付録 2.7.4-52 治験薬の投与中止に至った有害事象（いずれかの投与群で発現割合 0%超）

006 試験（APaT 集団）

	Control		MK-3475 combined	
	n	(%)	n	(%)
Subjects in population	256		555	
with one or more adverse events	34	(13.3)	50	(9.0)
with no adverse events	222	(86.7)	505	(91.0)
Blood and lymphatic system disorders	**0**	**(0.0)**	**1**	**(0.2)**
Thrombocytopenia	0	(0.0)	1	(0.2)
Cardiac disorders	**0**	**(0.0)**	**3**	**(0.5)**
Cardiac failure	0	(0.0)	1	(0.2)
Cardiac failure congestive	0	(0.0)	1	(0.2)
Myocardial infarction	0	(0.0)	1	(0.2)
Endocrine disorders	**1**	**(0.4)**	**1**	**(0.2)**
Adrenal insufficiency	0	(0.0)	1	(0.2)
Hypopituitarism	1	(0.4)	0	(0.0)
Gastrointestinal disorders	**14**	**(5.5)**	**12**	**(2.2)**
Autoimmune pancreatitis	0	(0.0)	1	(0.2)
Colitis	9	(3.5)	8	(1.4)
Diarrhoea	5	(2.0)	1	(0.2)
Enterocolitis	1	(0.4)	0	(0.0)
Oesophagitis	0	(0.0)	1	(0.2)
Salivary gland disorder	0	(0.0)	1	(0.2)
General disorders and administration site conditions	**1**	**(0.4)**	**2**	**(0.4)**
Death	0	(0.0)	1	(0.2)
Facial pain	1	(0.4)	0	(0.0)
General physical health deterioration	0	(0.0)	1	(0.2)
Hepatobiliary disorders	**5**	**(2.0)**	**5**	**(0.9)**
Autoimmune hepatitis	1	(0.4)	2	(0.4)
Bile duct obstruction	1	(0.4)	0	(0.0)
Cholangitis	1	(0.4)	0	(0.0)
Drug-induced liver injury	0	(0.0)	1	(0.2)
Hepatic function abnormal	0	(0.0)	1	(0.2)

C Confidential

付録 2.7.4-52 治験薬の投与中止に至った有害事象（いずれかの投与群で発現割合 0%超）
006 試験（APaT 集団）（続き）

	Control		MK-3475 combined	
	n	(%)	n	(%)
Hepatobiliary disorders	**5**	**(2.0)**	**5**	**(0.9)**
Hepatitis	0	(0.0)	1	(0.2)
Hepatocellular injury	2	(0.8)	0	(0.0)
Liver disorder	1	(0.4)	0	(0.0)
Immune system disorders	**1**	**(0.4)**	**2**	**(0.4)**
Anaphylactoid reaction	0	(0.0)	1	(0.2)
Drug hypersensitivity	0	(0.0)	1	(0.2)
Hypersensitivity	1	(0.4)	0	(0.0)
Infections and infestations	**1**	**(0.4)**	**3**	**(0.5)**
Colonic abscess	1	(0.4)	0	(0.0)
Encephalitis	0	(0.0)	1	(0.2)
Lung infection	0	(0.0)	1	(0.2)
Soft tissue infection	0	(0.0)	1	(0.2)
Injury, poisoning and procedural complications	**0**	**(0.0)**	**1**	**(0.2)**
Facial bones fracture	0	(0.0)	1	(0.2)
Investigations	**2**	**(0.8)**	**1**	**(0.2)**
Alanine aminotransferase increased	1	(0.4)	0	(0.0)
Aspartate aminotransferase increased	1	(0.4)	0	(0.0)
Blood alkaline phosphatase increased	1	(0.4)	0	(0.0)
Lipase increased	0	(0.0)	1	(0.2)
Metabolism and nutrition disorders	**1**	**(0.4)**	**3**	**(0.5)**
Gout	0	(0.0)	1	(0.2)
Hypercalcaemia	1	(0.4)	0	(0.0)
Hypoalbuminaemia	0	(0.0)	1	(0.2)
Malnutrition	0	(0.0)	1	(0.2)
Type 1 diabetes mellitus	0	(0.0)	1	(0.2)
Musculoskeletal and connective tissue disorders	**2**	**(0.8)**	**2**	**(0.4)**
Arthralgia	1	(0.4)	1	(0.2)

