	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Pain	0	(0.0)	1	(0.1)	2	(0.3)	0	(0.0)
Peripheral swelling	2	(0.6)	6	(0.9)	2	(0.3)	0	(0.0)
Hepatobiliary disorders	**0**	**(0.0)**	**4**	**(0.6)**	**2**	**(0.3)**	**1**	**(0.3)**
Drug-induced liver injury	0	(0.0)	2	(0.3)	0	(0.0)	0	(0.0)
Hepatic fibrosis	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Hepatic steatosis	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)
Hepatitis	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)

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Phase 2 and 3: Placebo-Controlled Safety Pool
All Subjects as Treated

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	n	(%)	n	(%)	n	(%)	n	(%)
Hepatomegaly	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Immune system disorders								
Allergic oedema	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Drug hypersensitivity	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)
Food allergy	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Seasonal allergy	1	(0.3)	0	(0.0)	2	(0.3)	0	(0.0)
Infections and infestations								
Abscess limb	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Abscess neck	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Acarodermatitis	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Asymptomatic bacteriuria	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Bacterial vaginosis	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Bronchitis viral	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Conjunctivitis	0	(0.0)	4	(0.6)	0	(0.0)	0	(0.0)
Cystitis	1	(0.3)	4	(0.6)	1	(0.1)	0	(0.0)
Ear infection	0	(0.0)	2	(0.3)	1	(0.1)	0	(0.0)
Epiglottitis	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Folliculitis	2	(0.6)	2	(0.3)	6	(0.8)	0	(0.0)
Fungal skin infection	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Gastrointestinal infection	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.3)
Gingival abscess	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Gingivitis	0	(0.0)	1	(0.1)	1	(0.1)	1	(0.3)

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	n	(%)	n	(%)	n	(%)	n	(%)
Herpes simplex	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Herpes zoster	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Hordeolum	0	(0.0)	1	(0.1)	1	(0.1)	5	(1.6)
Impetigo	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)
Lower respiratory tract infection	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Myringitis	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Oral candidiasis	0	(0.0)	1	(0.1)	2	(0.3)	0	(0.0)
Oral herpes	1	(0.3)	4	(0.6)	1	(0.1)	3	(1.0)
Otitis externa	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Otitis media	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Papilloma viral infection	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Paronychia	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Periodontitis	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Pharyngitis	2	(0.6)	6	(0.9)	2	(0.3)	1	(0.3)
Pulpitis dental	1	(0.3)	0	(0.0)	2	(0.3)	0	(0.0)
Rash pustular	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)
Rhinitis	2	(0.6)	5	(0.7)	4	(0.6)	3	(1.0)
Skin candida	0	(0.0)	1	(0.1)	2	(0.3)	0	(0.0)
Staphylococcal infection	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Subcutaneous abscess	0	(0.0)	1	(0.1)	2	(0.3)	0	(0.0)
Sweat gland infection	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Tinea pedis	0	(0.0)	2	(0.3)	2	(0.3)	0	(0.0)

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	n	(%)	n	(%)	n	(%)	n	(%)
Tinea versicolour	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.3)
Tonsillitis	1	(0.3)	3	(0.4)	2	(0.3)	1	(0.3)
Tooth infection	1	(0.3)	2	(0.3)	1	(0.1)	4	(1.3)
Tracheitis	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Trichophytosis	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Vaginal infection	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Viral pharyngitis	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Viral rhinitis	0	(0.0)	1	(0.1)	2	(0.3)	0	(0.0)
Viral upper respiratory tract infection	1	(0.3)	2	(0.3)	2	(0.3)	2	(0.6)
Vulvovaginal candidiasis	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Wound infection	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Injury, poisoning and procedural complications								
Accidental overdose	2	(0.6)	4	(0.6)	6	(0.8)	3	(1.0)
Animal bite	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Animal scratch	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Arthropod bite	1	(0.3)	1	(0.1)	2	(0.3)	0	(0.0)
Bone contusion	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Cartilage injury	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Concussion	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Drug administration error	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Facial bones fracture	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Fall	0	(0.0)	2	(0.3)	3	(0.4)	0	(0.0)

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Phase 2 and 3: Placebo-Controlled Safety Pool
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	n	(%)	n	(%)	n	(%)	n	(%)
Foot fracture	0	(0.0)	1	(0.1)	3	(0.4)	1	(0.3)
Joint dislocation	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Joint injury	1	(0.3)	3	(0.4)	0	(0.0)	0	(0.0)
Laceration	1	(0.3)	1	(0.1)	2	(0.3)	0	(0.0)
Ligament sprain	0	(0.0)	1	(0.1)	2	(0.3)	0	(0.0)
Muscle strain	2	(0.6)	5	(0.7)	3	(0.4)	0	(0.0)
Post procedural haematoma	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Procedural pain	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Rib fracture	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Road traffic accident	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Skin abrasion	0	(0.0)	3	(0.4)	1	(0.1)	0	(0.0)
Soft tissue injury	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Sunburn	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)
Traumatic haemorrhage	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Wound	1	(0.3)	0	(0.0)	3	(0.4)	0	(0.0)
Investigations								
Alanine aminotransferase increased	2	(0.6)	4	(0.6)	3	(0.4)	1	(0.3)
Aspartate aminotransferase increased	0	(0.0)	4	(0.6)	2	(0.3)	0	(0.0)
Blood chloride decreased	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Blood cholesterol increased	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Blood creatinine increased	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Blood lactate dehydrogenase increased	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)

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	n	(%)	n	(%)	n	(%)	n	(%)
Blood sodium decreased	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Blood triglycerides increased	0	(0.0)	3	(0.4)	0	(0.0)	0	(0.0)
Blood urine present	0	(0.0)	3	(0.4)	0	(0.0)	0	(0.0)
Electrocardiogram Q wave abnormal	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Electrocardiogram QRS complex abnormal	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Electrocardiogram QT prolonged	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)
Electrocardiogram abnormal	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)
Eosinophil count increased	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Gamma-glutamyltransferase increased	2	(0.6)	4	(0.6)	2	(0.3)	2	(0.6)
Gastric pH decreased	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Glucose urine present	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Hepatic enzyme increased	0	(0.0)	1	(0.1)	2	(0.3)	1	(0.3)
High density lipoprotein increased	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Liver function test abnormal	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Neutrophil count increased	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Protein urine present	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Red blood cells urine	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Red blood cells urine positive	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Urine analysis abnormal	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)
White blood cells urine positive	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Metabolism and nutrition disorders								
Gout	0	(0.0)	2	(0.3)	0	(0.0)	0	(0.0)

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	n	(%)	n	(%)	n	(%)	n	(%)
Hypercholesterolaemia	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)
Hyperglycaemia	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Hyperlipidaemia	0	(0.0)	4	(0.6)	1	(0.1)	0	(0.0)
Hypertriglyceridaemia	0	(0.0)	2	(0.3)	1	(0.1)	1	(0.3)
Iron deficiency	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Type 2 diabetes mellitus	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.3)
Musculoskeletal and connective tissue disorders								
Ankle deformity	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Arthropathy	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Bursitis	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Exostosis	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Intervertebral disc degeneration	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Joint crepitation	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Joint stiffness	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Limb discomfort	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Muscle spasms	2	(0.6)	0	(0.0)	5	(0.7)	1	(0.3)
Muscle tightness	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Muscular weakness	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)
Musculoskeletal pain	1	(0.3)	1	(0.1)	6	(0.8)	2	(0.6)
Myalgia	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.6)
Neck pain	0	(0.0)	0	(0.0)	3	(0.4)	0	(0.0)
Osteoarthritis	0	(0.0)	0	(0.0)	3	(0.4)	0	(0.0)

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	n	(%)	n	(%)	n	(%)	n	(%)
Pain in extremity	2	(0.6)	7	(1.0)	6	(0.8)	2	(0.6)
Periarthritis	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)
Rheumatic disorder	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Rotator cuff syndrome	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.3)
Spinal column stenosis	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Spinal osteoarthritis	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Spinal pain	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Wrist deformity	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**1**	**(0.3)**	**7**	**(1.0)**	**3**	**(0.4)**	**3**	**(1.0)**
Acrochordon	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Basal cell carcinoma	0	(0.0)	2	(0.3)	1	(0.1)	1	(0.3)
Dysplastic naevus	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Seborrhoeic keratosis	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.3)
Skin papilloma	1	(0.3)	4	(0.6)	0	(0.0)	0	(0.0)
Nervous system disorders								
Alcoholic seizure	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Balance disorder	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Carotid artery stenosis	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Cervicobrachial syndrome	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)
Dysgeusia	0	(0.0)	2	(0.3)	2	(0.3)	0	(0.0)
Hyperaesthesia	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Hypertonia	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)

Subjects With Adverse Events
(Incidence < 1% in Both MK-3222 Groups and One or More MK-3222 Groups is More Frequently than in the Placebo Group)
Phase 2 and 3: Placebo-Controlled Safety Pool
All Subjects as Treated

	Placebo		MK-3222 100 mg		MK-3222 200 mg		Etanercept 50 mg	
	n	(%)	n	(%)	n	(%)	n	(%)
Hypoaesthesia	1	(0.3)	2	(0.3)	0	(0.0)	1	(0.3)
Hypotonia	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Intercostal neuralgia	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Lethargy	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.3)
Loss of consciousness	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Migraine with aura	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Muscle contractions involuntary	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Nerve compression	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Nervous system disorder	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Parosmia	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Sciatica	0	(0.0)	0	(0.0)	3	(0.4)	0	(0.0)
Sinus headache	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Somnolence	1	(0.3)	1	(0.1)	2	(0.3)	0	(0.0)
Syncope	0	(0.0)	2	(0.3)	0	(0.0)	0	(0.0)
Tension headache	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Visual field defect	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Pregnancy, puerperium and perinatal conditions	**0**	**(0.0)**	**1**	**(0.1)**	**1**	**(0.1)**	**0**	**(0.0)**
Abortion	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Abortion spontaneous	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Psychiatric disorders								
Adjustment disorder	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Alcohol abuse	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)

Subjects With Adverse Events
(Incidence < 1% in Both MK-3222 Groups and One or More MK-3222 Groups is More Frequently than in the Placebo Group)
Phase 2 and 3: Placebo-Controlled Safety Pool
All Subjects as Treated

	Placebo		MK-3222 100 mg		MK-3222 200 mg		Etanercept 50 mg	
	n	(%)	n	(%)	n	(%)	n	(%)
Anxiety	0	(0.0)	3	(0.4)	1	(0.1)	0	(0.0)
Depression	0	(0.0)	2	(0.3)	3	(0.4)	1	(0.3)
Insomnia	2	(0.6)	4	(0.6)	7	(1.0)	2	(0.6)
Irritability	0	(0.0)	2	(0.3)	0	(0.0)	0	(0.0)
Libido decreased	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Major depression	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Mood swings	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)
Suicide attempt	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Renal and urinary disorders								
Bladder pain	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Calculus ureteric	1	(0.3)	2	(0.3)	0	(0.0)	0	(0.0)
Haematuria	0	(0.0)	3	(0.4)	3	(0.4)	0	(0.0)
Nephrolithiasis	0	(0.0)	2	(0.3)	1	(0.1)	0	(0.0)
Nitrituria	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Proteinuria	2	(0.6)	4	(0.6)	1	(0.1)	1	(0.3)
Renal colic	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)
Renal failure	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Renal pain	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Reproductive system and breast disorders								
Bartholin's cyst	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Breast cyst	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Breast inflammation	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)

Subjects With Adverse Events
(Incidence < 1% in Both MK-3222 Groups and One or More MK-3222 Groups is More Frequently than in the Placebo Group)
Phase 2 and 3: Placebo-Controlled Safety Pool
All Subjects as Treated

	Placebo		MK-3222 100 mg		MK-3222 200 mg		Etanercept 50 mg	
	n	(%)	n	(%)	n	(%)	n	(%)
Breast pain	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Erectile dysfunction	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Genital discomfort	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Gynaecomastia	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Menstruation delayed	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)
Menstruation irregular	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Ovarian cyst	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Spontaneous penile erection	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Testicular cyst	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Testicular pain	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Uterine haemorrhage	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Respiratory, thoracic and mediastinal disorders								
Asthma	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Bronchitis chronic	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Catarrh	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Chronic obstructive pulmonary disease	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Dry throat	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)
Dysphonia	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)
Dyspnoea exertional	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Emphysema	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Laryngeal pain	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Nasal dryness	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.3)

Subjects With Adverse Events
(Incidence < 1% in Both MK-3222 Groups and One or More MK-3222 Groups is More Frequently than in the Placebo Group)
Phase 2 and 3: Placebo-Controlled Safety Pool
All Subjects as Treated

	Placebo		MK-3222 100 mg		MK-3222 200 mg		Etanercept 50 mg	
	n	(%)	n	(%)	n	(%)	n	(%)
Nasal oedema	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Oropharyngeal discomfort	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Paranasal sinus hypersecretion	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)
Pneumothorax	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Productive cough	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.3)
Respiratory tract congestion	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)
Rhinitis allergic	0	(0.0)	2	(0.3)	2	(0.3)	2	(0.6)
Rhonchi	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Tonsillar hypertrophy	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Upper-airway cough syndrome	0	(0.0)	2	(0.3)	0	(0.0)	0	(0.0)
Skin and subcutaneous tissue disorders								
Acne	1	(0.3)	2	(0.3)	1	(0.1)	2	(0.6)
Alopecia	2	(0.6)	4	(0.6)	4	(0.6)	0	(0.0)
Blister	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Dermal cyst	0	(0.0)	1	(0.1)	2	(0.3)	0	(0.0)
Dermatitis	0	(0.0)	0	(0.0)	2	(0.3)	0	(0.0)
Dry skin	0	(0.0)	2	(0.3)	0	(0.0)	0	(0.0)
Ecchymosis	0	(0.0)	2	(0.3)	0	(0.0)	1	(0.3)
Eczema	1	(0.3)	4	(0.6)	2	(0.3)	2	(0.6)
Erythema	2	(0.6)	0	(0.0)	4	(0.6)	2	(0.6)
Hyperhidrosis	0	(0.0)	2	(0.3)	1	(0.1)	1	(0.3)
Miliaria	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)

Subjects With Adverse Events
(Incidence < 1% in Both MK-3222 Groups and One or More MK-3222 Groups is More Frequently than in the Placebo Group)
Phase 2 and 3: Placebo-Controlled Safety Pool
All Subjects as Treated

	Placebo		MK-3222 100 mg		MK-3222 200 mg		Etanercept 50 mg	
	n	(%)	n	(%)	n	(%)	n	(%)
Neurodermatitis	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Papule	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.3)
Photosensitivity reaction	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Polymorphic light eruption	1	(0.3)	0	(0.0)	2	(0.3)	0	(0.0)
Pruritus generalised	0	(0.0)	1	(0.1)	1	(0.1)	0	(0.0)
Rash	0	(0.0)	3	(0.4)	3	(0.4)	0	(0.0)
Rash papular	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Rash papulosquamous	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Rosacea	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Seborrhoeic dermatitis	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Skin atrophy	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Skin odour abnormal	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Skin swelling	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Skin tightness	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Swelling face	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Social circumstances	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.1)**	**0**	**(0.0)**
Menarche	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Surgical and medical procedures	**0**	**(0.0)**	**1**	**(0.1)**	**0**	**(0.0)**	**0**	**(0.0)**
Renal stone removal	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Vascular disorders								
Arteriosclerosis	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Flushing	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)
Hypotension	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Lymphoedema	0	(0.0)	0	(0.0)	1	(0.1)	0	(0.0)
Pallor	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.3)
Peripheral arterial occlusive disease	0	(0.0)	1	(0.1)	0	(0.0)	0	(0.0)

[Source: 5.3.5.3-10]

付録 2.7.4-42
臨床検査値の経時的変動の要約 - 生化学検査
第 IIb 相及び第 III 相試験：ベース試験の安全性併合解析 - 継続曝露
1 回以上投与された被験者

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Albumin (gm/dL)								
Week 4	continuous exposure MK-3222 100 mg	251	4.5 (0.3)	[3.6, 5.2]	4.5 (0.3)	[3.5, 5.3]	-0.0 (0.3)	[-1.1, 0.7]
	continuous exposure MK-3222 200 mg	206	4.5 (0.3)	[3.7, 5.1]	4.4 (0.3)	[3.1, 5.3]	-0.0 (0.3)	[-1.5, 0.7]
	continuous exposure MK-3222 100 / 200 mg	626	4.5 (0.3)	[3.6, 5.3]	4.5 (0.3)	[3.1, 5.3]	-0.0 (0.3)	[-1.5, 0.9]
Week 12/16	continuous exposure MK-3222 100 mg	251	4.5 (0.3)	[3.6, 5.2]	4.5 (0.3)	[3.2, 5.4]	-0.0 (0.2)	[-0.7, 0.7]
	continuous exposure MK-3222 200 mg	209	4.5 (0.3)	[3.7, 5.1]	4.5 (0.3)	[3.6, 5.1]	0.0 (0.2)	[-0.6, 0.7]
	continuous exposure MK-3222 100 / 200 mg	628	4.5 (0.3)	[3.6, 5.3]	4.5 (0.3)	[3.1, 5.7]	-0.0 (0.3)	[-1.1, 0.7]
Week 28	continuous exposure MK-3222 100 mg	250	4.5 (0.3)	[3.6, 5.2]	4.5 (0.3)	[3.0, 5.2]	0.0 (0.2)	[-0.9, 0.9]
	continuous exposure MK-3222 200 mg	210	4.5 (0.3)	[3.7, 5.1]	4.5 (0.3)	[3.8, 5.3]	0.0 (0.3)	[-0.8, 0.7]
	continuous exposure MK-3222 100 / 200 mg	631	4.5 (0.3)	[3.6, 5.3]	4.5 (0.3)	[3.0, 5.5]	0.0 (0.3)	[-0.9, 0.9]
Week 52	continuous exposure MK-3222 100 mg	250	4.5 (0.3)	[3.6, 5.2]	4.6 (0.3)	[3.5, 5.3]	0.0 (0.3)	[-0.7, 1.0]
	continuous exposure MK-3222 200 mg	207	4.5 (0.3)	[3.7, 5.1]	4.6 (0.3)	[3.9, 5.3]	0.1 (0.3)	[-1.0, 0.9]
	continuous exposure MK-3222 100 / 200 mg	624	4.5 (0.3)	[3.6, 5.3]	4.6 (0.3)	[3.3, 5.3]	0.1 (0.3)	[-1.0, 1.0]

Summary of Laboratory Assessment over Time - Chemistry
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Alkaline Phosphatase (IU/L)								
Week 4	continuous exposure MK-3222 100 mg	251	76.3 (23.9)	[23.0, 201.0]	74.4 (23.6)	[23.0, 216.0]	-1.9 (8.6)	[-72.0, 29.0]
	continuous exposure MK-3222 200 mg	205	75.7 (21.9)	[26.0, 139.0]	74.6 (22.1)	[28.0, 147.0]	-1.1 (7.6)	[-28.0, 25.0]
	continuous exposure MK-3222 100 / 200 mg	625	75.7 (22.7)	[23.0, 201.0]	74.0 (22.0)	[23.0, 216.0]	-1.7 (9.3)	[-113.0, 29.0]
Week 12/16	continuous exposure MK-3222 100 mg	251	76.4 (24.0)	[23.0, 201.0]	73.6 (23.8)	[23.0, 233.0]	-2.8 (12.8)	[-87.0, 99.0]
	continuous exposure MK-3222 200 mg	209	75.9 (21.5)	[27.0, 139.0]	73.1 (22.0)	[29.0, 139.0]	-2.8 (8.6)	[-29.0, 32.0]
	continuous exposure MK-3222 100 / 200 mg	628	75.8 (22.5)	[23.0, 201.0]	72.8 (21.9)	[21.0, 233.0]	-3.0 (11.9)	[-127.0, 99.0]
Week 28	continuous exposure MK-3222 100 mg	250	76.4 (24.0)	[23.0, 201.0]	74.1 (25.2)	[22.0, 301.0]	-2.3 (12.5)	[-66.0, 100.0]
	continuous exposure MK-3222 200 mg	210	75.8 (21.7)	[26.0, 139.0]	73.5 (22.7)	[30.0, 147.0]	-2.3 (10.6)	[-45.0, 35.0]
	continuous exposure MK-3222 100 / 200 mg	631	75.8 (22.6)	[23.0, 201.0]	73.4 (22.6)	[16.0, 301.0]	-2.4 (12.3)	[-139.0, 100.0]
Week 52	continuous exposure MK-3222 100 mg	250	76.4 (24.0)	[23.0, 201.0]	73.2 (21.2)	[23.0, 151.0]	-3.1 (12.1)	[-71.0, 42.0]
	continuous exposure MK-3222 200 mg	207	75.5 (21.1)	[26.0, 139.0]	73.2 (21.1)	[31.0, 141.0]	-2.3 (11.8)	[-40.0, 34.0]
	continuous exposure MK-3222 100 / 200 mg	624	75.6 (22.4)	[23.0, 201.0]	73.2 (20.5)	[23.0, 151.0]	-2.3 (13.1)	[-134.0, 42.0]