C Confidential

付録 2.7.4-52 治験薬の投与中止に至った有害事象（いずれかの投与群で発現割合 0%超）
006 試験（APaT 集団）（続き）

	Control		MK-3475 combined	
	n	(%)	n	(%)
Musculoskeletal and connective tissue disorders	**2**	**(0.8)**	**2**	**(0.4)**
Myalgia	1	(0.4)	0	(0.0)
Rheumatoid arthritis	1	(0.4)	0	(0.0)
Sjogren's syndrome	0	(0.0)	1	(0.2)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**2**	**(0.8)**	**6**	**(1.1)**
Chronic lymphocytic leukaemia	1	(0.4)	0	(0.0)
Intracranial tumour haemorrhage	0	(0.0)	2	(0.4)
Lymphangiosis carcinomatosa	0	(0.0)	1	(0.2)
Metastases to central nervous system	0	(0.0)	2	(0.4)
Metastatic malignant melanoma	0	(0.0)	1	(0.2)
Tumour haemorrhage	1	(0.4)	0	(0.0)
Nervous system disorders	**1**	**(0.4)**	**6**	**(1.1)**
Cognitive disorder	0	(0.0)	1	(0.2)
Dizziness	1	(0.4)	0	(0.0)
Epilepsy	0	(0.0)	1	(0.2)
Guillain-Barre syndrome	0	(0.0)	1	(0.2)
Haemorrhage intracranial	0	(0.0)	1	(0.2)
Optic neuritis	0	(0.0)	1	(0.2)
Partial seizures	0	(0.0)	1	(0.2)
Polyneuropathy	0	(0.0)	1	(0.2)
Psychiatric disorders	**0**	**(0.0)**	**2**	**(0.4)**
Completed suicide	0	(0.0)	1	(0.2)
Depression	0	(0.0)	1	(0.2)
Renal and urinary disorders	**1**	**(0.4)**	**1**	**(0.2)**
Renal failure	0	(0.0)	1	(0.2)
Tubulointerstitial nephritis	1	(0.4)	0	(0.0)
Respiratory, thoracic and mediastinal disorders	**1**	**(0.4)**	**4**	**(0.7)**
Cough	0	(0.0)	1	(0.2)

C Confidential

付録 2.7.4-52 治験薬の投与中止に至った有害事象（いずれかの投与群で発現割合 0%超）
006 試験（APaT 集団）（続き）

	Control		MK-3475 combined	
	n	(%)	n	(%)
Respiratory, thoracic and mediastinal disorders	**1**	**(0.4)**	**4**	**(0.7)**
Dyspnoea	0	(0.0)	1	(0.2)
Hypoxia	1	(0.4)	0	(0.0)
Pneumonitis	0	(0.0)	1	(0.2)
Pulmonary embolism	0	(0.0)	1	(0.2)
Skin and subcutaneous tissue disorders	**2**	**(0.8)**	**2**	**(0.4)**
Psoriasis	0	(0.0)	1	(0.2)
Rash	1	(0.4)	0	(0.0)
Rash maculo-papular	1	(0.4)	0	(0.0)
Vitiligo	0	(0.0)	1	(0.2)

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.
MedDRA preferred terms 'Malignant neoplasm progression' and 'Neoplasm progression' not related to the drug are excluded.
AEs were followed 30 days after last dose of study
(Database Cutoff Date: 03SEP2014).

Data Source: [資料5.3.5.1.2: P006V01]

C Confidential

付録 2.7.4-53 治験薬の投与中止に至った有害事象の一覧

006 試験（APaT 集団）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
Control									
Trial Number=3475-006, Site Number=0004, Subject ID=366682, Gender=F, Race=White, Age=73 Years, Rel Day of Study Medication Discontinuance†=43									
366682	Treatment Cycle 2	26	Diarrhoea	4.96 Months	3	Y	Y	Discontinued	Resolved
Trial Number=3475-006, Site Number=0005, Subject ID=360125, Gender=F, Race=White, Age=71 Years, Rel Day of Study Medication Discontinuance†=1									
360125	Safety Follow-up	2	Hypersensitivity	15 Hours	2	N	Y	Discontinued	Resolved
Trial Number=3475-006, Site Number=0007, Subject ID=366167, Gender=F, Race=White, Age=52 Years, Rel Day of Study Medication Discontinuance†=44									
366167	Treatment Cycle 2	41	Colitis	3.75 Months	3	Y	Y	Discontinued	Resolved
Trial Number=3475-006, Site Number=0100, Subject ID=364670, Gender=F, Race=White, Age=55 Years, Rel Day of Study Medication Discontinuance†=43									
364670	Safety Follow-up	63	Liver disorder	5.29 Months	2	N	Y	Discontinued	Resolved
Trial Number=3475-006, Site Number=0102, Subject ID=366755, Gender=F, Race=White, Age=80 Years, Rel Day of Study Medication Discontinuance†=22									
366755	Safety Follow-up	50	Chronic lymphocytic leukaemia	Continuing	2	Y	N	Discontinued	Not Resolved
Trial Number=3475-006, Site Number=0300, Subject ID=363094, Gender=F, Race=White, Age=53 Years, Rel Day of Study Medication Discontinuance†=25									
363094	Treatment Cycle 1	4	Rheumatoid arthritis	2.79 Months	2	N	N	Discontinued	Resolved
Trial Number=3475-006, Site Number=0605, Subject ID=360281, Gender=M, Race=White, Age=83 Years, Rel Day of Study Medication Discontinuance†=20									
360281	Safety Follow-up	33	Hypercalcaemia	2.43 Weeks	4	Y	N	Discontinued	Resolved
Trial Number=3475-006, Site Number=0605, Subject ID=364560, Gender=F, Race=White, Age=81 Years, Rel Day of Study Medication Discontinuance†=64									
364560	Safety Follow-up	65	Colonic abscess	1.28 Months	3	Y	Y	Discontinued	Resolved

C Confidential

付録 2.7.4-53 治験薬の投与中止に至った有害事象の一覧

006 試験（APaT 集団）（続き）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
Control									
Trial Number=3475-006, Site Number=0612, Subject ID=360849, Gender=M, Race=White, Age=67 Years, Rel Day of Study Medication Discontinuance†=25									
360849	Safety Follow-up	28	Rash	1.31 Months	4	Y	Y	Discontinued	Resolved
Trial Number=3475-006, Site Number=0612, Subject ID=364286, Gender=M, Race=White, Age=57 Years, Rel Day of Study Medication Discontinuance†=22									
364286	Safety Follow-up	43	Hepatocellular injury	Continuing	3	Y	Y	Discontinued	Not Resolved
Trial Number=3475-006, Site Number=0612, Subject ID=366743, Gender=F, Race=White, Age=67 Years, Rel Day of Study Medication Discontinuance†=67									
366743	Treatment Cycle 2	41	Hepatocellular injury	1.87 Months	3	Y	Y	Discontinued	Resolved
Trial Number=3475-006, Site Number=0702, Subject ID=361483, Gender=F, Race=White, Age=68 Years, Rel Day of Study Medication Discontinuance†=22									
361483	Safety Follow-up	27	Colitis	Continuing	4	Y	Y	Discontinued	Not Resolved
Trial Number=3475-006, Site Number=0900, Subject ID=368171, Gender=M, Race=White, Age=60 Years, Rel Day of Study Medication Discontinuance†=43									
368171	Safety Follow-up	62	Hypoxia	2 Days	5	Y	N	Discontinued	Fatal
Trial Number=3475-006, Site Number=1400, Subject ID=366198, Gender=F, Race=White, Age=63 Years, Rel Day of Study Medication Discontinuance†=22									
366198	Safety Follow-up	25	Diarrhoea	2.3 Months	3	Y	Y	Discontinued	Resolved
Trial Number=3475-006, Site Number=1502, Subject ID=361277, Gender=F, Race=White, Age=78 Years, Rel Day of Study Medication Discontinuance†=65									
361277	Safety Follow-up	76	Enterocolitis	3.43 Weeks	3	Y	Y	Discontinued	Resolved
Trial Number=3475-006, Site Number=1502, Subject ID=369073, Gender=F, Race=White, Age=55 Years, Rel Day of Study Medication Discontinuance†=22									
369073	Treatment Cycle 1	21 21	Alanine aminotransferase increased Aspartate aminotransferase increased	2.04 Months 1.18 Months	4 3	Y Y	Y Y	Discontinued Discontinued	Resolved Resolved