Summary of Laboratory Assessment over Time - Chemistry
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Alanine Aminotransferase (IU/L)								
Week 4	continuous exposure MK-3222 100 mg	251	28.2 (18.9)	[7.0, 190.0]	27.6 (15.3)	[6.0, 91.0]	-0.6 (15.5)	[-143.0, 72.0]
	continuous exposure MK-3222 200 mg	206	26.7 (17.5)	[4.0, 173.0]	26.8 (15.7)	[6.0, 114.0]	0.1 (14.9)	[-145.0, 64.0]
	continuous exposure MK-3222 100 / 200 mg	626	27.8 (19.4)	[4.0, 190.0]	27.2 (16.8)	[6.0, 215.0]	-0.5 (16.1)	[-153.0, 72.0]
Week 12/16	continuous exposure MK-3222 100 mg	251	28.1 (18.9)	[7.0, 190.0]	26.8 (15.8)	[7.0, 112.0]	-1.3 (16.2)	[-162.0, 66.0]
	continuous exposure MK-3222 200 mg	209	26.8 (17.8)	[4.0, 173.0]	27.0 (16.6)	[5.0, 100.0]	0.2 (15.5)	[-148.0, 70.0]
	continuous exposure MK-3222 100 / 200 mg	627	27.8 (19.5)	[4.0, 190.0]	26.6 (15.7)	[5.0, 112.0]	-1.2 (16.6)	[-162.0, 70.0]
Week 28	continuous exposure MK-3222 100 mg	249	28.1 (19.0)	[7.0, 190.0]	27.5 (17.5)	[6.0, 126.0]	-0.6 (18.7)	[-165.0, 91.0]
	continuous exposure MK-3222 200 mg	210	26.8 (17.7)	[4.0, 173.0]	28.0 (19.1)	[6.0, 149.0]	1.2 (18.6)	[-141.0, 101.0]
	continuous exposure MK-3222 100 / 200 mg	629	27.7 (19.5)	[4.0, 190.0]	27.6 (17.8)	[6.0, 149.0]	-0.2 (19.0)	[-165.0, 101.0]
Week 52	continuous exposure MK-3222 100 mg	249	28.1 (19.0)	[7.0, 190.0]	29.2 (19.9)	[7.0, 192.0]	1.0 (20.6)	[-160.0, 175.0]
	continuous exposure MK-3222 200 mg	207	26.8 (17.8)	[4.0, 173.0]	28.0 (17.4)	[5.0, 107.0]	1.2 (17.8)	[-144.0, 75.0]
	continuous exposure MK-3222 100 / 200 mg	622	27.7 (19.5)	[4.0, 190.0]	28.7 (18.5)	[5.0, 192.0]	1.0 (19.8)	[-163.0, 175.0]

Summary of Laboratory Assessment over Time - Chemistry
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Aspartate Aminotransferase (IU/L)								
Week 4	continuous exposure MK-3222 100 mg	251	23.7 (11.4)	[11.0, 115.0]	24.0 (13.5)	[8.0, 172.0]	0.3 (13.0)	[-86.0, 116.0]
	continuous exposure MK-3222 200 mg	206	22.7 (11.1)	[10.0, 124.0]	23.2 (9.4)	[10.0, 79.0]	0.5 (10.7)	[-100.0, 54.0]
	continuous exposure MK-3222 100 / 200 mg	625	23.6 (12.0)	[8.0, 124.0]	23.7 (12.6)	[8.0, 172.0]	0.1 (11.8)	[-100.0, 116.0]
Week 12/16	continuous exposure MK-3222 100 mg	251	23.7 (11.4)	[11.0, 115.0]	23.3 (12.2)	[12.0, 149.0]	-0.4 (12.6)	[-84.0, 128.0]
	continuous exposure MK-3222 200 mg	209	22.8 (11.1)	[10.0, 124.0]	23.5 (12.2)	[11.0, 131.0]	0.7 (12.5)	[-103.0, 111.0]
	continuous exposure MK-3222 100 / 200 mg	627	23.6 (12.0)	[8.0, 124.0]	23.3 (11.6)	[10.0, 149.0]	-0.3 (12.4)	[-103.0, 128.0]
Week 28	continuous exposure MK-3222 100 mg	249	23.6 (11.3)	[11.0, 115.0]	23.4 (11.8)	[8.0, 102.0]	-0.2 (12.3)	[-94.0, 74.0]
	continuous exposure MK-3222 200 mg	210	22.8 (11.0)	[10.0, 124.0]	23.6 (16.6)	[7.0, 220.0]	0.8 (17.3)	[-98.0, 185.0]
	continuous exposure MK-3222 100 / 200 mg	629	23.6 (11.9)	[8.0, 124.0]	23.5 (13.7)	[7.0, 220.0]	-0.0 (14.3)	[-98.0, 185.0]
Week 52	continuous exposure MK-3222 100 mg	249	23.7 (11.4)	[11.0, 115.0]	24.6 (24.0)	[10.0, 374.0]	0.9 (23.9)	[-89.0, 342.0]
	continuous exposure MK-3222 200 mg	207	22.8 (11.1)	[10.0, 124.0]	23.0 (10.5)	[10.0, 82.0]	0.2 (12.1)	[-100.0, 63.0]
	continuous exposure MK-3222 100 / 200 mg	622	23.6 (11.9)	[8.0, 124.0]	23.9 (17.7)	[10.0, 374.0]	0.4 (18.1)	[-100.0, 342.0]

Summary of Laboratory Assessment over Time - Chemistry
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Blood Urea Nitrogen (mg/dL)								
Week 4	continuous exposure MK-3222 100 mg	251	14.0 (4.5)	[5.0, 46.0]	13.8 (3.6)	[4.0, 25.0]	-0.2 (3.8)	[-32.0, 9.0]
	continuous exposure MK-3222 200 mg	206	13.5 (4.0)	[5.0, 26.0]	13.5 (4.1)	[5.0, 30.0]	0.1 (3.6)	[-14.0, 15.0]
	continuous exposure MK-3222 100 / 200 mg	626	14.0 (4.4)	[5.0, 46.0]	13.9 (4.0)	[4.0, 30.0]	-0.1 (3.9)	[-32.0, 15.0]
Week 12/16	continuous exposure MK-3222 100 mg	251	14.0 (4.5)	[5.0, 46.0]	14.0 (4.0)	[6.0, 27.0]	0.0 (4.1)	[-32.0, 10.0]
	continuous exposure MK-3222 200 mg	209	13.6 (4.0)	[5.0, 26.0]	13.9 (4.2)	[4.0, 27.0]	0.3 (3.8)	[-13.0, 16.0]
	continuous exposure MK-3222 100 / 200 mg	628	14.0 (4.4)	[5.0, 46.0]	14.2 (4.0)	[4.0, 27.0]	0.2 (4.0)	[-32.0, 16.0]
Week 28	continuous exposure MK-3222 100 mg	249	14.0 (4.5)	[5.0, 46.0]	13.8 (3.7)	[5.0, 26.0]	-0.2 (4.1)	[-31.0, 10.0]
	continuous exposure MK-3222 200 mg	210	13.6 (4.0)	[5.0, 26.0]	14.0 (4.0)	[6.0, 27.0]	0.5 (3.6)	[-15.0, 9.0]
	continuous exposure MK-3222 100 / 200 mg	630	14.0 (4.4)	[5.0, 46.0]	14.0 (3.9)	[5.0, 30.0]	0.1 (4.0)	[-31.0, 10.0]
Week 52	continuous exposure MK-3222 100 mg	250	14.0 (4.5)	[5.0, 46.0]	13.7 (3.8)	[5.0, 29.0]	-0.3 (4.2)	[-29.0, 16.0]
	continuous exposure MK-3222 200 mg	207	13.6 (4.0)	[5.0, 26.0]	13.5 (4.0)	[5.0, 27.0]	-0.1 (3.8)	[-14.0, 11.0]
	continuous exposure MK-3222 100 / 200 mg	624	14.0 (4.4)	[5.0, 46.0]	13.9 (4.0)	[5.0, 29.0]	-0.1 (4.0)	[-29.0, 16.0]

Summary of Laboratory Assessment over Time - Chemistry
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Calcium (mg/dL)								
Week 4	continuous exposure MK-3222 100 mg	251	9.5 (0.4)	[8.0, 11.1]	9.5 (0.4)	[8.2, 11.5]	-0.0 (0.4)	[-1.1, 1.5]
	continuous exposure MK-3222 200 mg	205	9.5 (0.4)	[8.5, 11.5]	9.5 (0.4)	[8.4, 11.4]	0.0 (0.3)	[-0.9, 0.9]
	continuous exposure MK-3222 100 / 200 mg	625	9.5 (0.4)	[8.0, 11.5]	9.5 (0.4)	[8.2, 11.5]	0.0 (0.4)	[-1.1, 1.5]
Week 12/16	continuous exposure MK-3222 100 mg	251	9.5 (0.4)	[8.0, 11.1]	9.5 (0.4)	[8.1, 11.3]	-0.0 (0.4)	[-1.3, 1.4]
	continuous exposure MK-3222 200 mg	209	9.5 (0.4)	[8.5, 11.5]	9.5 (0.4)	[8.5, 11.7]	0.1 (0.3)	[-0.9, 0.9]
	continuous exposure MK-3222 100 / 200 mg	628	9.5 (0.4)	[8.0, 11.5]	9.5 (0.4)	[8.1, 11.7]	0.0 (0.4)	[-1.3, 1.4]
Week 28	continuous exposure MK-3222 100 mg	250	9.5 (0.4)	[8.0, 11.1]	9.6 (0.4)	[8.3, 10.9]	0.1 (0.4)	[-0.9, 1.4]
	continuous exposure MK-3222 200 mg	210	9.5 (0.4)	[8.5, 11.5]	9.6 (0.4)	[8.4, 11.3]	0.1 (0.4)	[-0.8, 1.0]
	continuous exposure MK-3222 100 / 200 mg	631	9.5 (0.4)	[8.0, 11.5]	9.6 (0.4)	[8.3, 11.3]	0.1 (0.4)	[-1.1, 1.4]
Week 52	continuous exposure MK-3222 100 mg	250	9.5 (0.4)	[8.0, 11.1]	9.5 (0.4)	[8.5, 10.9]	-0.0 (0.4)	[-1.0, 1.5]
	continuous exposure MK-3222 200 mg	207	9.5 (0.4)	[8.5, 10.5]	9.5 (0.4)	[8.3, 10.4]	0.0 (0.4)	[-1.2, 1.2]
	continuous exposure MK-3222 100 / 200 mg	624	9.5 (0.4)	[8.0, 11.4]	9.5 (0.4)	[8.3, 11.0]	0.0 (0.4)	[-1.2, 1.5]

Summary of Laboratory Assessment over Time - Chemistry
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Cholesterol (mg/dL)								
Week 12/16	continuous exposure MK-3222 100 mg	248	198.9 (39.9)	[98.0, 363.0]	201.4 (50.8)	[106.3, 704.0]	2.5 (39.1)	[-103.0, 452.0]
	continuous exposure MK-3222 200 mg	208	198.3 (40.7)	[86.0, 334.0]	200.8 (41.0)	[94.0, 322.5]	2.5 (23.2)	[-51.0, 101.3]
	continuous exposure MK-3222 100 / 200 mg	623	198.8 (40.5)	[86.0, 363.0]	200.7 (44.6)	[94.0, 704.0]	1.9 (31.2)	[-103.0, 452.0]
Week 28	continuous exposure MK-3222 200 mg	1	212.3 ()	[212.3, 212.3]	200.3 ()	[200.3, 200.3]	-12.0 ()	[-12.0, -12.0]
	continuous exposure MK-3222 100 / 200 mg	3	214.4 (25.2)	[190.3, 240.5]	190.3 (31.4)	[155.1, 215.4]	-24.1 (11.6)	[-35.2, -12.0]
Week 52	continuous exposure MK-3222 100 mg	248	198.4 (40.0)	[98.0, 363.0]	198.1 (40.9)	[115.2, 390.0]	-0.2 (29.1)	[-92.0, 138.0]
	continuous exposure MK-3222 200 mg	209	198.8 (40.5)	[86.0, 334.0]	199.2 (42.3)	[101.3, 369.0]	0.3 (24.4)	[-133.0, 78.0]
	continuous exposure MK-3222 100 / 200 mg	625	198.6 (40.5)	[86.0, 363.0]	200.0 (42.8)	[101.3, 390.0]	1.4 (28.1)	[-133.0, 159.0]
Chloride (mmol/L)								
Week 4	continuous exposure MK-3222 100 mg	251	102.0 (2.6)	[92.0, 111.0]	101.9 (2.5)	[92.0, 109.0]	-0.2 (2.6)	[-11.0, 9.0]
	continuous exposure MK-3222 200 mg	205	102.0 (2.3)	[95.0, 108.0]	102.0 (2.4)	[93.0, 108.0]	0.0 (2.3)	[-8.0, 7.0]
	continuous exposure MK-3222 100 / 200 mg	625	101.9 (2.5)	[92.0, 111.0]	101.8 (2.5)	[92.0, 109.0]	-0.0 (2.4)	[-11.0, 9.0]

Summary of Laboratory Assessment over Time - Chemistry
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Chloride (mmol/L) (Continues)								
Week 12/16	continuous exposure MK-3222 100 mg	251	102.0 (2.6)	[92.0, 111.0]	102.0 (2.4)	[94.0, 112.0]	-0.0 (2.8)	[-11.0, 13.0]
	continuous exposure MK-3222 200 mg	209	102.0 (2.3)	[95.0, 108.0]	101.9 (2.3)	[93.0, 110.0]	-0.0 (2.2)	[-8.0, 7.0]
	continuous exposure MK-3222 100 / 200 mg	628	101.9 (2.5)	[92.0, 111.0]	101.9 (2.5)	[93.0, 112.0]	0.1 (2.5)	[-11.0, 13.0]
Week 28	continuous exposure MK-3222 100 mg	250	102.0 (2.6)	[92.0, 111.0]	101.3 (2.5)	[86.0, 108.0]	-0.8 (2.8)	[-16.0, 9.0]
	continuous exposure MK-3222 200 mg	210	102.0 (2.3)	[95.0, 108.0]	101.5 (2.4)	[93.0, 107.0]	-0.5 (2.7)	[-7.0, 6.0]
	continuous exposure MK-3222 100 / 200 mg	631	101.9 (2.5)	[92.0, 111.0]	101.3 (2.7)	[86.0, 109.0]	-0.5 (2.8)	[-16.0, 9.0]
Week 52	continuous exposure MK-3222 100 mg	250	102.1 (2.5)	[92.0, 111.0]	101.4 (2.1)	[95.0, 107.0]	-0.7 (2.8)	[-12.0, 12.0]
	continuous exposure MK-3222 200 mg	207	102.0 (2.3)	[95.0, 108.0]	101.3 (2.5)	[94.0, 107.0]	-0.7 (2.7)	[-10.0, 7.0]
	continuous exposure MK-3222 100 / 200 mg	624	101.9 (2.5)	[92.0, 111.0]	101.3 (2.4)	[87.0, 108.0]	-0.6 (2.7)	[-12.0, 12.0]
Creatinine (mg/dL)								
Week 4	continuous exposure MK-3222 100 mg	251	0.9 (0.2)	[0.4, 1.5]	0.9 (0.2)	[0.4, 1.5]	-0.0 (0.1)	[-0.5, 0.4]
	continuous exposure MK-3222 200 mg	207	0.9 (0.2)	[0.3, 1.4]	0.9 (0.2)	[0.3, 1.4]	0.0 (0.1)	[-0.5, 0.4]
	continuous exposure MK-3222 100 / 200 mg	627	0.9 (0.2)	[0.3, 1.5]	0.9 (0.2)	[0.3, 1.5]	-0.0 (0.1)	[-0.5, 0.4]

Summary of Laboratory Assessment over Time - Chemistry
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Creatinine (mg/dL) (Continues)								
Week 12/16	continuous exposure MK-3222 100 mg	251	0.9 (0.2)	[0.4, 1.5]	0.9 (0.2)	[0.4, 1.4]	-0.0 (0.1)	[-0.5, 0.3]
	continuous exposure MK-3222 200 mg	209	0.9 (0.2)	[0.3, 1.4]	0.9 (0.2)	[0.4, 1.3]	-0.0 (0.1)	[-0.4, 0.2]
	continuous exposure MK-3222 100 / 200 mg	628	0.9 (0.2)	[0.3, 1.5]	0.9 (0.2)	[0.4, 2.3]	-0.0 (0.1)	[-0.5, 1.2]
Week 28	continuous exposure MK-3222 100 mg	249	0.9 (0.2)	[0.4, 1.5]	0.8 (0.2)	[0.4, 1.4]	-0.1 (0.1)	[-0.5, 0.4]
	continuous exposure MK-3222 200 mg	210	0.9 (0.2)	[0.3, 1.4]	0.8 (0.2)	[0.4, 1.4]	-0.0 (0.1)	[-0.5, 0.2]
	continuous exposure MK-3222 100 / 200 mg	630	0.9 (0.2)	[0.3, 1.5]	0.8 (0.2)	[0.4, 1.8]	-0.0 (0.1)	[-0.6, 0.8]
Week 52	continuous exposure MK-3222 100 mg	251	0.9 (0.2)	[0.4, 1.5]	0.8 (0.2)	[0.4, 1.4]	-0.1 (0.1)	[-0.6, 0.4]
	continuous exposure MK-3222 200 mg	207	0.9 (0.2)	[0.3, 1.4]	0.8 (0.2)	[0.4, 1.3]	-0.1 (0.1)	[-0.6, 0.5]
	continuous exposure MK-3222 100 / 200 mg	625	0.9 (0.2)	[0.3, 1.5]	0.8 (0.2)	[0.4, 1.4]	-0.1 (0.1)	[-0.6, 0.5]
C-Reactive Protein (mg/dL)								
Week 4	continuous exposure MK-3222 100 mg	221	0.5 (1.6)	[0.0, 19.7]	0.6 (2.5)	[0.0, 35.0]	0.0 (2.6)	[-12.2, 34.7]
	continuous exposure MK-3222 200 mg	161	0.4 (0.6)	[0.0, 4.2]	0.3 (0.5)	[0.0, 3.8]	-0.1 (0.5)	[-3.4, 0.8]
	continuous exposure MK-3222 100 / 200 mg	502	0.5 (1.2)	[0.0, 19.7]	0.4 (1.7)	[0.0, 35.0]	-0.0 (1.8)	[-12.2, 34.7]

Summary of Laboratory Assessment over Time - Chemistry
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
C-Reactive Protein (mg/dL) (Continues)								
Week 12/16	continuous exposure MK-3222 100 mg	221	0.5 (1.6)	[0.0, 19.7]	0.4 (0.7)	[0.0, 7.7]	-0.2 (1.5)	[-16.6, 7.6]
	continuous exposure MK-3222 200 mg	162	0.4 (0.6)	[0.0, 4.2]	0.3 (0.5)	[0.0, 4.5]	-0.1 (0.6)	[-3.4, 4.0]
	continuous exposure MK-3222 100 / 200 mg	503	0.5 (1.2)	[0.0, 19.7]	0.3 (0.6)	[0.0, 7.7]	-0.1 (1.1)	[-16.6, 7.6]
Week 28	continuous exposure MK-3222 100 mg	220	0.5 (1.6)	[0.0, 19.7]	0.3 (0.4)	[0.0, 2.2]	-0.2 (1.5)	[-18.4, 0.8]
	continuous exposure MK-3222 200 mg	164	0.4 (0.6)	[0.0, 4.2]	0.3 (0.4)	[0.0, 4.4]	-0.1 (0.5)	[-3.4, 1.2]
	continuous exposure MK-3222 100 / 200 mg	505	0.5 (1.2)	[0.0, 19.7]	0.3 (0.4)	[0.0, 4.4]	-0.1 (1.1)	[-18.4, 4.0]
Week 52	continuous exposure MK-3222 100 mg	222	0.5 (1.6)	[0.0, 19.7]	0.4 (0.6)	[0.0, 6.0]	-0.2 (1.7)	[-18.7, 5.7]
	continuous exposure MK-3222 200 mg	161	0.4 (0.6)	[0.0, 4.2]	0.3 (0.4)	[0.0, 3.3]	-0.1 (0.5)	[-3.4, 1.7]
	continuous exposure MK-3222 100 / 200 mg	500	0.5 (1.2)	[0.0, 19.7]	0.4 (0.6)	[0.0, 6.0]	-0.1 (1.2)	[-18.7, 5.7]
Gamma Glutamyl Transferase (IU/L)								
Week 4	continuous exposure MK-3222 100 mg	251	35.1 (39.9)	[6.0, 409.0]	34.4 (38.2)	[5.0, 361.0]	-0.7 (15.8)	[-91.0, 174.0]
	continuous exposure MK-3222 200 mg	207	32.0 (34.3)	[7.0, 369.0]	32.4 (37.0)	[5.0, 427.0]	0.4 (10.3)	[-44.0, 64.0]
	continuous exposure MK-3222 100 / 200 mg	627	33.7 (36.4)	[6.0, 409.0]	33.3 (34.9)	[5.0, 427.0]	-0.4 (16.0)	[-253.0, 174.0]