C Confidential

付録 2.7.4-53 治験薬の投与中止に至った有害事象の一覧

006 試験（APaT 集団）（続き）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
Control									
Trial Number=3475-006, Site Number=1506, Subject ID=362963, Gender=M, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=43									
362963	Safety Follow-up	61	Tumour haemorrhage	1.14 Weeks	5	Y	N	Discontinued	Fatal
Trial Number=3475-006, Site Number=1601, Subject ID=363241, Gender=F, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=43									
363241	Safety Follow-up	52	Diarrhoea	1.43 Weeks	2	N	Y	Discontinued	Resolved
Trial Number=3475-006, Site Number=1700, Subject ID=367140, Gender=F, Race=White, Age=65 Years, Rel Day of Study Medication Discontinuance†=43									
367140	Treatment Cycle 3	43	Hypopituitarism	1.54 Months	3	Y	Y	Discontinued	Sequelae
Trial Number=3475-006, Site Number=1700, Subject ID=367898, Gender=M, Race=White, Age=38 Years, Rel Day of Study Medication Discontinuance†=22									
367898	Safety Follow-up	26	Autoimmune hepatitis	2.57 Weeks	3	Y	Y	Discontinued	Resolved
Trial Number=3475-006, Site Number=1700, Subject ID=368071, Gender=M, Race=White, Age=79 Years, Rel Day of Study Medication Discontinuance†=25									
368071	Treatment Cycle 2	25	Colitis	2.1 Months	3	Y	Y	Discontinued	Sequelae
Trial Number=3475-006, Site Number=1700, Subject ID=368192, Gender=M, Race=White, Age=35 Years, Rel Day of Study Medication Discontinuance†=1									
368192	Safety Follow-up	16	Colitis	2 Weeks	3	Y	Y	Discontinued	Resolved
Trial Number=3475-006, Site Number=1703, Subject ID=361155, Gender=F, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=22									
361155	Safety Follow-up	46	Tubulointerstitial nephritis	1.97 Months	3	Y	N	Discontinued	Sequelae
Trial Number=3475-006, Site Number=1706, Subject ID=362616, Gender=M, Race=White, Age=45 Years, Rel Day of Study Medication Discontinuance†=44									
362616	Safety Follow-up	46	Diarrhoea	3.61 Months	3	Y	Y	Discontinued	Resolved

Confidential

付録 2.7.4-53 治験薬の投与中止に至った有害事象の一覧

006 試験（APaT 集団）（続き）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
Control									
Trial Number=3475-006, Site Number=1807, Subject ID=362386, Gender=M, Race=White, Age=78 Years, Rel Day of Study Medication Discontinuance†=47									
362386	Treatment Cycle 2	26	Facial pain	Continuing	3	N	N	Discontinued	Not Resolved
Trial Number=3475-006, Site Number=1808, Subject ID=364536, Gender=M, Race=White, Age=73 Years, Rel Day of Study Medication Discontinuance†=21									
364536	Safety Follow-up	24	Arthralgia	1.25 Months	3	N	Y	Discontinued	Resolved
		24	Myalgia	Continuing	3	N	Y	Discontinued	Not Resolved
Trial Number=3475-006, Site Number=1812, Subject ID=360032, Gender=F, Race=White, Age=69 Years, Rel Day of Study Medication Discontinuance†=1									
360032	Safety Follow-up	15	Colitis	1.35 Months	3	Y	Y	Discontinued	Resolved
Trial Number=3475-006, Site Number=1812, Subject ID=363484, Gender=M, Race=White, Age=53 Years, Rel Day of Study Medication Discontinuance†=43									
363484	Safety Follow-up	46	Colitis	2.69 Months	3	Y	Y	Discontinued	Resolved
Trial Number=3475-006, Site Number=1815, Subject ID=364581, Gender=F, Race=White, Age=63 Years, Rel Day of Study Medication Discontinuance†=20									
364581	Safety Follow-up	33	Colitis	1.25 Months	3	N	Y	Discontinued	Resolved
Trial Number=3475-006, Site Number=1816, Subject ID=361035, Gender=F, Race=White, Age=77 Years, Rel Day of Study Medication Discontinuance†=20									
361035	Safety Follow-up	34	Bile duct obstruction	2.14 Weeks	3	Y	N	Discontinued	Resolved
		34	Cholangitis	2.14 Weeks	3	Y	N	Discontinued	Resolved
		41	Blood alkaline phosphatase increased	2.86 Weeks	2	N	N	Discontinued	Resolved
Trial Number=3475-006, Site Number=1816, Subject ID=362422, Gender=F, Race=White, Age=61 Years, Rel Day of Study Medication Discontinuance†=22									
362422	Treatment Cycle 1	2	Rash maculo-papular	1.61 Months	2	N	N	Discontinued	Resolved