Summary of Laboratory Assessment over Time - Chemistry
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Gamma Glutamyl Transferase (IU/L) (Continues)								
Week 12/16	continuous exposure MK-3222 100 mg	251	34.9 (39.9)	[6.0, 409.0]	36.8 (54.9)	[5.0, 653.0]	1.9 (28.9)	[-98.0, 408.0]
	continuous exposure MK-3222 200 mg	209	32.5 (34.8)	[7.0, 369.0]	35.1 (48.6)	[7.0, 598.0]	2.6 (20.5)	[-54.0, 229.0]
	continuous exposure MK-3222 100 / 200 mg	628	33.9 (36.6)	[6.0, 409.0]	35.2 (46.8)	[5.0, 653.0]	1.3 (25.7)	[-298.0, 408.0]
Week 28	continuous exposure MK-3222 100 mg	250	34.9 (40.0)	[6.0, 409.0]	39.7 (65.5)	[6.0, 676.0]	4.8 (41.9)	[-194.0, 431.0]
	continuous exposure MK-3222 200 mg	210	32.4 (34.7)	[7.0, 369.0]	38.5 (55.2)	[6.0, 535.0]	6.1 (34.6)	[-62.0, 406.0]
	continuous exposure MK-3222 100 / 200 mg	631	33.8 (36.5)	[6.0, 409.0]	38.4 (55.6)	[6.0, 676.0]	4.6 (37.2)	[-306.0, 431.0]
Week 52	continuous exposure MK-3222 100 mg	251	33.6 (32.1)	[6.0, 274.0]	37.3 (44.1)	[7.0, 513.0]	3.7 (35.0)	[-158.0, 426.0]
	continuous exposure MK-3222 200 mg	207	30.7 (25.7)	[7.0, 173.0]	34.2 (32.6)	[6.0, 206.0]	3.5 (21.7)	[-81.0, 141.0]
	continuous exposure MK-3222 100 / 200 mg	625	32.6 (30.4)	[6.0, 335.0]	36.3 (38.4)	[6.0, 513.0]	3.7 (29.9)	[-294.0, 426.0]
Fasting Glucose (mg/dL)								
Week 4	continuous exposure MK-3222 100 mg	.	()	[,]	()	[,]	()	[,]
	continuous exposure MK-3222 100 / 200 mg	.	()	[,]	()	[,]	()	[,]

Summary of Laboratory Assessment over Time - Chemistry
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Fasting Glucose (mg/dL) (Continues)								
Week 12/16	continuous exposure MK-3222 100 mg	218	96.2 (18.5)	[61.0, 205.0]	98.0 (21.9)	[62.0, 231.0]	1.9 (17.5)	[-73.0, 104.0]
	continuous exposure MK-3222 200 mg	161	101.5 (30.4)	[60.0, 353.0]	102.0 (28.2)	[61.0, 266.0]	0.4 (26.5)	[-242.0, 69.0]
	continuous exposure MK-3222 100 / 200 mg	496	99.6 (27.9)	[43.0, 353.0]	99.6 (24.6)	[61.0, 266.0]	-0.1 (23.0)	[-242.0, 104.0]
Week 52	continuous exposure MK-3222 100 mg	216	96.1 (18.3)	[61.0, 205.0]	97.3 (17.6)	[50.0, 194.0]	1.2 (16.8)	[-61.0, 61.0]
	continuous exposure MK-3222 200 mg	160	101.7 (30.5)	[60.0, 353.0]	106.0 (40.4)	[50.0, 388.0]	4.3 (35.2)	[-120.0, 295.0]
	continuous exposure MK-3222 100 / 200 mg	491	99.4 (27.0)	[43.0, 353.0]	101.0 (29.5)	[40.0, 388.0]	1.6 (25.2)	[-120.0, 295.0]
Bicarbonate (mEq/L)								
Week 4	continuous exposure MK-3222 100 mg	251	24.8 (2.4)	[18.0, 31.0]	24.2 (2.7)	[15.0, 32.0]	-0.6 (2.4)	[-8.0, 8.0]
	continuous exposure MK-3222 200 mg	206	25.2 (2.4)	[18.0, 31.0]	24.6 (2.5)	[18.0, 31.0]	-0.6 (2.4)	[-7.0, 6.0]
	continuous exposure MK-3222 100 / 200 mg	626	25.1 (2.5)	[18.0, 33.0]	24.5 (2.7)	[15.0, 37.0]	-0.6 (2.6)	[-9.0, 8.0]
Week 12/16	continuous exposure MK-3222 100 mg	251	24.7 (2.4)	[18.0, 31.0]	25.3 (2.4)	[19.0, 32.0]	0.6 (2.6)	[-6.0, 11.0]
	continuous exposure MK-3222 200 mg	209	25.1 (2.4)	[18.0, 31.0]	25.9 (2.6)	[19.0, 33.0]	0.7 (2.7)	[-6.0, 9.0]
	continuous exposure MK-3222 100 / 200 mg	628	25.0 (2.5)	[18.0, 33.0]	25.6 (2.6)	[18.0, 39.0]	0.6 (2.8)	[-8.0, 13.0]

Summary of Laboratory Assessment over Time - Chemistry
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Bicarbonate (mEq/L) (Continues)								
Week 28	continuous exposure MK-3222 100 mg	250	24.8 (2.4)	[18.0, 31.0]	24.9 (2.5)	[18.0, 32.0]	0.1 (2.6)	[-7.0, 6.0]
	continuous exposure MK-3222 200 mg	210	25.1 (2.4)	[18.0, 31.0]	25.4 (2.6)	[18.0, 32.0]	0.2 (2.6)	[-8.0, 8.0]
	continuous exposure MK-3222 100 / 200 mg	631	25.1 (2.5)	[18.0, 33.0]	25.1 (2.6)	[16.0, 32.0]	0.1 (2.7)	[-10.0, 8.0]
Week 52	continuous exposure MK-3222 100 mg	250	24.8 (2.4)	[18.0, 31.0]	24.9 (2.2)	[19.0, 31.0]	0.1 (2.7)	[-8.0, 9.0]
	continuous exposure MK-3222 200 mg	207	25.1 (2.4)	[18.0, 31.0]	25.4 (2.4)	[18.0, 32.0]	0.2 (2.6)	[-7.0, 7.0]
	continuous exposure MK-3222 100 / 200 mg	624	25.0 (2.5)	[18.0, 33.0]	25.2 (2.5)	[16.0, 33.0]	0.1 (2.8)	[-9.0, 11.0]
Potassium (mEq/L)								
Week 4	continuous exposure MK-3222 100 mg	250	4.3 (0.3)	[3.1, 5.3]	4.3 (0.4)	[3.4, 5.5]	0.0 (0.4)	[-1.3, 1.4]
	continuous exposure MK-3222 200 mg	205	4.3 (0.4)	[3.2, 5.7]	4.3 (0.4)	[2.8, 5.6]	-0.0 (0.4)	[-1.6, 1.3]
	continuous exposure MK-3222 100 / 200 mg	624	4.3 (0.3)	[3.1, 5.7]	4.3 (0.4)	[2.8, 5.8]	-0.0 (0.4)	[-1.6, 1.4]
Week 12/16	continuous exposure MK-3222 100 mg	249	4.3 (0.3)	[3.1, 5.3]	4.3 (0.4)	[3.4, 5.5]	0.0 (0.3)	[-0.8, 1.0]
	continuous exposure MK-3222 200 mg	209	4.3 (0.4)	[3.2, 5.7]	4.3 (0.4)	[3.4, 5.4]	-0.0 (0.4)	[-1.4, 1.1]
	continuous exposure MK-3222 100 / 200 mg	625	4.3 (0.4)	[3.1, 5.7]	4.3 (0.4)	[3.4, 5.5]	0.0 (0.4)	[-1.4, 1.1]

Summary of Laboratory Assessment over Time - Chemistry
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Potassium (mEq/L) (Continues)								
Week 28	continuous exposure MK-3222 100 mg	249	4.3 (0.3)	[3.1, 5.3]	4.3 (0.4)	[3.2, 5.3]	0.1 (0.4)	[-1.0, 1.4]
	continuous exposure MK-3222 200 mg	210	4.3 (0.4)	[3.2, 5.7]	4.3 (0.4)	[3.3, 5.6]	0.1 (0.4)	[-1.5, 1.2]
	continuous exposure MK-3222 100 / 200 mg	629	4.3 (0.3)	[3.1, 5.7]	4.3 (0.4)	[3.2, 5.6]	0.0 (0.4)	[-1.5, 1.4]
Week 52	continuous exposure MK-3222 100 mg	247	4.3 (0.3)	[3.1, 5.3]	4.3 (0.4)	[3.2, 5.8]	0.1 (0.4)	[-0.9, 1.9]
	continuous exposure MK-3222 200 mg	207	4.3 (0.4)	[3.2, 5.7]	4.3 (0.3)	[3.4, 5.4]	0.0 (0.4)	[-1.4, 1.0]
	continuous exposure MK-3222 100 / 200 mg	620	4.3 (0.3)	[3.1, 5.7]	4.3 (0.4)	[3.2, 6.3]	0.1 (0.4)	[-1.4, 2.2]
Lactate Dehydrogenase (IU/L)								
Week 4	continuous exposure MK-3222 100 mg	251	175.9 (39.0)	[77.0, 461.0]	172.5 (37.6)	[74.0, 389.0]	-3.3 (31.8)	[-213.0, 181.0]
	continuous exposure MK-3222 200 mg	207	168.8 (33.2)	[71.0, 289.0]	166.2 (31.7)	[72.0, 297.0]	-2.7 (25.2)	[-117.0, 114.0]
	continuous exposure MK-3222 100 / 200 mg	626	172.0 (35.6)	[71.0, 461.0]	168.5 (34.0)	[72.0, 389.0]	-3.5 (27.2)	[-213.0, 181.0]
Week 12/16	continuous exposure MK-3222 100 mg	251	176.1 (39.0)	[77.0, 461.0]	169.1 (34.6)	[80.0, 405.0]	-7.0 (35.5)	[-255.0, 210.0]
	continuous exposure MK-3222 200 mg	209	169.0 (33.3)	[71.0, 289.0]	164.7 (30.9)	[61.0, 265.0]	-4.3 (24.6)	[-82.0, 75.0]
	continuous exposure MK-3222 100 / 200 mg	628	172.4 (35.7)	[71.0, 461.0]	167.8 (35.4)	[61.0, 453.0]	-4.6 (31.6)	[-255.0, 210.0]

Summary of Laboratory Assessment over Time - Chemistry
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Lactate Dehydrogenase (IU/L) (Continues)								
Week 28	continuous exposure MK-3222 100 mg	250	175.9 (38.9)	[77.0, 461.0]	169.6 (36.6)	[74.0, 424.0]	-6.3 (36.1)	[-263.0, 221.0]
	continuous exposure MK-3222 200 mg	210	169.1 (33.4)	[71.0, 289.0]	164.5 (36.9)	[62.0, 440.0]	-4.7 (32.1)	[-115.0, 279.0]
	continuous exposure MK-3222 100 / 200 mg	631	172.2 (35.7)	[71.0, 461.0]	166.9 (36.0)	[62.0, 440.0]	-5.4 (32.7)	[-263.0, 279.0]
Week 52	continuous exposure MK-3222 100 mg	250	175.9 (39.1)	[77.0, 461.0]	168.4 (37.0)	[66.0, 443.0]	-7.5 (36.7)	[-255.0, 262.0]
	continuous exposure MK-3222 200 mg	207	169.6 (33.3)	[71.0, 289.0]	160.7 (31.8)	[63.0, 284.0]	-8.9 (27.3)	[-109.0, 135.0]
	continuous exposure MK-3222 100 / 200 mg	624	172.1 (35.4)	[71.0, 461.0]	165.0 (34.8)	[63.0, 443.0]	-7.1 (31.8)	[-255.0, 262.0]
Non-Fasting Glucose (mg/dL)								
Week 4	continuous exposure MK-3222 100 mg	221	98.1 (24.1)	[57.0, 308.0]	100.5 (27.6)	[51.0, 253.0]	2.3 (22.2)	[-95.0, 126.0]
	continuous exposure MK-3222 200 mg	159	100.2 (28.3)	[64.0, 282.0]	106.8 (40.7)	[65.0, 340.0]	6.7 (28.5)	[-66.0, 166.0]
	continuous exposure MK-3222 100 / 200 mg	500	99.5 (29.5)	[57.0, 421.0]	102.9 (33.1)	[51.0, 340.0]	3.3 (25.2)	[-170.0, 166.0]
Week 12/16	continuous exposure MK-3222 100 mg	2	97.0 (5.7)	[93.0, 101.0]	89.0 (0.0)	[89.0, 89.0]	-8.0 (5.7)	[-12.0, -4.0]
	continuous exposure MK-3222 200 mg	2	74.5 (4.9)	[71.0, 78.0]	90.0 (2.8)	[88.0, 92.0]	15.5 (2.1)	[14.0, 17.0]
	continuous exposure MK-3222 100 / 200 mg	4	85.8 (13.7)	[71.0, 101.0]	89.5 (1.7)	[88.0, 92.0]	3.8 (14.0)	[-12.0, 17.0]

Summary of Laboratory Assessment over Time - Chemistry
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Non-Fasting Glucose (mg/dL) (Continues)								
Week 28	continuous exposure MK-3222 100 mg	220	98.0 (24.2)	[57.0, 308.0]	100.2 (27.1)	[53.0, 267.0]	2.2 (21.4)	[-129.0, 90.0]
	continuous exposure MK-3222 200 mg	163	99.9 (28.1)	[64.0, 282.0]	103.1 (29.7)	[61.0, 262.0]	3.2 (22.4)	[-115.0, 88.0]
	continuous exposure MK-3222 100 / 200 mg	503	99.4 (29.4)	[57.0, 421.0]	102.1 (32.4)	[53.0, 411.0]	2.7 (22.7)	[-129.0, 138.0]
Week 52	continuous exposure MK-3222 100 mg	3	97.3 (1.5)	[96.0, 99.0]	102.3 (15.5)	[91.0, 120.0]	5.0 (16.1)	[-8.0, 23.0]
	continuous exposure MK-3222 200 mg	2	101.5 (20.5)	[87.0, 116.0]	108.5 (24.7)	[91.0, 126.0]	7.0 (4.2)	[4.0, 10.0]
	continuous exposure MK-3222 100 / 200 mg	6	97.8 (9.9)	[87.0, 116.0]	102.0 (16.6)	[88.0, 126.0]	4.2 (11.1)	[-8.0, 23.0]
Phosphorus (mg/dL)								
Week 4	continuous exposure MK-3222 100 mg	250	3.3 (0.5)	[2.0, 5.0]	3.4 (0.5)	[2.2, 5.1]	0.0 (0.5)	[-1.2, 1.7]
	continuous exposure MK-3222 200 mg	206	3.4 (0.5)	[2.0, 5.1]	3.3 (0.5)	[1.9, 4.7]	-0.1 (0.5)	[-1.7, 1.5]
	continuous exposure MK-3222 100 / 200 mg	625	3.4 (0.5)	[1.9, 6.1]	3.4 (0.5)	[1.9, 5.1]	-0.0 (0.5)	[-1.8, 2.2]
Week 12/16	continuous exposure MK-3222 100 mg	250	3.3 (0.5)	[2.0, 5.0]	3.4 (0.5)	[1.3, 5.1]	0.0 (0.5)	[-1.8, 1.4]
	continuous exposure MK-3222 200 mg	209	3.4 (0.5)	[2.0, 5.1]	3.4 (0.5)	[1.8, 5.6]	-0.0 (0.5)	[-2.2, 1.4]
	continuous exposure MK-3222 100 / 200 mg	627	3.4 (0.5)	[1.9, 6.1]	3.4 (0.5)	[1.3, 5.6]	0.0 (0.5)	[-2.2, 1.6]

Summary of Laboratory Assessment over Time - Chemistry
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Phosphorus (mg/dL) (Continues)								
Week 28	continuous exposure MK-3222 100 mg	248	3.3 (0.5)	[2.0, 5.0]	3.4 (0.5)	[2.1, 5.1]	0.0 (0.6)	[-2.2, 1.5]
	continuous exposure MK-3222 200 mg	210	3.4 (0.5)	[2.0, 5.1]	3.4 (0.5)	[1.9, 5.0]	0.0 (0.5)	[-2.0, 1.4]
	continuous exposure MK-3222 100 / 200 mg	628	3.4 (0.5)	[1.9, 6.1]	3.4 (0.5)	[1.9, 5.1]	0.0 (0.6)	[-2.2, 2.1]
Week 52	continuous exposure MK-3222 100 mg	248	3.3 (0.5)	[2.0, 5.0]	3.4 (0.6)	[1.7, 5.7]	0.0 (0.6)	[-1.6, 2.2]
	continuous exposure MK-3222 200 mg	207	3.4 (0.5)	[2.0, 5.1]	3.4 (0.5)	[1.6, 5.0]	-0.0 (0.6)	[-1.7, 2.0]
	continuous exposure MK-3222 100 / 200 mg	622	3.4 (0.6)	[1.9, 6.1]	3.4 (0.6)	[1.6, 5.8]	0.0 (0.6)	[-2.2, 2.2]
Protein (gm/dL)								
Week 4	continuous exposure MK-3222 100 mg	251	7.3 (0.4)	[6.2, 8.6]	7.2 (0.4)	[6.3, 8.2]	-0.1 (0.3)	[-1.3, 0.8]
	continuous exposure MK-3222 200 mg	206	7.2 (0.4)	[6.3, 8.3]	7.2 (0.4)	[4.9, 8.4]	-0.0 (0.4)	[-3.0, 1.1]
	continuous exposure MK-3222 100 / 200 mg	626	7.2 (0.4)	[6.0, 8.9]	7.2 (0.4)	[4.9, 8.4]	-0.1 (0.4)	[-3.0, 1.1]
Week 12/16	continuous exposure MK-3222 100 mg	251	7.3 (0.4)	[6.2, 8.6]	7.2 (0.4)	[6.0, 8.2]	-0.1 (0.4)	[-1.2, 0.8]
	continuous exposure MK-3222 200 mg	209	7.2 (0.4)	[6.3, 8.3]	7.1 (0.4)	[6.4, 8.6]	-0.1 (0.3)	[-0.9, 1.2]
	continuous exposure MK-3222 100 / 200 mg	628	7.2 (0.4)	[6.0, 8.9]	7.2 (0.4)	[6.0, 8.6]	-0.1 (0.4)	[-1.7, 1.2]

Summary of Laboratory Assessment over Time - Chemistry
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Protein (gm/dL) (Continues)								
Week 28	continuous exposure MK-3222 100 mg	250	7.3 (0.4)	[6.2, 8.6]	7.2 (0.4)	[6.3, 8.1]	-0.1 (0.3)	[-1.2, 0.9]
	continuous exposure MK-3222 200 mg	210	7.2 (0.4)	[6.3, 8.3]	7.2 (0.4)	[6.1, 8.6]	-0.0 (0.3)	[-0.9, 1.5]
	continuous exposure MK-3222 100 / 200 mg	631	7.2 (0.4)	[6.0, 8.9]	7.2 (0.4)	[6.1, 8.6]	-0.1 (0.4)	[-1.5, 1.5]
Week 52	continuous exposure MK-3222 100 mg	250	7.3 (0.4)	[6.2, 8.6]	7.2 (0.4)	[6.2, 8.4]	-0.1 (0.4)	[-1.0, 1.1]
	continuous exposure MK-3222 200 mg	207	7.2 (0.4)	[6.3, 8.3]	7.2 (0.4)	[5.9, 9.0]	-0.0 (0.4)	[-1.0, 0.9]
	continuous exposure MK-3222 100 / 200 mg	624	7.2 (0.4)	[6.0, 8.9]	7.2 (0.4)	[5.9, 9.0]	-0.1 (0.4)	[-1.2, 1.6]
Sodium (mEq/L)								
Week 4	continuous exposure MK-3222 100 mg	251	141.2 (2.4)	[132.0, 153.0]	141.0 (2.3)	[131.0, 147.0]	-0.3 (2.3)	[-12.0, 6.0]
	continuous exposure MK-3222 200 mg	205	140.8 (2.1)	[135.0, 147.0]	140.9 (2.3)	[134.0, 148.0]	0.1 (2.2)	[-8.0, 5.0]
	continuous exposure MK-3222 100 / 200 mg	625	140.9 (2.2)	[132.0, 153.0]	140.9 (2.4)	[131.0, 157.0]	-0.0 (2.3)	[-12.0, 14.0]
Week 12/16	continuous exposure MK-3222 100 mg	251	141.2 (2.4)	[132.0, 153.0]	141.0 (2.2)	[135.0, 148.0]	-0.2 (2.4)	[-12.0, 9.0]
	continuous exposure MK-3222 200 mg	209	140.8 (2.1)	[135.0, 147.0]	140.8 (2.1)	[134.0, 149.0]	-0.0 (1.9)	[-5.0, 5.0]
	continuous exposure MK-3222 100 / 200 mg	628	140.9 (2.2)	[132.0, 153.0]	140.8 (2.1)	[134.0, 149.0]	-0.1 (2.2)	[-12.0, 9.0]