C Confidential

付録 2.7.4-53 治験薬の投与中止に至った有害事象の一覧

006 試験（APaT 集団）（続き）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
Control									
Trial Number=3475-006, Site Number=1824, Subject ID=361753, Gender=M, Race=White, Age=60 Years, Rel Day of Study Medication Discontinuance†=42									
361753	Safety Follow-up	53	Diarrhoea	5 Days	2	Y	Y	Discontinued	Resolved
		56	Colitis	3.22 Months	3	Y	Y	Discontinued	Resolved
Trial Number=3475-006, Site Number=1900, Subject ID=364587, Gender=F, Race=White, Age=59 Years, Rel Day of Study Medication Discontinuance†=1									
364587	Safety Follow-up	8	Colitis	1.18 Months	4	Y	Y	Discontinued	Resolved
Trial Number=3475-006, Site Number=1900, Subject ID=368479, Gender=M, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance†=22									
368479	Safety Follow-up	25	Dizziness	Unknown	1	N	N	Discontinued	Unknown
MK-3475 10 mg/kg Q2W									
Trial Number=3475-006, Site Number=0001, Subject ID=362146, Gender=M, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance†=182									
362146	Safety Follow-up	193	Death	23 Hours	5	Y	N	Discontinued	Fatal
Trial Number=3475-006, Site Number=0101, Subject ID=361468, Gender=F, Race=White, Age=61 Years, Rel Day of Study Medication Discontinuance†=91									
361468	Treatment Cycle 7	91	Myocardial infarction	1.65 Hours	5	Y	N	Discontinued	Fatal
Trial Number=3475-006, Site Number=0102, Subject ID=362910, Gender=F, Race=White, Age=72 Years, Rel Day of Study Medication Discontinuance†=12									
362910	Safety Follow-up	38	Lymphangiosis carcinomatosa	1.28 Months	5	Y	N	Discontinued	Fatal
Trial Number=3475-006, Site Number=0403, Subject ID=360347, Gender=M, Race=White, Age=46 Years, Rel Day of Study Medication Discontinuance†=86									
360347	Safety Follow-up	97	Encephalitis	1.43 Weeks	3	Y	Y	Discontinued	Resolved

C Confidential

付録 2.7.4-53 治験薬の投与中止に至った有害事象の一覧

006 試験（APaT 集団）（続き）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q2W									
Trial Number=3475-006, Site Number=0501, Subject ID=368971, Gender=F, Race=White, Age=54 Years, Rel Day of Study Medication Discontinuance†=1									
368971	Safety Follow-up	4	Hepatic function abnormal	4.14 Weeks	2	N	N	Discontinued	Unknown
		4	Malnutrition	4.14 Weeks	3	N	N	Discontinued	Unknown
		4	Metastatic malignant melanoma	4.14 Weeks	5	Y	N	Discontinued	Fatal
		15	Hypoalbuminaemia	Continuing	3	N	N	Discontinued	Not Resolved
Trial Number=3475-006, Site Number=0504, Subject ID=361989, Gender=F, Race=Multiple, Age=69 Years, Rel Day of Study Medication Discontinuance†=42									
361989	Safety Follow-up	50	Facial bones fracture	1.14 Weeks	4	Y	N	Discontinued	Resolved
Trial Number=3475-006, Site Number=0605, Subject ID=360713, Gender=M, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=153									
360713	Treatment Cycle 9	125	Colitis	2.5 Months	3	Y	Y	Discontinued	Resolved
Trial Number=3475-006, Site Number=0605, Subject ID=362930, Gender=M, Race=White, Age=59 Years, Rel Day of Study Medication Discontinuance†=85									
362930	Safety Follow-up	87	Colitis	1.12 Months	3	Y	Y	Discontinued	Resolved
Trial Number=3475-006, Site Number=0704, Subject ID=360742, Gender=F, Race=White, Age=83 Years, Rel Day of Study Medication Discontinuance†=154									
360742	Safety Follow-up	162	Epilepsy	3 Days	3	Y	Y	Discontinued	Resolved
Trial Number=3475-006, Site Number=0704, Subject ID=366882, Gender=M, Race=White, Age=77 Years, Rel Day of Study Medication Discontinuance†=144									
366882	Safety Follow-up	158	Adrenal insufficiency	Continuing	4	Y	Y	Discontinued	Not Resolved
Trial Number=3475-006, Site Number=1301, Subject ID=368724, Gender=M, Race=White, Age=73 Years, Rel Day of Study Medication Discontinuance†=204									
368724	Treatment Cycle 14	184	Gout	Continuing	3	Y	N	Discontinued	Not Resolved