Summary of Laboratory Assessment over Time - Chemistry
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Sodium (mEq/L) (Continues)								
Week 28	continuous exposure MK-3222 100 mg	250	141.3 (2.4)	[132.0, 153.0]	140.7 (2.5)	[125.0, 149.0]	-0.6 (2.5)	[-17.0, 7.0]
	continuous exposure MK-3222 200 mg	210	140.8 (2.1)	[135.0, 147.0]	140.7 (2.3)	[134.0, 149.0]	-0.2 (2.3)	[-8.0, 8.0]
	continuous exposure MK-3222 100 / 200 mg	630	140.9 (2.2)	[132.0, 153.0]	140.6 (2.4)	[125.0, 149.0]	-0.3 (2.4)	[-17.0, 8.0]
Week 52	continuous exposure MK-3222 100 mg	250	141.3 (2.4)	[132.0, 153.0]	140.6 (2.1)	[133.0, 150.0]	-0.6 (2.4)	[-11.0, 8.0]
	continuous exposure MK-3222 200 mg	207	140.9 (2.1)	[135.0, 147.0]	140.4 (2.2)	[133.0, 147.0]	-0.4 (2.2)	[-6.0, 5.0]
	continuous exposure MK-3222 100 / 200 mg	624	141.0 (2.2)	[132.0, 153.0]	140.4 (2.2)	[132.0, 150.0]	-0.5 (2.3)	[-11.0, 8.0]
Triglycerides (mg/dL)								
Week 12/16	continuous exposure MK-3222 100 mg	219	162.3 (134.7)	[41.0, 1688.0]	172.3 (142.4)	[39.0, 1570.0]	10.0 (90.3)	[-310.0, 637.0]
	continuous exposure MK-3222 200 mg	161	149.7 (88.5)	[34.0, 549.0]	164.8 (90.1)	[42.0, 606.0]	15.1 (68.1)	[-275.0, 292.0]
	continuous exposure MK-3222 100 / 200 mg	498	156.6 (115.4)	[34.0, 1688.0]	169.1 (127.6)	[39.0, 1570.0]	12.4 (87.3)	[-338.0, 704.0]
Week 52	continuous exposure MK-3222 100 mg	219	162.4 (134.8)	[41.0, 1688.0]	167.8 (114.9)	[36.0, 989.0]	5.4 (99.2)	[-699.0, 431.0]
	continuous exposure MK-3222 200 mg	163	148.5 (88.1)	[34.0, 549.0]	159.7 (98.5)	[39.0, 579.0]	11.2 (81.5)	[-347.0, 380.0]
	continuous exposure MK-3222 100 / 200 mg	500	155.8 (115.2)	[34.0, 1688.0]	168.7 (127.4)	[36.0, 1586.0]	12.8 (112.5)	[-699.0, 1438.0]

Summary of Laboratory Assessment over Time - Chemistry
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Bilirubin (mg/dL)								
Week 4	continuous exposure MK-3222 100 mg	251	0.5 (0.2)	[0.1, 1.5]	0.4 (0.2)	[0.1, 1.7]	-0.0 (0.2)	[-0.8, 1.0]
	continuous exposure MK-3222 200 mg	206	0.5 (0.3)	[0.1, 2.3]	0.5 (0.3)	[0.1, 1.9]	-0.0 (0.2)	[-0.9, 0.6]
	continuous exposure MK-3222 100 / 200 mg	626	0.5 (0.3)	[0.1, 3.4]	0.5 (0.3)	[0.1, 2.7]	-0.0 (0.2)	[-0.9, 1.0]
Week 12/16	continuous exposure MK-3222 100 mg	251	0.5 (0.2)	[0.1, 1.5]	0.5 (0.2)	[0.1, 1.7]	-0.0 (0.2)	[-0.8, 1.1]
	continuous exposure MK-3222 200 mg	209	0.5 (0.3)	[0.1, 2.3]	0.5 (0.3)	[0.1, 2.1]	-0.0 (0.2)	[-0.7, 0.8]
	continuous exposure MK-3222 100 / 200 mg	628	0.5 (0.3)	[0.1, 3.4]	0.5 (0.3)	[0.1, 2.2]	-0.0 (0.2)	[-1.2, 1.1]
Week 28	continuous exposure MK-3222 100 mg	249	0.5 (0.2)	[0.1, 1.5]	0.5 (0.2)	[0.1, 1.5]	-0.0 (0.2)	[-0.8, 0.7]
	continuous exposure MK-3222 200 mg	210	0.5 (0.3)	[0.1, 2.3]	0.5 (0.3)	[0.1, 2.2]	-0.0 (0.2)	[-0.7, 1.4]
	continuous exposure MK-3222 100 / 200 mg	630	0.5 (0.3)	[0.1, 3.4]	0.5 (0.3)	[0.1, 2.8]	-0.0 (0.2)	[-0.8, 1.4]
Week 52	continuous exposure MK-3222 100 mg	247	0.5 (0.2)	[0.1, 1.5]	0.5 (0.3)	[0.1, 2.0]	-0.0 (0.2)	[-0.6, 1.0]
	continuous exposure MK-3222 200 mg	206	0.5 (0.3)	[0.1, 2.3]	0.5 (0.3)	[0.1, 2.1]	-0.0 (0.2)	[-0.7, 0.9]
	continuous exposure MK-3222 100 / 200 mg	618	0.5 (0.3)	[0.1, 3.4]	0.5 (0.3)	[0.1, 3.2]	-0.0 (0.2)	[-0.7, 1.0]

Baseline is defined as last value obtained prior to the first dose of study medication during treatment phase.
Values for fasting glucose are blank at week 4 because it was not scheduled for assessment.
For Phosphorus, the unit conversion took place when generating this table.
N: number of subjects with non-missing baseline and post-baseline values at the given time point.
SD=Standard deviation; Min=Minimum; Max=Maximum.
[Source: 5.3.5.3-10]

付録 2.7.4-43
臨床検査値の経時的変動の要約 - 血液学的検査
第 IIb 相及び第 III 相試験：ベース試験の安全性併合解析 - 継続曝露
1 回以上投与された被験者

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Basophils/Leukocytes (%)								
Week 4	continuous exposure MK-3222 100 mg	222	0.4 (0.2)	[0.0, 1.1]	0.4 (0.2)	[0.0, 1.3]	0.0 (0.3)	[-1.1, 0.9]
	continuous exposure MK-3222 200 mg	163	0.4 (0.2)	[0.0, 1.4]	0.4 (0.2)	[0.0, 1.4]	0.0 (0.2)	[-0.6, 1.1]
	continuous exposure MK-3222 100 / 200 mg	504	0.4 (0.2)	[0.0, 2.0]	0.4 (0.2)	[0.0, 1.4]	0.0 (0.3)	[-1.6, 1.1]
Week 12/16	continuous exposure MK-3222 100 mg	220	0.4 (0.2)	[0.0, 1.1]	0.4 (0.3)	[0.0, 2.7]	0.0 (0.3)	[-0.9, 2.2]
	continuous exposure MK-3222 200 mg	162	0.4 (0.2)	[0.0, 1.4]	0.4 (0.3)	[0.0, 2.7]	0.0 (0.3)	[-0.9, 2.1]
	continuous exposure MK-3222 100 / 200 mg	502	0.4 (0.2)	[0.0, 2.0]	0.4 (0.3)	[0.0, 2.7]	0.0 (0.3)	[-1.4, 2.2]
Week 28	continuous exposure MK-3222 100 mg	219	0.4 (0.2)	[0.0, 1.1]	0.4 (0.3)	[0.0, 2.0]	0.0 (0.3)	[-0.9, 1.7]
	continuous exposure MK-3222 200 mg	161	0.4 (0.2)	[0.0, 1.4]	0.4 (0.4)	[0.0, 3.6]	0.0 (0.4)	[-1.1, 3.3]
	continuous exposure MK-3222 100 / 200 mg	499	0.4 (0.2)	[0.0, 2.0]	0.4 (0.3)	[0.0, 3.6]	0.0 (0.4)	[-1.6, 3.3]
Week 52	continuous exposure MK-3222 100 mg	220	0.4 (0.2)	[0.0, 1.1]	0.4 (0.3)	[0.0, 3.2]	0.0 (0.3)	[-0.8, 2.9]
	continuous exposure MK-3222 200 mg	159	0.4 (0.2)	[0.0, 1.4]	0.4 (0.3)	[0.0, 1.8]	0.0 (0.3)	[-0.8, 1.6]
	continuous exposure MK-3222 100 / 200 mg	496	0.4 (0.2)	[0.0, 2.0]	0.4 (0.3)	[0.0, 3.2]	0.0 (0.3)	[-1.5, 2.9]

Summary of Laboratory Assessment over Time - Hematology
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Eosinophils (10[3]/microL)								
Week 4	continuous exposure MK-3222 100 mg	251	0.2 (0.2)	[0.0, 1.4]	0.2 (0.2)	[0.0, 1.0]	-0.0 (0.1)	[-1.2, 0.5]
	continuous exposure MK-3222 200 mg	207	0.2 (0.2)	[0.0, 1.2]	0.2 (0.2)	[0.0, 1.9]	-0.0 (0.1)	[-0.4, 1.3]
	continuous exposure MK-3222 100 / 200 mg	625	0.2 (0.2)	[0.0, 1.4]	0.2 (0.2)	[0.0, 1.9]	-0.0 (0.1)	[-1.2, 1.3]
Week 12/16	continuous exposure MK-3222 100 mg	249	0.2 (0.2)	[0.0, 1.4]	0.2 (0.1)	[0.0, 1.1]	-0.0 (0.1)	[-0.9, 0.5]
	continuous exposure MK-3222 200 mg	209	0.2 (0.2)	[0.0, 1.2]	0.2 (0.1)	[0.0, 1.0]	-0.0 (0.1)	[-0.5, 0.3]
	continuous exposure MK-3222 100 / 200 mg	626	0.2 (0.2)	[0.0, 1.4]	0.2 (0.1)	[0.0, 1.1]	-0.0 (0.1)	[-0.9, 0.5]
Week 28	continuous exposure MK-3222 100 mg	247	0.2 (0.2)	[0.0, 1.4]	0.2 (0.1)	[0.0, 0.8]	-0.0 (0.2)	[-1.3, 0.6]
	continuous exposure MK-3222 200 mg	207	0.2 (0.2)	[0.0, 1.2]	0.2 (0.2)	[0.0, 2.2]	0.0 (0.2)	[-0.5, 2.0]
	continuous exposure MK-3222 100 / 200 mg	621	0.2 (0.2)	[0.0, 1.4]	0.2 (0.2)	[0.0, 2.2]	-0.0 (0.2)	[-1.3, 2.0]
Week 52	continuous exposure MK-3222 100 mg	249	0.2 (0.2)	[0.0, 1.4]	0.2 (0.1)	[0.0, 0.8]	-0.0 (0.1)	[-1.2, 0.6]
	continuous exposure MK-3222 200 mg	203	0.2 (0.2)	[0.0, 1.2]	0.2 (0.1)	[0.0, 0.7]	-0.0 (0.1)	[-0.6, 0.5]
	continuous exposure MK-3222 100 / 200 mg	618	0.2 (0.2)	[0.0, 1.4]	0.2 (0.1)	[0.0, 0.8]	-0.0 (0.1)	[-1.2, 0.6]

Summary of Laboratory Assessment over Time - Hematology
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Eosinophils/Leukocytes (%)								
Week 4	continuous exposure MK-3222 100 mg	222	2.7 (2.1)	[0.1, 13.7]	2.7 (2.0)	[0.0, 14.6]	0.0 (1.4)	[-8.9, 4.5]
	continuous exposure MK-3222 200 mg	163	2.6 (1.9)	[0.0, 11.5]	2.5 (1.9)	[0.0, 11.6]	-0.2 (1.2)	[-4.7, 3.8]
	continuous exposure MK-3222 100 / 200 mg	504	2.6 (1.9)	[0.0, 13.7]	2.6 (2.0)	[0.0, 17.5]	-0.0 (1.4)	[-8.9, 11.1]
Week 12/16	continuous exposure MK-3222 100 mg	220	2.7 (2.1)	[0.1, 13.7]	2.7 (2.0)	[0.1, 12.3]	0.0 (1.6)	[-5.7, 6.3]
	continuous exposure MK-3222 200 mg	162	2.6 (1.9)	[0.0, 11.5]	2.4 (2.0)	[0.0, 17.0]	-0.2 (1.3)	[-5.3, 5.5]
	continuous exposure MK-3222 100 / 200 mg	502	2.6 (1.9)	[0.0, 13.7]	2.5 (1.9)	[0.0, 17.0]	-0.1 (1.4)	[-5.7, 6.3]
Week 28	continuous exposure MK-3222 100 mg	219	2.7 (2.1)	[0.1, 13.7]	2.6 (1.9)	[0.1, 13.2]	-0.1 (1.7)	[-9.8, 7.6]
	continuous exposure MK-3222 200 mg	161	2.6 (1.9)	[0.0, 11.5]	2.9 (2.7)	[0.0, 22.8]	0.3 (2.3)	[-6.0, 20.7]
	continuous exposure MK-3222 100 / 200 mg	499	2.6 (1.9)	[0.0, 13.7]	2.7 (2.2)	[0.0, 22.8]	0.1 (1.9)	[-9.8, 20.7]
Week 52	continuous exposure MK-3222 100 mg	220	2.7 (2.1)	[0.1, 13.7]	2.7 (1.9)	[0.1, 9.6]	0.0 (1.8)	[-8.6, 7.4]
	continuous exposure MK-3222 200 mg	159	2.6 (1.9)	[0.0, 11.5]	2.6 (1.7)	[0.1, 10.6]	0.0 (1.5)	[-6.7, 4.3]
	continuous exposure MK-3222 100 / 200 mg	496	2.6 (1.9)	[0.0, 13.7]	2.6 (1.8)	[0.1, 10.6]	0.0 (1.6)	[-8.6, 7.4]

Summary of Laboratory Assessment over Time - Hematology
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Hematocrit (%)								
Week 4	continuous exposure MK-3222 100 mg	251	44.5 (3.8)	[31.8, 52.8]	44.4 (3.8)	[32.4, 55.6]	-0.0 (2.0)	[-5.4, 8.9]
	continuous exposure MK-3222 200 mg	207	44.2 (3.7)	[32.7, 58.8]	44.2 (3.7)	[32.9, 60.5]	0.0 (2.1)	[-9.4, 7.5]
	continuous exposure MK-3222 100 / 200 mg	625	44.3 (3.7)	[31.8, 58.8]	44.3 (3.7)	[32.4, 60.5]	-0.0 (2.0)	[-9.4, 8.9]
Week 12/16	continuous exposure MK-3222 100 mg	250	44.4 (3.8)	[31.8, 52.8]	44.4 (3.9)	[30.4, 55.7]	-0.0 (2.4)	[-12.3, 7.7]
	continuous exposure MK-3222 200 mg	209	44.2 (3.6)	[32.7, 58.8]	44.4 (3.8)	[35.0, 59.2]	0.2 (2.2)	[-6.2, 5.7]
	continuous exposure MK-3222 100 / 200 mg	627	44.3 (3.6)	[31.8, 58.8]	44.5 (3.8)	[30.4, 59.2]	0.2 (2.3)	[-12.3, 7.7]
Week 28	continuous exposure MK-3222 100 mg	247	44.5 (3.8)	[31.8, 52.8]	44.3 (3.7)	[32.1, 55.4]	-0.2 (2.3)	[-11.5, 7.0]
	continuous exposure MK-3222 200 mg	208	44.1 (3.5)	[32.7, 53.0]	44.2 (3.4)	[33.9, 53.1]	0.1 (2.3)	[-6.5, 9.6]
	continuous exposure MK-3222 100 / 200 mg	622	44.3 (3.6)	[31.8, 55.0]	44.3 (3.6)	[32.1, 55.4]	-0.0 (2.3)	[-11.5, 9.6]
Week 52	continuous exposure MK-3222 100 mg	249	44.5 (3.8)	[31.8, 52.8]	44.8 (4.0)	[30.9, 55.3]	0.3 (2.4)	[-7.0, 6.6]
	continuous exposure MK-3222 200 mg	204	44.2 (3.6)	[32.7, 58.8]	44.5 (3.4)	[35.5, 58.5]	0.3 (2.4)	[-6.1, 10.6]
	continuous exposure MK-3222 100 / 200 mg	620	44.3 (3.6)	[31.8, 58.8]	44.7 (3.8)	[28.4, 58.5]	0.3 (2.4)	[-9.4, 10.6]

Summary of Laboratory Assessment over Time - Hematology
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Hemoglobin (gm/dL)								
Week 4	continuous exposure MK-3222 100 mg	251	14.7 (1.4)	[9.7, 17.9]	14.7 (1.3)	[10.1, 17.6]	-0.0 (0.6)	[-1.8, 3.0]
	continuous exposure MK-3222 200 mg	207	14.6 (1.3)	[10.2, 18.5]	14.6 (1.3)	[10.6, 19.0]	0.0 (0.6)	[-2.8, 2.1]
	continuous exposure MK-3222 100 / 200 mg	625	14.7 (1.3)	[9.7, 18.7]	14.7 (1.3)	[10.1, 19.0]	-0.0 (0.6)	[-2.8, 3.0]
Week 12/16	continuous exposure MK-3222 100 mg	250	14.7 (1.4)	[9.7, 17.9]	14.6 (1.4)	[9.7, 18.2]	-0.0 (0.7)	[-3.8, 2.2]
	continuous exposure MK-3222 200 mg	209	14.6 (1.3)	[10.2, 18.5]	14.6 (1.3)	[10.7, 19.0]	0.0 (0.7)	[-2.3, 2.1]
	continuous exposure MK-3222 100 / 200 mg	627	14.7 (1.3)	[9.7, 18.7]	14.7 (1.3)	[9.7, 19.0]	0.0 (0.7)	[-3.8, 2.9]
Week 28	continuous exposure MK-3222 100 mg	247	14.7 (1.4)	[9.7, 17.9]	14.7 (1.3)	[9.7, 18.1]	-0.0 (0.7)	[-3.1, 1.9]
	continuous exposure MK-3222 200 mg	208	14.6 (1.2)	[10.2, 17.3]	14.6 (1.2)	[11.2, 17.2]	-0.0 (0.7)	[-1.5, 1.8]
	continuous exposure MK-3222 100 / 200 mg	622	14.7 (1.3)	[9.7, 18.7]	14.7 (1.3)	[9.7, 18.6]	-0.0 (0.7)	[-3.1, 2.8]
Week 52	continuous exposure MK-3222 100 mg	249	14.7 (1.4)	[9.7, 17.9]	14.8 (1.4)	[9.4, 18.5]	0.1 (0.7)	[-2.0, 2.1]
	continuous exposure MK-3222 200 mg	204	14.6 (1.3)	[10.2, 18.5]	14.7 (1.2)	[11.4, 18.6]	0.1 (0.8)	[-1.6, 4.1]
	continuous exposure MK-3222 100 / 200 mg	620	14.7 (1.3)	[9.7, 18.7]	14.8 (1.3)	[8.8, 18.7]	0.1 (0.8)	[-3.5, 4.1]

Summary of Laboratory Assessment over Time - Hematology
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Lymphocytes (10[3]/microL)								
Week 4	continuous exposure MK-3222 100 mg	251	1.9 (0.7)	[0.6, 6.1]	1.9 (0.7)	[0.5, 5.5]	0.1 (0.4)	[-1.4, 1.7]
	continuous exposure MK-3222 200 mg	207	1.8 (0.7)	[0.4, 4.1]	1.9 (0.6)	[0.5, 4.2]	0.1 (0.4)	[-1.6, 1.4]
	continuous exposure MK-3222 100 / 200 mg	625	1.8 (0.7)	[0.4, 6.1]	1.9 (0.7)	[0.5, 6.4]	0.1 (0.4)	[-1.6, 3.5]
Week 12/16	continuous exposure MK-3222 100 mg	249	1.9 (0.7)	[0.6, 6.1]	2.0 (0.7)	[0.7, 5.7]	0.1 (0.4)	[-1.4, 1.5]
	continuous exposure MK-3222 200 mg	209	1.8 (0.6)	[0.4, 4.1]	1.9 (0.6)	[0.7, 4.0]	0.1 (0.4)	[-1.8, 1.2]
	continuous exposure MK-3222 100 / 200 mg	626	1.8 (0.7)	[0.4, 6.1]	1.9 (0.6)	[0.5, 5.7]	0.1 (0.4)	[-1.8, 1.5]
Week 28	continuous exposure MK-3222 100 mg	247	1.9 (0.7)	[0.6, 6.1]	2.0 (0.7)	[0.5, 7.0]	0.1 (0.5)	[-1.6, 1.9]
	continuous exposure MK-3222 200 mg	207	1.8 (0.7)	[0.4, 4.1]	1.9 (0.6)	[0.7, 4.0]	0.1 (0.4)	[-1.7, 1.6]
	continuous exposure MK-3222 100 / 200 mg	621	1.8 (0.7)	[0.4, 6.1]	1.9 (0.7)	[0.5, 7.0]	0.1 (0.5)	[-1.7, 1.9]
Week 52	continuous exposure MK-3222 100 mg	249	1.9 (0.7)	[0.6, 6.1]	1.9 (0.7)	[0.7, 7.5]	0.1 (0.4)	[-1.1, 1.7]
	continuous exposure MK-3222 200 mg	203	1.8 (0.7)	[0.4, 4.1]	1.8 (0.6)	[0.5, 3.7]	0.0 (0.5)	[-2.2, 1.8]
	continuous exposure MK-3222 100 / 200 mg	618	1.8 (0.7)	[0.4, 6.1]	1.9 (0.7)	[0.5, 7.5]	0.1 (0.4)	[-2.2, 2.9]

Summary of Laboratory Assessment over Time - Hematology
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Lymphocytes/Leukocytes (%)								
Week 4	continuous exposure MK-3222 100 mg	222	25.6 (8.0)	[7.7, 55.8]	27.4 (7.7)	[3.2, 55.7]	1.7 (5.7)	[-18.7, 17.7]
	continuous exposure MK-3222 200 mg	163	26.1 (7.9)	[10.2, 59.4]	27.2 (8.1)	[9.1, 58.3]	1.1 (6.5)	[-22.5, 22.7]
	continuous exposure MK-3222 100 / 200 mg	504	26.0 (7.6)	[7.7, 59.4]	27.3 (7.7)	[3.2, 58.3]	1.3 (6.2)	[-22.5, 31.3]
Week 12/16	continuous exposure MK-3222 100 mg	220	25.8 (8.0)	[7.7, 55.8]	28.7 (7.8)	[7.4, 57.1]	2.9 (6.7)	[-27.2, 27.6]
	continuous exposure MK-3222 200 mg	162	26.0 (8.0)	[10.2, 59.4]	27.6 (7.1)	[12.7, 48.3]	1.6 (6.9)	[-22.1, 22.7]
	continuous exposure MK-3222 100 / 200 mg	502	26.1 (7.6)	[7.7, 59.4]	28.2 (7.6)	[7.4, 57.1]	2.1 (6.8)	[-27.2, 27.6]
Week 28	continuous exposure MK-3222 100 mg	219	25.6 (8.0)	[7.7, 55.8]	28.0 (7.7)	[7.4, 53.8]	2.5 (6.8)	[-15.3, 26.3]
	continuous exposure MK-3222 200 mg	161	26.1 (8.0)	[10.2, 59.4]	28.1 (7.0)	[10.8, 47.6]	2.0 (6.1)	[-14.8, 23.9]
	continuous exposure MK-3222 100 / 200 mg	499	26.1 (7.7)	[7.7, 59.4]	28.3 (7.6)	[7.4, 58.0]	2.2 (6.7)	[-15.3, 36.8]
Week 52	continuous exposure MK-3222 100 mg	220	25.8 (8.0)	[7.7, 55.8]	28.0 (7.9)	[9.6, 64.9]	2.3 (6.3)	[-12.4, 25.6]
	continuous exposure MK-3222 200 mg	159	25.9 (8.1)	[10.2, 59.4]	27.4 (7.4)	[5.7, 53.3]	1.4 (7.0)	[-22.2, 27.5]
	continuous exposure MK-3222 100 / 200 mg	496	26.1 (7.7)	[7.7, 59.4]	28.0 (7.4)	[5.7, 64.9]	1.9 (6.4)	[-22.2, 27.5]

Summary of Laboratory Assessment over Time - Hematology
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Leukocytes (10[3]/microL)								
Week 4	continuous exposure MK-3222 100 mg	251	7.5 (2.2)	[3.1, 17.5]	7.3 (2.2)	[3.1, 17.3]	-0.3 (1.7)	[-10.5, 9.2]
	continuous exposure MK-3222 200 mg	207	7.1 (2.2)	[3.4, 21.6]	7.0 (1.8)	[3.2, 12.3]	-0.1 (1.6)	[-10.2, 6.6]
	continuous exposure MK-3222 100 / 200 mg	625	7.3 (2.2)	[3.1, 21.6]	7.1 (2.1)	[3.1, 17.3]	-0.2 (1.6)	[-10.5, 9.2]
Week 12/16	continuous exposure MK-3222 100 mg	250	7.5 (2.1)	[3.1, 17.5]	7.1 (2.1)	[3.4, 19.3]	-0.4 (1.9)	[-9.9, 14.0]
	continuous exposure MK-3222 200 mg	209	7.1 (2.2)	[3.4, 21.6]	7.0 (2.1)	[3.7, 20.1]	-0.1 (1.5)	[-5.7, 4.6]
	continuous exposure MK-3222 100 / 200 mg	627	7.3 (2.1)	[2.8, 21.6]	7.0 (2.1)	[3.0, 20.1]	-0.3 (1.7)	[-9.9, 14.0]
Week 28	continuous exposure MK-3222 100 mg	247	7.6 (2.2)	[3.1, 17.5]	7.3 (2.4)	[3.4, 23.5]	-0.2 (1.9)	[-9.6, 10.4]
	continuous exposure MK-3222 200 mg	208	7.0 (2.2)	[3.4, 21.6]	6.8 (1.8)	[3.7, 11.9]	-0.2 (1.7)	[-13.2, 3.0]
	continuous exposure MK-3222 100 / 200 mg	622	7.3 (2.2)	[2.8, 21.6]	7.1 (2.1)	[2.9, 23.5]	-0.2 (1.7)	[-13.2, 10.4]
Week 52	continuous exposure MK-3222 100 mg	249	7.5 (2.2)	[3.1, 17.5]	7.0 (2.0)	[2.8, 15.8]	-0.5 (1.8)	[-10.1, 7.5]
	continuous exposure MK-3222 200 mg	204	7.0 (2.2)	[3.4, 21.6]	6.7 (2.1)	[2.9, 21.7]	-0.4 (2.1)	[-13.1, 10.6]
	continuous exposure MK-3222 100 / 200 mg	620	7.3 (2.2)	[2.8, 21.6]	6.9 (2.1)	[2.7, 21.7]	-0.4 (1.8)	[-13.1, 10.6]

Summary of Laboratory Assessment over Time - Hematology
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Erythrocytes (10[6]/microL)								
Week 4	continuous exposure MK-3222 100 mg	251	4.9 (0.4)	[3.7, 6.8]	4.9 (0.4)	[3.3, 6.9]	-0.0 (0.2)	[-0.5, 1.4]
	continuous exposure MK-3222 200 mg	207	4.8 (0.4)	[3.6, 6.1]	4.8 (0.4)	[3.3, 6.2]	0.0 (0.2)	[-0.9, 0.8]
	continuous exposure MK-3222 100 / 200 mg	625	4.8 (0.4)	[3.6, 6.9]	4.8 (0.4)	[3.3, 7.1]	-0.0 (0.2)	[-0.9, 1.4]
Week 12/16	continuous exposure MK-3222 100 mg	250	4.9 (0.4)	[3.7, 6.8]	4.8 (0.5)	[2.8, 7.0]	-0.0 (0.2)	[-1.2, 0.7]
	continuous exposure MK-3222 200 mg	209	4.8 (0.4)	[3.6, 6.1]	4.8 (0.4)	[3.7, 6.2]	0.0 (0.2)	[-0.7, 0.7]
	continuous exposure MK-3222 100 / 200 mg	627	4.8 (0.4)	[3.6, 6.9]	4.8 (0.5)	[2.8, 7.0]	0.0 (0.2)	[-1.2, 0.9]
Week 28	continuous exposure MK-3222 100 mg	247	4.9 (0.5)	[3.7, 6.8]	4.8 (0.5)	[3.6, 6.8]	-0.0 (0.2)	[-1.0, 0.6]
	continuous exposure MK-3222 200 mg	208	4.8 (0.4)	[3.6, 5.9]	4.8 (0.4)	[3.5, 5.8]	-0.0 (0.2)	[-0.6, 0.6]
	continuous exposure MK-3222 100 / 200 mg	622	4.8 (0.4)	[3.6, 6.9]	4.8 (0.4)	[3.4, 7.1]	-0.0 (0.2)	[-1.0, 0.8]
Week 52	continuous exposure MK-3222 100 mg	249	4.9 (0.5)	[3.7, 6.8]	4.9 (0.5)	[3.6, 6.9]	0.0 (0.3)	[-0.8, 0.7]
	continuous exposure MK-3222 200 mg	204	4.8 (0.4)	[3.6, 6.1]	4.8 (0.4)	[3.5, 6.1]	0.0 (0.2)	[-0.6, 0.7]
	continuous exposure MK-3222 100 / 200 mg	620	4.8 (0.4)	[3.6, 6.8]	4.9 (0.4)	[3.5, 6.9]	0.0 (0.2)	[-0.9, 1.0]

Summary of Laboratory Assessment over Time - Hematology
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Platelet (10[3]/microL)								
Week 4	continuous exposure MK-3222 100 mg	246	242.3 (57.3)	[102.0, 438.0]	238.5 (58.9)	[110.0, 443.0]	-3.8 (34.4)	[-167.0, 136.0]
	continuous exposure MK-3222 200 mg	202	243.7 (53.8)	[118.0, 391.0]	239.9 (51.2)	[121.0, 397.0]	-3.8 (27.3)	[-132.0, 112.0]
	continuous exposure MK-3222 100 / 200 mg	614	240.9 (55.2)	[102.0, 438.0]	236.8 (54.7)	[110.0, 443.0]	-4.1 (31.0)	[-167.0, 136.0]
Week 12/16	continuous exposure MK-3222 100 mg	245	241.9 (57.4)	[102.0, 438.0]	232.3 (53.2)	[107.0, 419.0]	-9.6 (29.4)	[-122.0, 98.0]
	continuous exposure MK-3222 200 mg	208	240.3 (56.3)	[36.0, 391.0]	232.3 (53.5)	[53.0, 427.0]	-7.9 (29.4)	[-113.0, 98.0]
	continuous exposure MK-3222 100 / 200 mg	619	239.5 (56.5)	[36.0, 438.0]	231.2 (52.7)	[53.0, 427.0]	-8.3 (29.2)	[-122.0, 98.0]
Week 28	continuous exposure MK-3222 100 mg	241	242.4 (57.2)	[102.0, 438.0]	236.7 (53.8)	[99.0, 387.0]	-5.7 (32.6)	[-209.0, 75.0]
	continuous exposure MK-3222 200 mg	206	240.7 (56.8)	[36.0, 391.0]	238.0 (54.8)	[56.0, 440.0]	-2.7 (26.8)	[-82.0, 91.0]
	continuous exposure MK-3222 100 / 200 mg	613	240.0 (56.6)	[36.0, 438.0]	235.7 (53.4)	[56.0, 440.0]	-4.3 (30.2)	[-209.0, 119.0]
Week 52	continuous exposure MK-3222 100 mg	246	242.4 (57.4)	[102.0, 438.0]	238.3 (54.4)	[113.0, 390.0]	-4.0 (37.0)	[-181.0, 115.0]
	continuous exposure MK-3222 200 mg	202	240.1 (56.7)	[36.0, 391.0]	233.3 (52.1)	[94.0, 430.0]	-6.8 (36.9)	[-166.0, 129.0]
	continuous exposure MK-3222 100 / 200 mg	615	239.6 (56.5)	[36.0, 438.0]	234.7 (52.8)	[94.0, 430.0]	-5.0 (35.2)	[-181.0, 129.0]

Summary of Laboratory Assessment over Time - Hematology
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Monocytes (10[3]/microL)								
Week 4	continuous exposure MK-3222 100 mg	251	0.5 (0.2)	[0.1, 1.3]	0.5 (0.2)	[0.1, 1.0]	-0.0 (0.2)	[-0.9, 0.5]
	continuous exposure MK-3222 200 mg	207	0.5 (0.2)	[0.1, 1.2]	0.4 (0.2)	[0.1, 1.2]	-0.0 (0.2)	[-0.7, 0.4]
	continuous exposure MK-3222 100 / 200 mg	625	0.5 (0.2)	[0.0, 1.3]	0.4 (0.2)	[0.1, 1.2]	-0.0 (0.2)	[-0.9, 0.6]
Week 12/16	continuous exposure MK-3222 100 mg	249	0.5 (0.2)	[0.1, 1.3]	0.4 (0.2)	[0.1, 1.2]	-0.0 (0.2)	[-0.8, 0.8]
	continuous exposure MK-3222 200 mg	209	0.5 (0.2)	[0.1, 1.2]	0.4 (0.2)	[0.1, 1.1]	-0.0 (0.1)	[-0.6, 0.3]
	continuous exposure MK-3222 100 / 200 mg	626	0.5 (0.2)	[0.0, 1.3]	0.4 (0.2)	[0.1, 1.2]	-0.0 (0.2)	[-0.8, 0.8]
Week 28	continuous exposure MK-3222 100 mg	247	0.5 (0.2)	[0.1, 1.3]	0.5 (0.2)	[0.1, 1.5]	-0.0 (0.2)	[-0.6, 0.5]
	continuous exposure MK-3222 200 mg	207	0.4 (0.2)	[0.1, 1.2]	0.4 (0.2)	[0.1, 1.2]	-0.0 (0.2)	[-1.0, 0.4]
	continuous exposure MK-3222 100 / 200 mg	621	0.5 (0.2)	[0.0, 1.3]	0.4 (0.2)	[0.0, 1.5]	-0.0 (0.2)	[-1.0, 0.7]
Week 52	continuous exposure MK-3222 100 mg	249	0.5 (0.2)	[0.1, 1.3]	0.5 (0.2)	[0.1, 0.9]	-0.0 (0.2)	[-0.8, 0.4]
	continuous exposure MK-3222 200 mg	203	0.5 (0.2)	[0.1, 1.2]	0.4 (0.2)	[0.1, 1.1]	-0.0 (0.2)	[-1.0, 0.5]
	continuous exposure MK-3222 100 / 200 mg	618	0.5 (0.2)	[0.1, 1.3]	0.4 (0.2)	[0.1, 1.1]	-0.0 (0.2)	[-1.0, 0.5]

Summary of Laboratory Assessment over Time - Hematology
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Monocytes/Leukocytes (%)								
Week 4	continuous exposure MK-3222 100 mg	222	6.4 (2.0)	[1.5, 15.0]	6.6 (2.3)	[0.8, 19.4]	0.1 (2.3)	[-8.0, 11.2]
	continuous exposure MK-3222 200 mg	163	6.5 (2.1)	[1.6, 13.8]	6.3 (2.0)	[2.0, 15.1]	-0.1 (1.8)	[-5.3, 6.9]
	continuous exposure MK-3222 100 / 200 mg	504	6.5 (2.1)	[0.0, 15.1]	6.5 (2.2)	[0.6, 19.4]	-0.0 (2.1)	[-8.0, 13.1]
Week 12/16	continuous exposure MK-3222 100 mg	220	6.4 (2.0)	[1.5, 15.0]	6.5 (2.4)	[1.2, 15.6]	0.0 (2.2)	[-6.8, 8.2]
	continuous exposure MK-3222 200 mg	162	6.5 (2.1)	[1.6, 13.8]	6.1 (1.8)	[1.8, 13.9]	-0.4 (1.8)	[-5.4, 4.0]
	continuous exposure MK-3222 100 / 200 mg	502	6.5 (2.1)	[0.0, 15.3]	6.4 (2.2)	[1.2, 15.6]	-0.1 (2.2)	[-6.8, 12.7]
Week 28	continuous exposure MK-3222 100 mg	219	6.4 (2.0)	[1.5, 15.0]	6.4 (2.0)	[1.8, 14.3]	-0.0 (2.1)	[-7.9, 8.0]
	continuous exposure MK-3222 200 mg	161	6.4 (2.0)	[1.6, 12.8]	6.4 (2.1)	[1.2, 14.3]	-0.0 (2.1)	[-7.4, 7.2]
	continuous exposure MK-3222 100 / 200 mg	499	6.4 (2.1)	[0.0, 15.3]	6.4 (2.2)	[1.2, 18.1]	-0.0 (2.3)	[-7.9, 12.7]
Week 52	continuous exposure MK-3222 100 mg	220	6.5 (2.0)	[1.5, 15.0]	6.7 (2.1)	[2.2, 13.5]	0.2 (2.2)	[-7.4, 7.9]
	continuous exposure MK-3222 200 mg	159	6.5 (2.1)	[1.6, 13.8]	6.3 (2.2)	[1.2, 13.6]	-0.2 (2.0)	[-6.6, 7.8]
	continuous exposure MK-3222 100 / 200 mg	496	6.5 (2.1)	[1.3, 15.3]	6.6 (2.2)	[1.2, 13.6]	0.1 (2.0)	[-7.4, 7.9]

Summary of Laboratory Assessment over Time - Hematology
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Neutrophils (10[3]/microL)								
Week 4	continuous exposure MK-3222 100 mg	251	5.0 (1.8)	[1.4, 14.0]	4.6 (1.9)	[1.5, 15.9]	-0.3 (1.6)	[-9.5, 9.5]
	continuous exposure MK-3222 200 mg	207	4.6 (1.8)	[1.5, 16.9]	4.5 (1.5)	[1.4, 10.4]	-0.1 (1.6)	[-11.1, 7.2]
	continuous exposure MK-3222 100 / 200 mg	625	4.8 (1.8)	[1.4, 16.9]	4.6 (1.7)	[1.4, 15.9]	-0.2 (1.5)	[-11.1, 9.5]
Week 12/16	continuous exposure MK-3222 100 mg	249	4.9 (1.7)	[1.4, 14.0]	4.5 (1.8)	[1.4, 16.6]	-0.5 (1.8)	[-9.0, 13.8]
	continuous exposure MK-3222 200 mg	209	4.6 (1.8)	[1.5, 16.9]	4.5 (1.7)	[1.8, 14.6]	-0.2 (1.4)	[-5.8, 4.6]
	continuous exposure MK-3222 100 / 200 mg	626	4.8 (1.7)	[1.0, 16.9]	4.5 (1.8)	[1.3, 16.6]	-0.3 (1.6)	[-9.0, 13.8]
Week 28	continuous exposure MK-3222 100 mg	247	5.0 (1.8)	[1.4, 14.0]	4.7 (1.9)	[1.4, 18.4]	-0.3 (1.7)	[-9.0, 9.0]
	continuous exposure MK-3222 200 mg	207	4.6 (1.8)	[1.5, 16.9]	4.3 (1.4)	[1.3, 8.9]	-0.3 (1.6)	[-12.6, 3.4]
	continuous exposure MK-3222 100 / 200 mg	621	4.8 (1.8)	[1.0, 16.9]	4.5 (1.7)	[0.7, 18.4]	-0.3 (1.6)	[-12.6, 9.0]
Week 52	continuous exposure MK-3222 100 mg	249	4.9 (1.8)	[1.4, 14.0]	4.4 (1.6)	[1.0, 13.3]	-0.5 (1.6)	[-9.5, 7.2]
	continuous exposure MK-3222 200 mg	203	4.6 (1.8)	[1.5, 16.9]	4.3 (1.8)	[1.2, 18.7]	-0.4 (1.9)	[-12.8, 10.6]
	continuous exposure MK-3222 100 / 200 mg	618	4.8 (1.8)	[1.0, 16.9]	4.4 (1.7)	[1.0, 18.7]	-0.4 (1.7)	[-12.8, 10.6]

Summary of Laboratory Assessment over Time - Hematology
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Neutrophils/Leukocytes (%)								
Week 4	continuous exposure MK-3222 100 mg	222	64.9 (8.7)	[31.7, 86.3]	63.0 (8.7)	[34.2, 92.5]	-1.9 (6.8)	[-20.9, 28.1]
	continuous exposure MK-3222 200 mg	163	64.4 (8.6)	[32.4, 85.2]	63.6 (8.6)	[34.2, 86.7]	-0.8 (7.5)	[-27.0, 26.4]
	continuous exposure MK-3222 100 / 200 mg	504	64.5 (8.3)	[31.7, 86.3]	63.3 (8.5)	[34.2, 92.5]	-1.2 (7.0)	[-27.6, 28.1]
Week 12/16	continuous exposure MK-3222 100 mg	220	64.7 (8.6)	[31.7, 86.3]	61.7 (8.7)	[33.5, 85.8]	-3.0 (7.8)	[-33.7, 32.5]
	continuous exposure MK-3222 200 mg	162	64.6 (8.6)	[32.4, 85.2]	63.5 (7.7)	[37.6, 80.8]	-1.1 (7.6)	[-24.5, 26.6]
	continuous exposure MK-3222 100 / 200 mg	502	64.4 (8.4)	[31.7, 86.3]	62.5 (8.4)	[33.5, 87.6]	-1.9 (7.7)	[-33.7, 32.5]
Week 28	continuous exposure MK-3222 100 mg	219	65.0 (8.7)	[31.7, 86.3]	62.6 (8.3)	[33.9, 85.7]	-2.4 (7.8)	[-25.3, 22.5]
	continuous exposure MK-3222 200 mg	161	64.6 (8.7)	[32.4, 85.2]	62.3 (7.7)	[43.0, 79.2]	-2.3 (7.0)	[-26.7, 17.0]
	continuous exposure MK-3222 100 / 200 mg	499	64.5 (8.4)	[31.7, 86.3]	62.2 (8.4)	[24.6, 85.7]	-2.3 (7.8)	[-45.9, 22.5]
Week 52	continuous exposure MK-3222 100 mg	220	64.7 (8.7)	[31.7, 86.3]	62.2 (8.8)	[28.5, 84.1]	-2.5 (7.8)	[-31.2, 20.1]
	continuous exposure MK-3222 200 mg	159	64.7 (8.8)	[32.4, 85.2]	63.3 (8.2)	[37.1, 87.3]	-1.3 (8.0)	[-30.5, 25.4]
	continuous exposure MK-3222 100 / 200 mg	496	64.4 (8.5)	[31.7, 86.3]	62.4 (8.2)	[28.5, 87.3]	-2.0 (7.6)	[-31.2, 25.4]

Baseline is defined as last value obtained prior to the first dose of study medication during treatment phase.
For RBC and Platelet, the unit conversion took place when generating this table
N: number of subjects with non-missing baseline and post-baseline values at the given time point.
SD=Standard deviation; Min=Minimum; Max=Maximum.
[Source: 5.3.5.3-10]

付録 2.7.4-44
臨床検査値の経時的変動の要約 - 尿検査
第 IIb 相及び第 III 相試験：ベース試験の安全性併合解析 - 継続曝露
1 回以上投与された被験者

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Non-Fasting Glucose (mmol/L)								
Week 4	continuous exposure MK-3222 100 mg	3	15.7 (11.2)	[5.6, 27.8]	11.1 (4.8)	[5.6, 13.9]	-4.6 (8.0)	[-13.9, 0.0]
	continuous exposure MK-3222 200 mg	4	34.7 (13.9)	[27.8, 55.5]	25.7 (21.9)	[5.6, 55.5]	-9.0 (25.2)	[-27.8, 27.8]
	continuous exposure MK-3222 100 / 200 mg	10	29.7 (15.6)	[5.6, 55.5]	20.5 (14.9)	[5.6, 55.5]	-9.2 (16.8)	[-27.8, 27.8]
Week 12/16	continuous exposure MK-3222 100 mg	1	27.8 ()	[27.8, 27.8]	27.8 ()	[27.8, 27.8]	0.0 ()	[0.0, 0.0]
	continuous exposure MK-3222 200 mg	3	27.8 (0.0)	[27.8, 27.8]	38.9 (28.8)	[5.6, 55.5]	11.1 (28.8)	[-22.2, 27.8]
	continuous exposure MK-3222 100 / 200 mg	6	32.4 (11.3)	[27.8, 55.5]	25.9 (24.5)	[5.6, 55.5]	-6.5 (30.9)	[-50.0, 27.8]
Week 28	continuous exposure MK-3222 100 mg	.	()	[,]	()	[,]	()	[,]
	continuous exposure MK-3222 200 mg	1	27.8 ()	[27.8, 27.8]	55.5 ()	[55.5, 55.5]	27.8 ()	[27.8, 27.8]
	continuous exposure MK-3222 100 / 200 mg	4	34.7 (13.9)	[27.8, 55.5]	43.0 (25.0)	[5.6, 55.5]	8.3 (24.2)	[-22.2, 27.8]
Week 52	continuous exposure MK-3222 100 mg	.	()	[,]	()	[,]	()	[,]
	continuous exposure MK-3222 200 mg	2	27.8 (0.0)	[27.8, 27.8]	5.6 (0.0)	[5.6, 5.6]	-22.2 (0.0)	[-22.2, -22.2]
	continuous exposure MK-3222 100 / 200 mg	5	33.3 (12.4)	[27.8, 55.5]	21.6 (21.0)	[5.6, 55.5]	-11.7 (11.2)	[-22.2, 0.0]

Summary of Laboratory Assessment over Time - Urinalysis
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Ketones								
Week 4	continuous exposure MK-3222 100 mg	.	()	[,]	()	[,]	()	[,]
	continuous exposure MK-3222 200 mg	1	15.0 ()	[15.0, 15.0]	15.0 ()	[15.0, 15.0]	0.0 ()	[0.0, 0.0]
	continuous exposure MK-3222 100 / 200 mg	1	15.0 ()	[15.0, 15.0]	15.0 ()	[15.0, 15.0]	0.0 ()	[0.0, 0.0]
Week 12/16	continuous exposure MK-3222 100 mg	.	()	[,]	()	[,]	()	[,]
	continuous exposure MK-3222 200 mg	.	()	[,]	()	[,]	()	[,]
	continuous exposure MK-3222 100 / 200 mg	.	()	[,]	()	[,]	()	[,]
Week 28	continuous exposure MK-3222 100 mg	2	27.5 (17.7)	[15.0, 40.0]	15.0 (0.0)	[15.0, 15.0]	-12.5 (17.7)	[-25.0, 0.0]
	continuous exposure MK-3222 200 mg	.	()	[,]	()	[,]	()	[,]
	continuous exposure MK-3222 100 / 200 mg	2	27.5 (17.7)	[15.0, 40.0]	15.0 (0.0)	[15.0, 15.0]	-12.5 (17.7)	[-25.0, 0.0]
Week 52	continuous exposure MK-3222 100 mg	.	()	[,]	()	[,]	()	[,]
	continuous exposure MK-3222 200 mg	.	()	[,]	()	[,]	()	[,]
	continuous exposure MK-3222 100 / 200 mg	.	()	[,]	()	[,]	()	[,]

Summary of Laboratory Assessment over Time - Urinalysis
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

			Baseline		Value		Change From Baseline	
Visit	Treatment	N	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
pH								
Week 4	continuous exposure MK-3222 100 mg	90	6.1 (0.5)	[5.0, 7.5]	6.2 (0.6)	[5.5, 8.0]	0.1 (0.7)	[-1.5, 2.5]
	continuous exposure MK-3222 200 mg	87	6.2 (0.5)	[5.5, 7.5]	6.1 (0.4)	[5.5, 7.0]	-0.1 (0.5)	[-1.5, 1.5]
	continuous exposure MK-3222 100 / 200 mg	254	6.1 (0.5)	[5.0, 7.5]	6.2 (0.5)	[5.5, 8.0]	0.0 (0.6)	[-1.5, 2.5]
Week 12/16	continuous exposure MK-3222 100 mg	88	6.1 (0.5)	[5.0, 7.0]	6.1 (0.5)	[5.0, 7.5]	0.1 (0.6)	[-1.5, 2.0]
	continuous exposure MK-3222 200 mg	79	6.2 (0.5)	[5.0, 7.5]	6.2 (0.5)	[5.5, 8.5]	0.0 (0.6)	[-1.5, 2.5]
	continuous exposure MK-3222 100 / 200 mg	232	6.1 (0.5)	[5.0, 7.5]	6.2 (0.5)	[5.0, 8.5]	0.0 (0.6)	[-1.5, 2.5]
Week 28	continuous exposure MK-3222 100 mg	91	6.1 (0.4)	[5.0, 7.5]	6.1 (0.5)	[5.5, 8.5]	0.0 (0.6)	[-1.0, 2.5]
	continuous exposure MK-3222 200 mg	75	6.2 (0.5)	[5.5, 7.5]	6.1 (0.5)	[5.0, 8.0]	-0.1 (0.6)	[-1.5, 1.5]
	continuous exposure MK-3222 100 / 200 mg	228	6.1 (0.5)	[5.0, 7.5]	6.1 (0.5)	[5.0, 8.5]	-0.0 (0.6)	[-1.5, 2.5]
Week 52	continuous exposure MK-3222 100 mg	90	6.1 (0.4)	[5.0, 7.5]	6.0 (0.5)	[5.5, 7.5]	-0.1 (0.5)	[-1.0, 1.5]
	continuous exposure MK-3222 200 mg	65	6.3 (0.6)	[5.5, 7.5]	6.0 (0.5)	[5.5, 7.5]	-0.2 (0.5)	[-1.5, 1.0]
	continuous exposure MK-3222 100 / 200 mg	215	6.2 (0.5)	[5.0, 7.5]	6.0 (0.4)	[5.5, 7.5]	-0.1 (0.5)	[-1.5, 1.5]

Summary of Laboratory Assessment over Time - Urinalysis
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Specific Gravity								
Week 4	continuous exposure MK-3222 100 mg	90	1.0 (0.0)	[1.0, 1.0]	1.0 (0.0)	[1.0, 1.0]	-0.0 (0.0)	[-0.0, 0.0]
	continuous exposure MK-3222 200 mg	87	1.0 (0.0)	[1.0, 1.0]	1.0 (0.0)	[1.0, 1.0]	-0.0 (0.0)	[-0.0, 0.0]
	continuous exposure MK-3222 100 / 200 mg	254	1.0 (0.0)	[1.0, 1.0]	1.0 (0.0)	[1.0, 1.0]	-0.0 (0.0)	[-0.0, 0.0]
Week 12/16	continuous exposure MK-3222 100 mg	88	1.0 (0.0)	[1.0, 1.0]	1.0 (0.0)	[1.0, 1.0]	0.0 (0.0)	[-0.0, 0.0]
	continuous exposure MK-3222 200 mg	79	1.0 (0.0)	[1.0, 1.0]	1.0 (0.0)	[1.0, 1.0]	0.0 (0.0)	[-0.0, 0.0]
	continuous exposure MK-3222 100 / 200 mg	232	1.0 (0.0)	[1.0, 1.0]	1.0 (0.0)	[1.0, 1.0]	0.0 (0.0)	[-0.0, 0.0]
Week 28	continuous exposure MK-3222 100 mg	91	1.0 (0.0)	[1.0, 1.0]	1.0 (0.0)	[1.0, 1.0]	-0.0 (0.0)	[-0.0, 0.0]
	continuous exposure MK-3222 200 mg	75	1.0 (0.0)	[1.0, 1.0]	1.0 (0.0)	[1.0, 1.0]	-0.0 (0.0)	[-0.0, 0.0]
	continuous exposure MK-3222 100 / 200 mg	228	1.0 (0.0)	[1.0, 1.0]	1.0 (0.0)	[1.0, 1.0]	-0.0 (0.0)	[-0.0, 0.0]
Week 52	continuous exposure MK-3222 100 mg	90	1.0 (0.0)	[1.0, 1.0]	1.0 (0.0)	[1.0, 1.0]	0.0 (0.0)	[-0.0, 0.0]
	continuous exposure MK-3222 200 mg	65	1.0 (0.0)	[1.0, 1.0]	1.0 (0.0)	[1.0, 1.0]	-0.0 (0.0)	[-0.0, 0.0]
	continuous exposure MK-3222 100 / 200 mg	215	1.0 (0.0)	[1.0, 1.0]	1.0 (0.0)	[1.0, 1.0]	0.0 (0.0)	[-0.0, 0.0]

Summary of Laboratory Assessment over Time - Urinalysis
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Protein								
Week 4	continuous exposure MK-3222 100 mg	5	86.0 (31.3)	[30.0, 100.0]	72.0 (38.3)	[30.0, 100.0]	-14.0 (31.3)	[-70.0, 0.0]
	continuous exposure MK-3222 200 mg	6	65.0 (38.3)	[30.0, 100.0]	53.3 (36.1)	[30.0, 100.0]	-11.7 (28.6)	[-70.0, 0.0]
	continuous exposure MK-3222 100 / 200 mg	16	65.0 (36.1)	[30.0, 100.0]	56.3 (35.0)	[30.0, 100.0]	-8.8 (35.0)	[-70.0, 70.0]
Week 12/16	continuous exposure MK-3222 100 mg	6	53.3 (36.1)	[30.0, 100.0]	53.3 (36.1)	[30.0, 100.0]	0.0 (0.0)	[0.0, 0.0]
	continuous exposure MK-3222 200 mg	5	58.0 (38.3)	[30.0, 100.0]	58.0 (38.3)	[30.0, 100.0]	0.0 (0.0)	[0.0, 0.0]
	continuous exposure MK-3222 100 / 200 mg	15	53.3 (34.2)	[30.0, 100.0]	71.3 (71.6)	[30.0, 300.0]	18.0 (69.7)	[0.0, 270.0]
Week 28	continuous exposure MK-3222 100 mg	4	82.5 (35.0)	[30.0, 100.0]	47.5 (35.0)	[30.0, 100.0]	-35.0 (40.4)	[-70.0, 0.0]
	continuous exposure MK-3222 200 mg	4	65.0 (40.4)	[30.0, 100.0]	47.5 (35.0)	[30.0, 100.0]	-17.5 (35.0)	[-70.0, 0.0]
	continuous exposure MK-3222 100 / 200 mg	11	68.2 (36.6)	[30.0, 100.0]	49.1 (32.7)	[30.0, 100.0]	-19.1 (32.7)	[-70.0, 0.0]
Week 52	continuous exposure MK-3222 100 mg	5	72.0 (38.3)	[30.0, 100.0]	72.0 (38.3)	[30.0, 100.0]	0.0 (0.0)	[0.0, 0.0]
	continuous exposure MK-3222 200 mg	2	100.0 (0.0)	[100.0, 100.0]	65.0 (49.5)	[30.0, 100.0]	-35.0 (49.5)	[-70.0, 0.0]
	continuous exposure MK-3222 100 / 200 mg	11	68.2 (36.6)	[30.0, 100.0]	61.8 (36.6)	[30.0, 100.0]	-6.4 (37.8)	[-70.0, 70.0]

Baseline is defined as last value obtained prior to the first dose of study medication during treatment phase.
N: number of subjects with non-missing baseline and post-baseline values at the given time point.
SD=Standard deviation; Min=Minimum ; Max=Maximum.
[Source: 5.3.5.3-10]

付録 2.7.4-45
バイタルサインの経時的変動の要約
第 IIb 相及び第 III 相試験：ベース試験の安全性併合解析 - 継続曝露
1 回以上投与された被験者

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Diastolic Blood Pressure (mmHg)								
Week 4	continuous exposure MK-3222 100 mg	252	80.1 (9.9)	[27.0, 110.0]	79.9 (9.8)	[52.0, 108.0]	-0.2 (9.4)	[-28.0, 43.0]
	continuous exposure MK-3222 200 mg	211	79.5 (8.9)	[56.0, 102.0]	79.1 (8.6)	[58.0, 101.0]	-0.4 (7.4)	[-26.0, 22.0]
	continuous exposure MK-3222 100 / 200 mg	634	79.6 (9.4)	[27.0, 110.0]	79.4 (9.4)	[52.0, 108.0]	-0.2 (8.5)	[-28.0, 43.0]
Week 8	continuous exposure MK-3222 100 mg	250	79.9 (9.8)	[27.0, 110.0]	79.9 (9.8)	[59.0, 117.0]	-0.1 (9.7)	[-33.0, 41.0]
	continuous exposure MK-3222 200 mg	212	79.5 (8.9)	[56.0, 102.0]	79.1 (9.0)	[48.0, 110.0]	-0.5 (8.6)	[-25.0, 22.0]
	continuous exposure MK-3222 100 / 200 mg	630	79.5 (9.4)	[27.0, 110.0]	79.2 (9.2)	[48.0, 117.0]	-0.3 (9.1)	[-33.0, 41.0]
Week 12	continuous exposure MK-3222 100 mg	250	80.0 (9.8)	[27.0, 110.0]	79.4 (9.7)	[58.0, 106.0]	-0.7 (9.7)	[-25.0, 37.0]
	continuous exposure MK-3222 200 mg	210	79.4 (8.9)	[56.0, 102.0]	78.9 (8.9)	[52.0, 108.0]	-0.5 (8.3)	[-24.0, 25.0]
	continuous exposure MK-3222 100 / 200 mg	631	79.6 (9.4)	[27.0, 110.0]	79.1 (9.3)	[51.0, 108.0]	-0.5 (9.1)	[-26.0, 37.0]
Week 16	continuous exposure MK-3222 100 mg	252	80.1 (9.9)	[27.0, 110.0]	79.7 (9.4)	[54.0, 112.0]	-0.4 (9.4)	[-37.0, 41.0]
	continuous exposure MK-3222 200 mg	211	79.5 (8.9)	[56.0, 102.0]	79.1 (9.4)	[53.0, 109.0]	-0.4 (9.1)	[-27.0, 28.0]
	continuous exposure MK-3222 100 / 200 mg	634	79.6 (9.4)	[27.0, 110.0]	79.2 (9.2)	[53.0, 112.0]	-0.4 (9.0)	[-37.0, 41.0]

Summary of Vital Signs Over Time
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Diastolic Blood Pressure (mmHg) (Continues)								
Week 28	continuous exposure MK-3222 100 mg	253	80.1 (9.9)	[27.0, 110.0]	79.4 (9.4)	[52.0, 103.0]	-0.7 (9.7)	[-28.0, 57.0]
	continuous exposure MK-3222 200 mg	210	79.6 (8.9)	[56.0, 102.0]	78.9 (9.3)	[40.0, 115.0]	-0.7 (9.3)	[-40.0, 27.0]
	continuous exposure MK-3222 100 / 200 mg	633	79.6 (9.4)	[27.0, 110.0]	79.2 (9.4)	[40.0, 115.0]	-0.4 (9.5)	[-40.0, 57.0]
Week 40	continuous exposure MK-3222 100 mg	253	80.1 (9.9)	[27.0, 110.0]	79.5 (9.5)	[59.0, 104.0]	-0.5 (9.3)	[-25.0, 43.0]
	continuous exposure MK-3222 200 mg	211	79.5 (8.9)	[56.0, 102.0]	79.3 (9.7)	[42.0, 110.0]	-0.3 (9.8)	[-28.0, 38.0]
	continuous exposure MK-3222 100 / 200 mg	635	79.6 (9.4)	[27.0, 110.0]	79.5 (9.6)	[42.0, 128.0]	-0.1 (9.6)	[-30.0, 43.0]
Week 52	continuous exposure MK-3222 100 mg	252	80.0 (9.9)	[27.0, 110.0]	79.8 (10.0)	[52.0, 109.0]	-0.3 (10.0)	[-27.0, 49.0]
	continuous exposure MK-3222 200 mg	209	79.5 (9.0)	[56.0, 102.0]	78.6 (8.7)	[48.0, 100.0]	-0.9 (9.2)	[-39.0, 23.0]
	continuous exposure MK-3222 100 / 200 mg	630	79.6 (9.4)	[27.0, 110.0]	79.3 (9.5)	[48.0, 110.0]	-0.3 (9.5)	[-39.0, 49.0]
Systolic Blood Pressure (mmHg)								
Week 4	continuous exposure MK-3222 100 mg	252	129.2 (13.2)	[92.0, 168.0]	128.4 (13.6)	[98.0, 176.0]	-0.8 (11.5)	[-30.0, 44.0]
	continuous exposure MK-3222 200 mg	211	128.9 (13.4)	[90.0, 170.0]	128.7 (14.6)	[94.0, 169.0]	-0.3 (11.5)	[-46.0, 32.0]
	continuous exposure MK-3222 100 / 200 mg	634	128.5 (13.5)	[90.0, 170.0]	128.2 (14.2)	[94.0, 176.0]	-0.3 (11.7)	[-46.0, 44.0]

Summary of Vital Signs Over Time
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Systolic Blood Pressure (mmHg) (Continues)								
Week 8	continuous exposure MK-3222 100 mg	250	129.2 (13.2)	[92.0, 168.0]	129.2 (13.7)	[98.0, 180.0]	0.0 (12.0)	[-40.0, 37.0]
	continuous exposure MK-3222 200 mg	212	129.0 (13.4)	[90.0, 170.0]	128.2 (14.6)	[90.0, 180.0]	-0.8 (12.4)	[-44.0, 36.0]
	continuous exposure MK-3222 100 / 200 mg	630	128.5 (13.5)	[90.0, 170.0]	128.3 (13.9)	[90.0, 180.0]	-0.2 (11.7)	[-44.0, 37.0]
Week 12	continuous exposure MK-3222 100 mg	250	129.3 (13.1)	[92.0, 168.0]	128.1 (13.5)	[90.0, 178.0]	-1.2 (12.3)	[-40.0, 38.0]
	continuous exposure MK-3222 200 mg	210	128.9 (13.4)	[90.0, 170.0]	127.0 (13.8)	[100.0, 164.0]	-1.9 (11.6)	[-38.0, 30.0]
	continuous exposure MK-3222 100 / 200 mg	631	128.5 (13.5)	[90.0, 170.0]	127.1 (13.7)	[85.0, 178.0]	-1.5 (11.9)	[-45.0, 38.0]
Week 16	continuous exposure MK-3222 100 mg	252	129.3 (13.2)	[92.0, 168.0]	127.2 (13.3)	[96.0, 166.0]	-2.0 (12.1)	[-38.0, 36.0]
	continuous exposure MK-3222 200 mg	211	129.0 (13.4)	[90.0, 170.0]	126.3 (13.4)	[100.0, 166.0]	-2.7 (12.4)	[-50.0, 22.0]
	continuous exposure MK-3222 100 / 200 mg	634	128.6 (13.5)	[90.0, 170.0]	126.2 (13.4)	[90.0, 166.0]	-2.4 (12.8)	[-63.0, 37.0]
Week 28	continuous exposure MK-3222 100 mg	253	129.3 (13.2)	[92.0, 168.0]	127.5 (13.1)	[94.0, 183.0]	-1.8 (11.6)	[-40.0, 36.0]
	continuous exposure MK-3222 200 mg	210	129.0 (13.4)	[90.0, 170.0]	127.1 (14.2)	[92.0, 178.0]	-1.9 (13.1)	[-49.0, 34.0]
	continuous exposure MK-3222 100 / 200 mg	633	128.6 (13.5)	[90.0, 170.0]	127.1 (13.9)	[90.0, 183.0]	-1.5 (12.5)	[-49.0, 39.0]

Summary of Vital Signs Over Time
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Systolic Blood Pressure (mmHg) (Continues)								
Week 40	continuous exposure MK-3222 100 mg	253	129.3 (13.2)	[92.0, 168.0]	128.0 (14.1)	[92.0, 165.0]	-1.2 (13.2)	[-42.0, 40.0]
	continuous exposure MK-3222 200 mg	211	129.0 (13.4)	[90.0, 170.0]	127.9 (14.0)	[90.0, 194.0]	-1.1 (13.3)	[-44.0, 40.0]
	continuous exposure MK-3222 100 / 200 mg	635	128.6 (13.5)	[90.0, 170.0]	127.6 (14.4)	[90.0, 212.0]	-1.0 (13.6)	[-44.0, 72.0]
Week 52	continuous exposure MK-3222 100 mg	252	129.3 (13.2)	[92.0, 168.0]	127.9 (13.5)	[91.0, 167.0]	-1.4 (12.7)	[-32.0, 34.0]
	continuous exposure MK-3222 200 mg	209	129.0 (13.5)	[90.0, 170.0]	127.0 (13.7)	[87.0, 180.0]	-2.0 (13.3)	[-52.0, 44.0]
	continuous exposure MK-3222 100 / 200 mg	630	128.5 (13.5)	[90.0, 170.0]	127.5 (13.6)	[87.0, 180.0]	-1.0 (13.0)	[-52.0, 44.0]
Pulse Rate (beats/min)								
Week 4	continuous exposure MK-3222 100 mg	252	74.6 (10.6)	[51.0, 120.0]	73.0 (10.6)	[50.0, 105.0]	-1.6 (9.6)	[-36.0, 30.0]
	continuous exposure MK-3222 200 mg	211	72.3 (10.3)	[45.0, 114.0]	73.4 (10.3)	[44.0, 115.0]	1.1 (9.5)	[-26.0, 31.0]
	continuous exposure MK-3222 100 / 200 mg	634	73.2 (10.7)	[43.0, 120.0]	72.8 (10.6)	[44.0, 115.0]	-0.4 (9.7)	[-36.0, 31.0]
Week 8	continuous exposure MK-3222 100 mg	250	74.5 (10.6)	[51.0, 120.0]	72.6 (9.7)	[48.0, 101.0]	-1.9 (8.9)	[-32.0, 27.0]
	continuous exposure MK-3222 200 mg	212	72.3 (10.3)	[45.0, 114.0]	73.8 (10.2)	[47.0, 107.0]	1.5 (8.6)	[-31.0, 28.0]
	continuous exposure MK-3222 100 / 200 mg	630	73.1 (10.7)	[43.0, 120.0]	73.0 (10.2)	[47.0, 111.0]	-0.1 (9.1)	[-32.0, 36.0]

Summary of Vital Signs Over Time
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Pulse Rate (beats/min) (Continues)								
Week 12	continuous exposure MK-3222 100 mg	250	74.5 (10.4)	[51.0, 120.0]	72.6 (10.3)	[48.0, 108.0]	-1.9 (9.1)	[-32.0, 28.0]
	continuous exposure MK-3222 200 mg	210	72.4 (10.3)	[45.0, 114.0]	72.9 (10.7)	[44.0, 113.0]	0.5 (9.7)	[-27.0, 32.0]
	continuous exposure MK-3222 100 / 200 mg	631	73.2 (10.6)	[43.0, 120.0]	72.3 (10.9)	[44.0, 117.0]	-0.8 (9.8)	[-38.0, 32.0]
Week 16	continuous exposure MK-3222 100 mg	252	74.6 (10.6)	[51.0, 120.0]	72.7 (10.3)	[48.0, 105.0]	-1.9 (10.1)	[-32.0, 26.0]
	continuous exposure MK-3222 200 mg	211	72.4 (10.3)	[45.0, 114.0]	71.9 (11.2)	[44.0, 116.0]	-0.5 (9.9)	[-32.0, 36.0]
	continuous exposure MK-3222 100 / 200 mg	634	73.2 (10.7)	[43.0, 120.0]	72.5 (11.1)	[44.0, 135.0]	-0.7 (10.3)	[-32.0, 42.0]
Week 28	continuous exposure MK-3222 100 mg	253	74.6 (10.6)	[51.0, 120.0]	72.5 (9.5)	[52.0, 110.0]	-2.1 (9.5)	[-40.0, 28.0]
	continuous exposure MK-3222 200 mg	211	72.4 (10.3)	[45.0, 114.0]	72.2 (10.7)	[48.0, 116.0]	-0.2 (11.1)	[-31.0, 35.0]
	continuous exposure MK-3222 100 / 200 mg	634	73.2 (10.7)	[43.0, 120.0]	72.5 (10.2)	[48.0, 116.0]	-0.7 (10.5)	[-40.0, 37.0]
Week 40	continuous exposure MK-3222 100 mg	253	74.6 (10.6)	[51.0, 120.0]	74.3 (10.4)	[48.0, 108.0]	-0.3 (10.0)	[-32.0, 42.0]
	continuous exposure MK-3222 200 mg	211	72.3 (10.3)	[45.0, 114.0]	73.3 (10.0)	[40.0, 104.0]	1.1 (9.8)	[-28.0, 40.0]
	continuous exposure MK-3222 100 / 200 mg	635	73.2 (10.7)	[43.0, 120.0]	73.7 (10.5)	[40.0, 109.0]	0.5 (10.3)	[-34.0, 42.0]

Summary of Vital Signs Over Time
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Pulse Rate (beats/min) (Continues)								
Week 52	continuous exposure MK-3222 100 mg	252	74.6 (10.6)	[51.0, 120.0]	72.3 (10.1)	[52.0, 109.0]	-2.3 (10.0)	[-36.0, 30.0]
	continuous exposure MK-3222 200 mg	209	72.2 (10.3)	[45.0, 114.0]	70.8 (9.9)	[44.0, 100.0]	-1.3 (10.5)	[-36.0, 24.0]
	continuous exposure MK-3222 100 / 200 mg	629	73.1 (10.7)	[43.0, 120.0]	72.0 (10.6)	[44.0, 119.0]	-1.2 (10.4)	[-36.0, 48.0]
Respiratory Rate (breaths/min)								
Week 4	continuous exposure MK-3222 100 mg	251	15.8 (3.1)	[7.0, 29.0]	15.7 (2.9)	[6.0, 26.0]	-0.1 (2.4)	[-11.0, 9.0]
	continuous exposure MK-3222 200 mg	208	15.7 (2.8)	[8.0, 26.0]	15.8 (2.9)	[10.0, 27.0]	0.1 (2.2)	[-8.0, 8.0]
	continuous exposure MK-3222 100 / 200 mg	628	15.8 (3.4)	[7.0, 60.0]	15.7 (3.0)	[6.0, 33.0]	-0.1 (2.9)	[-44.0, 15.0]
Week 8	continuous exposure MK-3222 100 mg	249	15.8 (3.1)	[7.0, 29.0]	15.7 (2.7)	[10.0, 25.0]	-0.1 (2.6)	[-11.0, 10.0]
	continuous exposure MK-3222 200 mg	209	15.7 (2.8)	[8.0, 26.0]	15.7 (2.8)	[7.0, 26.0]	0.0 (2.4)	[-8.0, 8.0]
	continuous exposure MK-3222 100 / 200 mg	623	15.8 (3.4)	[7.0, 60.0]	15.7 (2.7)	[7.0, 26.0]	-0.1 (3.1)	[-44.0, 10.0]
Week 12	continuous exposure MK-3222 100 mg	249	15.8 (3.0)	[7.0, 29.0]	15.5 (2.7)	[10.0, 26.0]	-0.2 (2.7)	[-9.0, 9.0]
	continuous exposure MK-3222 200 mg	207	15.7 (2.8)	[8.0, 26.0]	15.9 (2.8)	[6.0, 26.0]	0.2 (2.7)	[-12.0, 10.0]
	continuous exposure MK-3222 100 / 200 mg	625	15.8 (3.4)	[7.0, 60.0]	15.7 (2.7)	[6.0, 26.0]	-0.1 (3.1)	[-44.0, 10.0]

Summary of Vital Signs Over Time
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Respiratory Rate (breaths/min) (Continues)								
Week 16	continuous exposure MK-3222 100 mg	251	15.8 (3.1)	[7.0, 29.0]	15.5 (2.7)	[9.0, 26.0]	-0.2 (2.6)	[-13.0, 9.0]
	continuous exposure MK-3222 200 mg	208	15.7 (2.8)	[8.0, 26.0]	15.8 (2.8)	[8.0, 26.0]	0.1 (2.4)	[-11.0, 8.0]
	continuous exposure MK-3222 100 / 200 mg	628	15.8 (3.4)	[7.0, 60.0]	15.7 (2.7)	[8.0, 26.0]	-0.1 (3.0)	[-40.0, 9.0]
Week 28	continuous exposure MK-3222 100 mg	251	15.8 (3.1)	[7.0, 29.0]	15.7 (2.6)	[10.0, 25.0]	-0.0 (2.8)	[-12.0, 9.0]
	continuous exposure MK-3222 200 mg	208	15.7 (2.8)	[8.0, 26.0]	15.8 (2.8)	[9.0, 28.0]	0.1 (2.8)	[-8.0, 10.0]
	continuous exposure MK-3222 100 / 200 mg	626	15.8 (3.4)	[7.0, 60.0]	15.8 (2.7)	[9.0, 28.0]	0.0 (3.3)	[-44.0, 10.0]
Week 40	continuous exposure MK-3222 100 mg	252	15.8 (3.1)	[7.0, 29.0]	15.5 (2.8)	[8.0, 27.0]	-0.3 (2.8)	[-13.0, 9.0]
	continuous exposure MK-3222 200 mg	208	15.7 (2.8)	[8.0, 26.0]	15.6 (2.8)	[7.0, 27.0]	-0.1 (2.4)	[-8.0, 8.0]
	continuous exposure MK-3222 100 / 200 mg	629	15.8 (3.4)	[7.0, 60.0]	15.6 (2.8)	[7.0, 27.0]	-0.2 (3.2)	[-44.0, 10.0]
Week 52	continuous exposure MK-3222 100 mg	251	15.8 (3.1)	[7.0, 29.0]	15.9 (3.0)	[6.0, 28.0]	0.1 (3.0)	[-14.0, 10.0]
	continuous exposure MK-3222 200 mg	206	15.7 (2.8)	[8.0, 26.0]	15.4 (2.7)	[10.0, 26.0]	-0.3 (2.7)	[-12.0, 6.0]
	continuous exposure MK-3222 100 / 200 mg	623	15.8 (3.4)	[7.0, 60.0]	15.6 (2.8)	[6.0, 28.0]	-0.1 (3.3)	[-44.0, 10.0]

Summary of Vital Signs Over Time
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Temperature (C)								
Week 4	continuous exposure MK-3222 100 mg	252	36.4 (0.4)	[35.1, 37.6]	36.4 (0.5)	[34.4, 37.4]	0.1 (0.4)	[-1.2, 1.4]
	continuous exposure MK-3222 200 mg	211	36.4 (0.5)	[34.4, 37.6]	36.4 (0.5)	[34.0, 37.4]	0.1 (0.4)	[-1.4, 2.6]
	continuous exposure MK-3222 100 / 200 mg	634	36.4 (0.4)	[34.4, 37.7]	36.4 (0.5)	[34.0, 37.6]	0.0 (0.4)	[-1.8, 2.6]
Week 8	continuous exposure MK-3222 100 mg	250	36.4 (0.4)	[35.1, 37.6]	36.4 (0.4)	[34.3, 37.4]	-0.0 (0.4)	[-1.5, 1.4]
	continuous exposure MK-3222 200 mg	212	36.4 (0.5)	[34.4, 37.6]	36.4 (0.4)	[34.3, 37.3]	-0.0 (0.5)	[-1.3, 2.1]
	continuous exposure MK-3222 100 / 200 mg	630	36.4 (0.4)	[34.4, 37.7]	36.4 (0.4)	[34.3, 37.6]	0.0 (0.4)	[-1.5, 2.1]
Week 12	continuous exposure MK-3222 100 mg	250	36.4 (0.4)	[35.1, 37.6]	36.4 (0.4)	[34.8, 37.5]	-0.0 (0.4)	[-1.2, 1.5]
	continuous exposure MK-3222 200 mg	210	36.4 (0.5)	[34.4, 37.6]	36.4 (0.5)	[34.0, 37.2]	0.0 (0.5)	[-2.9, 1.9]
	continuous exposure MK-3222 100 / 200 mg	631	36.4 (0.4)	[34.4, 37.7]	36.4 (0.5)	[34.0, 37.6]	-0.0 (0.5)	[-2.9, 1.9]
Week 16	continuous exposure MK-3222 100 mg	252	36.4 (0.4)	[35.1, 37.6]	36.4 (0.4)	[34.0, 37.2]	0.0 (0.4)	[-2.5, 1.5]
	continuous exposure MK-3222 200 mg	211	36.4 (0.5)	[34.4, 37.6]	36.4 (0.4)	[35.2, 37.7]	0.1 (0.5)	[-1.4, 2.4]
	continuous exposure MK-3222 100 / 200 mg	634	36.4 (0.4)	[34.4, 37.7]	36.4 (0.4)	[34.0, 37.7]	0.0 (0.4)	[-2.5, 2.4]

Summary of Vital Signs Over Time
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Temperature (C) (Continues)								
Week 28	continuous exposure MK-3222 100 mg	253	36.4 (0.4)	[35.1, 37.6]	36.4 (0.4)	[34.4, 37.3]	0.0 (0.4)	[-1.4, 1.5]
	continuous exposure MK-3222 200 mg	211	36.4 (0.5)	[34.4, 37.6]	36.4 (0.4)	[34.2, 37.2]	0.1 (0.5)	[-1.7, 2.4]
	continuous exposure MK-3222 100 / 200 mg	634	36.4 (0.5)	[34.4, 37.7]	36.4 (0.4)	[34.2, 37.4]	0.0 (0.5)	[-1.7, 2.4]
Week 40	continuous exposure MK-3222 100 mg	253	36.4 (0.4)	[35.1, 37.6]	36.4 (0.4)	[34.8, 37.1]	0.0 (0.5)	[-1.6, 1.2]
	continuous exposure MK-3222 200 mg	211	36.4 (0.5)	[34.4, 37.6]	36.4 (0.4)	[34.2, 37.3]	0.0 (0.5)	[-2.3, 2.3]
	continuous exposure MK-3222 100 / 200 mg	635	36.4 (0.4)	[34.4, 37.7]	36.4 (0.4)	[34.0, 37.3]	-0.0 (0.5)	[-2.3, 2.3]
Week 52	continuous exposure MK-3222 100 mg	252	36.4 (0.4)	[35.1, 37.6]	36.4 (0.4)	[34.7, 37.5]	0.0 (0.4)	[-1.1, 1.5]
	continuous exposure MK-3222 200 mg	209	36.4 (0.5)	[34.4, 37.6]	36.3 (0.4)	[34.6, 37.2]	-0.0 (0.5)	[-2.2, 2.7]
	continuous exposure MK-3222 100 / 200 mg	629	36.4 (0.4)	[34.4, 37.7]	36.4 (0.4)	[34.6, 37.5]	-0.0 (0.5)	[-2.2, 2.7]

N: number of subjects with non-missing baseline and post-baseline values at the given time point.
Baseline is defined as last value obtained prior to the first dose of study medication during treatment phase.
SD=Standard deviation; Min=Minimum ; Max=Maximum.
[Source: 5.3.5.3-10]

付録 2.7.4-46
心電図所見の経時的変動の要約
第 IIb 相及び第 III 相試験：ベース試験の安全性併合解析 - 継続曝露
1 回以上投与された被験者

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
PR Interval (msec)								
Week 4	continuous exposure MK-3222 100 mg	306	105.8 (47.7)	[41.0, 220.0]	105.6 (47.2)	[46.0, 218.0]	-0.2 (10.9)	[-60.0, 42.0]
	continuous exposure MK-3222 200 mg	281	117.1 (50.6)	[44.0, 266.0]	118.0 (49.1)	[47.0, 256.0]	1.0 (10.9)	[-36.0, 42.0]
	continuous exposure MK-3222 100 / 200 mg	707	105.6 (48.6)	[41.0, 266.0]	106.1 (47.6)	[45.0, 256.0]	0.5 (10.6)	[-60.0, 42.0]
Week 12	continuous exposure MK-3222 100 mg	302	107.0 (49.3)	[41.0, 312.0]	106.4 (49.0)	[0.0, 280.0]	-0.7 (15.4)	[-175.0, 44.0]
	continuous exposure MK-3222 200 mg	278	117.5 (50.6)	[44.0, 266.0]	118.8 (51.0)	[46.0, 258.0]	1.3 (10.5)	[-44.0, 30.0]
	continuous exposure MK-3222 100 / 200 mg	696	106.5 (49.3)	[41.0, 312.0]	107.0 (49.4)	[0.0, 280.0]	0.5 (13.0)	[-175.0, 44.0]
Week 28	continuous exposure MK-3222 100 mg	305	106.9 (49.2)	[41.0, 312.0]	106.6 (50.8)	[0.0, 392.0]	-0.3 (17.4)	[-211.0, 80.0]
	continuous exposure MK-3222 200 mg	276	117.7 (50.6)	[44.0, 266.0]	119.0 (50.8)	[42.0, 252.0]	1.3 (11.2)	[-38.0, 34.0]
	continuous exposure MK-3222 100 / 200 mg	698	106.4 (49.3)	[41.0, 312.0]	107.1 (49.9)	[0.0, 392.0]	0.7 (14.2)	[-211.0, 80.0]
Week 52/64	continuous exposure MK-3222 100 mg	299	106.5 (48.9)	[41.0, 312.0]	106.4 (50.9)	[43.0, 346.0]	-0.1 (13.5)	[-64.0, 86.0]
	continuous exposure MK-3222 200 mg	275	118.4 (50.6)	[44.0, 266.0]	120.7 (51.4)	[42.0, 250.0]	2.2 (12.5)	[-52.0, 52.0]
	continuous exposure MK-3222 100 / 200 mg	692	106.4 (49.2)	[41.0, 312.0]	107.5 (50.5)	[41.0, 346.0]	1.1 (12.7)	[-64.0, 86.0]

Summary of ECG Parameters over Time
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
QRS Interval (msec)								
Week 4	continuous exposure MK-3222 100 mg	323	78.2 (16.0)	[41.0, 126.0]	78.4 (15.9)	[46.0, 140.0]	0.2 (8.4)	[-21.0, 48.0]
	continuous exposure MK-3222 200 mg	298	80.4 (17.3)	[44.0, 158.0]	81.4 (17.0)	[40.0, 156.0]	1.0 (8.6)	[-32.0, 33.0]
	continuous exposure MK-3222 100 / 200 mg	745	77.8 (16.6)	[41.0, 158.0]	78.3 (16.4)	[40.0, 156.0]	0.5 (8.6)	[-32.0, 48.0]
Week 12	continuous exposure MK-3222 100 mg	321	78.5 (16.1)	[41.0, 126.0]	78.3 (16.1)	[45.0, 136.0]	-0.2 (8.4)	[-27.0, 39.0]
	continuous exposure MK-3222 200 mg	299	80.5 (17.3)	[44.0, 158.0]	80.6 (17.1)	[44.0, 148.0]	0.1 (8.7)	[-48.0, 39.0]
	continuous exposure MK-3222 100 / 200 mg	743	78.0 (16.6)	[41.0, 158.0]	78.0 (16.6)	[43.0, 148.0]	0.0 (8.9)	[-48.0, 39.0]
Week 28	continuous exposure MK-3222 100 mg	323	78.4 (16.2)	[41.0, 126.0]	78.5 (15.7)	[45.0, 124.0]	0.1 (8.9)	[-33.0, 36.0]
	continuous exposure MK-3222 200 mg	297	80.5 (17.2)	[44.0, 158.0]	80.8 (17.2)	[48.0, 154.0]	0.4 (9.0)	[-43.0, 30.0]
	continuous exposure MK-3222 100 / 200 mg	745	77.8 (16.7)	[41.0, 158.0]	78.3 (16.6)	[41.0, 154.0]	0.5 (9.3)	[-43.0, 48.0]
Week 52/64	continuous exposure MK-3222 100 mg	318	78.2 (16.2)	[41.0, 126.0]	77.7 (16.7)	[43.0, 132.0]	-0.6 (8.9)	[-28.0, 36.0]
	continuous exposure MK-3222 200 mg	298	80.5 (17.3)	[44.0, 158.0]	81.0 (17.6)	[42.0, 156.0]	0.5 (9.4)	[-34.0, 54.0]
	continuous exposure MK-3222 100 / 200 mg	739	77.8 (16.7)	[41.0, 158.0]	78.0 (17.0)	[41.0, 156.0]	0.2 (9.4)	[-34.0, 54.0]

Summary of ECG Parameters over Time
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
QRS Axis (degrees)								
Week 4	continuous exposure MK-3222 100 mg	254	626.6 (419.7)	[0.0, 1440.0]	619.7 (411.2)	[0.0, 1304.0]	-6.9 (98.7)	[-420.0, 336.0]
	continuous exposure MK-3222 200 mg	226	560.6 (438.6)	[0.0, 1272.0]	544.0 (423.3)	[0.0, 1239.0]	-16.5 (90.0)	[-358.0, 325.0]
	continuous exposure MK-3222 100 / 200 mg	588	632.5 (420.5)	[0.0, 1440.0]	622.4 (411.3)	[0.0, 1340.0]	-10.0 (101.7)	[-420.0, 336.0]
Week 12	continuous exposure MK-3222 100 mg	252	621.0 (421.0)	[0.0, 1440.0]	619.2 (420.5)	[1.0, 1333.0]	-1.8 (103.7)	[-440.0, 285.0]
	continuous exposure MK-3222 200 mg	227	560.7 (440.4)	[0.0, 1272.0]	555.0 (437.7)	[0.0, 1339.0]	-5.6 (98.2)	[-349.0, 480.0]
	continuous exposure MK-3222 100 / 200 mg	587	630.1 (422.0)	[0.0, 1440.0]	630.2 (424.5)	[0.0, 1407.0]	0.0 (111.3)	[-440.0, 560.0]
Week 28	continuous exposure MK-3222 100 mg	248	623.1 (421.0)	[0.0, 1440.0]	617.4 (414.0)	[1.0, 1333.0]	-5.7 (105.4)	[-369.0, 469.0]
	continuous exposure MK-3222 200 mg	224	556.7 (441.9)	[0.0, 1272.0]	547.8 (434.1)	[0.0, 1236.0]	-8.9 (102.5)	[-444.0, 360.0]
	continuous exposure MK-3222 100 / 200 mg	578	629.2 (423.2)	[0.0, 1440.0]	619.5 (415.3)	[0.0, 1428.0]	-9.7 (110.8)	[-567.0, 469.0]
Week 52/64	continuous exposure MK-3222 100 mg	248	627.5 (419.2)	[1.0, 1440.0]	632.0 (421.5)	[1.0, 1276.0]	4.5 (111.1)	[-480.0, 409.0]
	continuous exposure MK-3222 200 mg	222	557.0 (441.5)	[0.0, 1272.0]	561.3 (447.1)	[0.0, 1401.0]	4.2 (101.7)	[-280.0, 420.0]
	continuous exposure MK-3222 100 / 200 mg	576	631.2 (421.4)	[0.0, 1440.0]	631.1 (422.6)	[0.0, 1451.0]	-0.1 (113.8)	[-480.0, 420.0]

Summary of ECG Parameters over Time
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Atrial Rate (beats/min)								
Week 4	continuous exposure MK-3222 100 mg	283	138.4 (46.9)	[49.0, 378.0]	138.2 (46.3)	[49.0, 374.0]	-0.2 (13.0)	[-48.0, 46.0]
	continuous exposure MK-3222 200 mg	246	127.9 (49.5)	[45.0, 216.0]	128.5 (49.0)	[47.0, 218.0]	0.6 (14.9)	[-72.0, 66.0]
	continuous exposure MK-3222 100 / 200 mg	653	137.2 (46.7)	[45.0, 378.0]	137.4 (46.1)	[47.0, 374.0]	0.2 (14.7)	[-80.0, 104.0]
Week 12	continuous exposure MK-3222 100 mg	282	138.0 (46.7)	[49.0, 378.0]	136.9 (46.4)	[48.0, 280.0]	-1.0 (20.3)	[-198.0, 96.0]
	continuous exposure MK-3222 200 mg	247	128.4 (48.9)	[45.0, 216.0]	129.0 (49.0)	[41.0, 217.0]	0.6 (14.3)	[-54.0, 75.0]
	continuous exposure MK-3222 100 / 200 mg	656	137.1 (46.2)	[45.0, 378.0]	137.5 (46.3)	[41.0, 280.0]	0.4 (17.9)	[-198.0, 100.0]
Week 28	continuous exposure MK-3222 100 mg	278	138.8 (47.1)	[49.0, 378.0]	137.8 (46.1)	[48.0, 370.0]	-1.0 (13.5)	[-56.0, 40.0]
	continuous exposure MK-3222 200 mg	248	127.9 (49.2)	[45.0, 216.0]	128.0 (48.9)	[43.0, 222.0]	0.1 (16.4)	[-70.0, 80.0]
	continuous exposure MK-3222 100 / 200 mg	648	137.2 (46.6)	[45.0, 378.0]	137.2 (46.1)	[43.0, 370.0]	0.0 (15.8)	[-70.0, 92.0]
Week 52/64	continuous exposure MK-3222 100 mg	279	139.6 (46.5)	[49.0, 378.0]	139.5 (47.6)	[46.0, 378.0]	-0.1 (16.1)	[-50.0, 83.0]
	continuous exposure MK-3222 200 mg	245	128.5 (49.0)	[45.0, 216.0]	128.4 (49.9)	[48.0, 223.0]	-0.0 (16.1)	[-58.0, 75.0]
	continuous exposure MK-3222 100 / 200 mg	651	137.9 (46.1)	[45.0, 378.0]	138.0 (47.1)	[46.0, 378.0]	0.1 (16.7)	[-70.0, 96.0]

Summary of ECG Parameters over Time
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
RR Interval (msec)								
Week 4	continuous exposure MK-3222 100 mg	318	347.5 (387.6)	[60.0, 1398.0]	338.9 (376.4)	[60.0, 1352.0]	-8.6 (63.6)	[-358.0, 207.0]
	continuous exposure MK-3222 200 mg	276	436.3 (413.7)	[40.0, 1340.0]	431.5 (409.6)	[40.0, 1289.0]	-4.8 (80.0)	[-314.0, 332.0]
	continuous exposure MK-3222 100 / 200 mg	726	349.1 (385.7)	[0.0, 1398.0]	343.8 (378.7)	[40.0, 1352.0]	-5.3 (66.5)	[-358.0, 332.0]
Week 12	continuous exposure MK-3222 100 mg	317	344.5 (384.7)	[60.0, 1398.0]	340.3 (378.2)	[40.0, 1250.0]	-4.2 (55.6)	[-244.0, 233.0]
	continuous exposure MK-3222 200 mg	274	427.4 (409.1)	[40.0, 1340.0]	433.3 (414.9)	[40.0, 1263.0]	5.9 (77.3)	[-304.0, 420.0]
	continuous exposure MK-3222 100 / 200 mg	724	344.0 (381.5)	[0.0, 1398.0]	345.3 (382.5)	[40.0, 1263.0]	1.3 (62.1)	[-304.0, 420.0]
Week 28	continuous exposure MK-3222 100 mg	316	342.7 (384.2)	[60.0, 1398.0]	338.5 (379.6)	[48.0, 1269.0]	-4.2 (70.1)	[-338.0, 338.0]
	continuous exposure MK-3222 200 mg	273	428.5 (409.4)	[40.0, 1340.0]	431.0 (411.6)	[40.0, 1240.0]	2.4 (75.3)	[-360.0, 317.0]
	continuous exposure MK-3222 100 / 200 mg	720	342.8 (381.2)	[0.0, 1398.0]	343.3 (382.0)	[40.0, 1274.0]	0.5 (68.7)	[-360.0, 370.0]
Week 52/64	continuous exposure MK-3222 100 mg	315	338.5 (382.5)	[60.0, 1398.0]	342.2 (390.2)	[48.0, 1334.0]	3.7 (70.2)	[-331.0, 292.0]
	continuous exposure MK-3222 200 mg	274	427.5 (409.0)	[40.0, 1340.0]	439.4 (421.0)	[55.0, 1200.0]	12.0 (72.9)	[-297.0, 360.0]
	continuous exposure MK-3222 100 / 200 mg	723	339.6 (379.8)	[0.0, 1398.0]	346.3 (389.7)	[48.0, 1334.0]	6.7 (65.8)	[-331.0, 360.0]

Summary of ECG Parameters over Time
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
QT Interval (msec)								
Week 4	continuous exposure MK-3222 100 mg	345	386.7 (32.2)	[240.0, 553.0]	384.7 (28.9)	[310.0, 562.0]	-2.0 (23.5)	[-76.0, 120.0]
	continuous exposure MK-3222 200 mg	311	393.7 (29.8)	[332.0, 570.0]	389.4 (29.7)	[320.0, 532.0]	-4.3 (24.7)	[-108.0, 112.0]
	continuous exposure MK-3222 100 / 200 mg	792	390.2 (30.7)	[240.0, 570.0]	386.9 (29.9)	[260.0, 562.0]	-3.3 (24.0)	[-108.0, 120.0]
Week 12	continuous exposure MK-3222 100 mg	345	386.9 (32.1)	[240.0, 553.0]	388.4 (29.3)	[318.0, 545.0]	1.5 (24.9)	[-88.0, 160.0]
	continuous exposure MK-3222 200 mg	313	393.6 (29.7)	[332.0, 570.0]	393.5 (32.5)	[205.0, 477.0]	-0.1 (26.5)	[-188.0, 71.0]
	continuous exposure MK-3222 100 / 200 mg	794	390.2 (30.6)	[240.0, 570.0]	390.8 (30.6)	[205.0, 545.0]	0.6 (25.3)	[-188.0, 160.0]
Week 28	continuous exposure MK-3222 100 mg	346	386.9 (32.2)	[240.0, 553.0]	385.3 (30.1)	[259.0, 524.0]	-1.6 (27.3)	[-180.0, 80.0]
	continuous exposure MK-3222 200 mg	313	393.6 (29.7)	[332.0, 570.0]	392.4 (32.4)	[313.0, 614.0]	-1.2 (27.3)	[-118.0, 186.0]
	continuous exposure MK-3222 100 / 200 mg	795	390.3 (30.6)	[240.0, 570.0]	388.6 (31.4)	[259.0, 614.0]	-1.7 (26.8)	[-180.0, 186.0]
Week 52/64	continuous exposure MK-3222 100 mg	343	386.9 (32.3)	[240.0, 553.0]	389.0 (30.7)	[248.0, 542.0]	2.1 (27.1)	[-115.0, 88.0]
	continuous exposure MK-3222 200 mg	313	393.6 (29.4)	[332.0, 570.0]	393.6 (29.7)	[278.0, 472.0]	-0.0 (26.2)	[-152.0, 80.0]
	continuous exposure MK-3222 100 / 200 mg	795	390.3 (30.6)	[240.0, 570.0]	390.8 (30.4)	[248.0, 542.0]	0.5 (26.4)	[-152.0, 88.0]

Summary of ECG Parameters over Time
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
QTc Interval (msec)								
Week 4	continuous exposure MK-3222 100 mg	289	203.8 (187.1)	[0.0, 474.0]	203.3 (187.2)	[0.0, 500.0]	-0.5 (24.3)	[-232.0, 170.0]
	continuous exposure MK-3222 200 mg	270	242.8 (190.2)	[0.0, 573.0]	243.5 (188.8)	[0.0, 468.0]	0.7 (22.0)	[-129.0, 188.0]
	continuous exposure MK-3222 100 / 200 mg	671	203.0 (188.0)	[0.0, 573.0]	203.0 (187.5)	[0.0, 500.0]	0.0 (22.8)	[-232.0, 188.0]
Week 12	continuous exposure MK-3222 100 mg	285	208.1 (187.1)	[0.0, 474.0]	207.7 (188.1)	[0.0, 489.0]	-0.3 (22.7)	[-235.0, 95.0]
	continuous exposure MK-3222 200 mg	272	242.7 (190.1)	[0.0, 573.0]	245.3 (188.0)	[0.0, 474.0]	2.7 (23.2)	[-121.0, 227.0]
	continuous exposure MK-3222 100 / 200 mg	670	204.6 (188.0)	[0.0, 573.0]	205.3 (187.8)	[0.0, 489.0]	0.7 (22.4)	[-235.0, 227.0]
Week 28	continuous exposure MK-3222 100 mg	287	206.4 (187.4)	[0.0, 474.0]	207.9 (187.5)	[0.0, 484.0]	1.5 (23.1)	[-221.0, 125.0]
	continuous exposure MK-3222 200 mg	270	244.3 (189.9)	[0.0, 573.0]	246.0 (187.9)	[1.0, 470.0]	1.7 (22.6)	[-119.0, 213.0]
	continuous exposure MK-3222 100 / 200 mg	667	205.1 (188.2)	[0.0, 573.0]	206.0 (187.4)	[0.0, 484.0]	0.9 (22.4)	[-221.0, 213.0]
Week 52/64	continuous exposure MK-3222 100 mg	283	204.8 (187.2)	[0.0, 474.0]	206.2 (186.7)	[0.0, 482.0]	1.4 (24.7)	[-243.0, 123.0]
	continuous exposure MK-3222 200 mg	271	243.6 (189.9)	[0.0, 573.0]	244.8 (187.2)	[0.0, 477.0]	1.2 (24.0)	[-122.0, 195.0]
	continuous exposure MK-3222 100 / 200 mg	664	204.2 (188.1)	[0.0, 573.0]	204.9 (186.8)	[0.0, 482.0]	0.7 (23.8)	[-243.0, 195.0]

Summary of ECG Parameters over Time
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
QTc Interval Fridericia (msec)								
Week 4	continuous exposure MK-3222 100 mg	319	404.5 (28.1)	[240.0, 584.0]	405.3 (24.0)	[349.0, 537.0]	0.8 (22.5)	[-59.0, 120.0]
	continuous exposure MK-3222 200 mg	278	408.4 (24.4)	[343.0, 572.0]	407.9 (22.6)	[356.0, 502.0]	-0.5 (21.4)	[-122.0, 87.0]
	continuous exposure MK-3222 100 / 200 mg	727	406.4 (26.1)	[240.0, 584.0]	406.2 (23.8)	[307.0, 537.0]	-0.2 (21.8)	[-122.0, 120.0]
Week 12	continuous exposure MK-3222 100 mg	317	404.4 (28.1)	[240.0, 584.0]	406.5 (22.6)	[333.0, 507.0]	2.2 (23.1)	[-105.0, 167.0]
	continuous exposure MK-3222 200 mg	276	408.5 (24.3)	[343.0, 572.0]	408.0 (29.3)	[162.0, 551.0]	-0.5 (24.6)	[-201.0, 109.0]
	continuous exposure MK-3222 100 / 200 mg	726	406.4 (26.0)	[240.0, 584.0]	407.2 (25.5)	[162.0, 551.0]	0.9 (22.7)	[-201.0, 167.0]
Week 28	continuous exposure MK-3222 100 mg	317	404.3 (28.1)	[240.0, 584.0]	404.9 (23.9)	[301.0, 525.0]	0.6 (23.7)	[-152.0, 125.0]
	continuous exposure MK-3222 200 mg	276	408.3 (24.4)	[343.0, 572.0]	408.2 (25.3)	[315.0, 553.0]	-0.0 (22.2)	[-119.0, 171.0]
	continuous exposure MK-3222 100 / 200 mg	724	406.2 (26.0)	[240.0, 584.0]	406.4 (24.9)	[301.0, 553.0]	0.2 (22.4)	[-152.0, 171.0]
Week 52/64	continuous exposure MK-3222 100 mg	314	404.4 (28.2)	[240.0, 584.0]	405.0 (22.9)	[318.0, 492.0]	0.6 (25.3)	[-115.0, 131.0]
	continuous exposure MK-3222 200 mg	276	408.3 (24.3)	[343.0, 572.0]	407.3 (22.8)	[337.0, 498.0]	-1.0 (21.3)	[-155.0, 99.0]
	continuous exposure MK-3222 100 / 200 mg	724	406.3 (26.0)	[240.0, 584.0]	406.4 (23.3)	[318.0, 506.0]	0.2 (23.6)	[-155.0, 131.0]

Summary of ECG Parameters over Time
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
QTc Interval Bazett (msec)								
Week 4	continuous exposure MK-3222 100 mg	273	410.5 (27.4)	[327.0, 582.0]	410.5 (26.5)	[334.0, 534.0]	0.0 (22.2)	[-95.0, 89.0]
	continuous exposure MK-3222 200 mg	252	415.2 (27.4)	[352.0, 573.0]	414.4 (22.9)	[353.0, 499.0]	-0.8 (22.0)	[-129.0, 56.0]
	continuous exposure MK-3222 100 / 200 mg	632	413.0 (27.4)	[327.0, 582.0]	412.4 (25.0)	[334.0, 534.0]	-0.6 (22.2)	[-129.0, 89.0]
Week 12	continuous exposure MK-3222 100 mg	269	410.6 (27.6)	[327.0, 582.0]	412.3 (25.5)	[333.0, 496.0]	1.7 (20.6)	[-104.0, 82.0]
	continuous exposure MK-3222 200 mg	249	415.0 (27.3)	[352.0, 573.0]	414.4 (25.9)	[269.0, 551.0]	-0.6 (24.2)	[-139.0, 108.0]
	continuous exposure MK-3222 100 / 200 mg	624	412.9 (27.4)	[327.0, 582.0]	412.8 (26.2)	[269.0, 551.0]	-0.1 (22.7)	[-139.0, 108.0]
Week 28	continuous exposure MK-3222 100 mg	266	410.7 (27.7)	[327.0, 582.0]	410.3 (28.2)	[233.0, 500.0]	-0.4 (24.5)	[-149.0, 75.0]
	continuous exposure MK-3222 200 mg	246	415.0 (27.4)	[352.0, 573.0]	414.7 (24.4)	[347.0, 507.0]	-0.3 (22.4)	[-119.0, 67.0]
	continuous exposure MK-3222 100 / 200 mg	616	413.0 (27.6)	[327.0, 582.0]	412.5 (26.7)	[233.0, 511.0]	-0.5 (23.8)	[-149.0, 91.0]
Week 52/64	continuous exposure MK-3222 100 mg	265	410.3 (27.6)	[327.0, 582.0]	409.9 (25.2)	[330.0, 490.0]	-0.4 (24.4)	[-118.0, 100.0]
	continuous exposure MK-3222 200 mg	245	415.3 (27.2)	[352.0, 573.0]	411.4 (24.2)	[338.0, 476.0]	-3.9 (23.6)	[-166.0, 52.0]
	continuous exposure MK-3222 100 / 200 mg	614	412.9 (27.3)	[327.0, 582.0]	411.3 (25.2)	[330.0, 504.0]	-1.6 (24.3)	[-166.0, 107.0]

Summary of ECG Parameters over Time
Phase 2 and 3: Base Period Safety Pool - Continuous Exposure
All Subjects as Treated

Visit	Treatment	N	Baseline		Value		Change From Baseline	
			Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]	Mean (SD)	[Min, Max]
Ventricular Rate (beats/min)								
Week 4	continuous exposure MK-3222 100 mg	287	269.1 (163.4)	[42.0, 566.0]	269.5 (162.4)	[44.0, 518.0]	0.4 (17.0)	[-79.0, 80.0]
	continuous exposure MK-3222 200 mg	273	236.1 (170.9)	[44.0, 478.0]	235.6 (169.3)	[47.0, 475.0]	-0.6 (14.1)	[-82.0, 45.0]
	continuous exposure MK-3222 100 / 200 mg	670	269.5 (165.3)	[42.0, 566.0]	269.1 (164.0)	[44.0, 518.0]	-0.4 (15.8)	[-82.0, 80.0]
Week 12	continuous exposure MK-3222 100 mg	285	267.2 (164.0)	[42.0, 566.0]	268.2 (164.1)	[48.0, 469.0]	1.0 (16.0)	[-97.0, 80.0]
	continuous exposure MK-3222 200 mg	274	235.4 (170.7)	[44.0, 478.0]	235.1 (171.2)	[41.0, 521.0]	-0.3 (17.6)	[-157.0, 87.0]
	continuous exposure MK-3222 100 / 200 mg	668	268.1 (165.5)	[42.0, 566.0]	267.9 (165.6)	[41.0, 521.0]	-0.1 (17.0)	[-157.0, 87.0]
Week 28	continuous exposure MK-3222 100 mg	281	267.7 (163.9)	[42.0, 566.0]	266.7 (162.5)	[46.0, 474.0]	-1.0 (20.7)	[-148.0, 70.0]
	continuous exposure MK-3222 200 mg	269	234.8 (170.7)	[44.0, 478.0]	234.9 (170.7)	[43.0, 498.0]	0.1 (14.2)	[-46.0, 69.0]
	continuous exposure MK-3222 100 / 200 mg	657	268.5 (165.5)	[42.0, 566.0]	267.8 (164.8)	[43.0, 498.0]	-0.7 (17.9)	[-148.0, 83.0]
Week 52/64	continuous exposure MK-3222 100 mg	278	270.8 (163.0)	[42.0, 566.0]	270.1 (163.5)	[44.0, 464.0]	-0.7 (19.8)	[-112.0, 96.0]
	continuous exposure MK-3222 200 mg	267	235.0 (170.9)	[44.0, 478.0]	232.8 (170.4)	[48.0, 465.0]	-2.2 (13.6)	[-115.0, 40.0]
	continuous exposure MK-3222 100 / 200 mg	652	270.0 (165.1)	[42.0, 566.0]	268.6 (165.4)	[44.0, 494.0]	-1.3 (17.4)	[-115.0, 98.0]

N: number of subjects with non-missing baseline and post-baseline values at the given time point.
Baseline is defined as last value obtained prior to the first dose of study medication during treatment phase.
SD=Standard deviation; Min=Minimum ; Max=Maximum.
[Source: 5.3.5.3-10]