C Confidential

付録 2.7.4-53 治験薬の投与中止に至った有害事象の一覧

006 試験（APaT 集団）（続き）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q2W									
Trial Number=3475-006, Site Number=1402, Subject ID=361567, Gender=F, Race=White, Age=68 Years, Rel Day of Study Medication Discontinuance†=43									
361567	Safety Follow-up	58	Intracranial tumour haemorrhage	Continuing	4	Y	N	Discontinued	Not Resolved
Trial Number=3475-006, Site Number=1502, Subject ID=360464, Gender=M, Race=White, Age=59 Years, Rel Day of Study Medication Discontinuance†=15									
360464	Safety Follow-up	29	General physical health deterioration	Continuing	3	Y	N	Discontinued	Not Resolved
Trial Number=3475-006, Site Number=1600, Subject ID=368466, Gender=M, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=14									
368466	Treatment Cycle 2	14	Drug hypersensitivity	2.33 Hours	3	Y	Y	Discontinued	Resolved
Trial Number=3475-006, Site Number=1601, Subject ID=361821, Gender=F, Race=White, Age=45 Years, Rel Day of Study Medication Discontinuance†=337									
361821	Treatment Cycle 20	326	Sjogren's syndrome	Continuing	3	N	Y	Discontinued	Not Resolved
Trial Number=3475-006, Site Number=1705, Subject ID=365415, Gender=F, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=197									
365415	Safety Follow-up	204	Colitis	Continuing	3	Y	Y	Discontinued	Not Resolved
Trial Number=3475-006, Site Number=1710, Subject ID=364567, Gender=M, Race=White, Age=73 Years, Rel Day of Study Medication Discontinuance†=113									
364567	Safety Follow-up	116	Autoimmune pancreatitis	3.86 Weeks	3	Y	Y	Discontinued	Sequelae
Trial Number=3475-006, Site Number=1804, Subject ID=364814, Gender=F, Race=White, Age=84 Years, Rel Day of Study Medication Discontinuance†=196									
364814	Treatment Cycle 3	48	Psoriasis	Continuing	3	N	Y	Discontinued	Resolving
Trial Number=3475-006, Site Number=1823, Subject ID=360915, Gender=M, Race=White, Age=60 Years, Rel Day of Study Medication Discontinuance†=146									
360915	Safety Follow-up	162	Partial seizures	1.14 Weeks	3	Y	N	Discontinued	Resolved

C Confidential

付録 2.7.4-53 治験薬の投与中止に至った有害事象の一覧

006 試験（APaT 集団）（続き）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q2W									
Trial Number=3475-006, Site Number=1824, Subject ID=360306, Gender=M, Race=White, Age=71 Years, Rel Day of Study Medication Discontinuance†=183									
360306	Safety Follow-up	191	Autoimmune hepatitis	1.77 Months	3	Y	Y	Discontinued	Resolved
MK-3475 10 mg/kg Q3W									
Trial Number=3475-006, Site Number=0001, Subject ID=368720, Gender=M, Race=White, Age=63 Years, Rel Day of Study Medication Discontinuance†=254									
368720	Safety Follow-up	262	Haemorrhage intracranial	3.86 Weeks	2	Y	N	Discontinued	Resolved
		279	Cognitive disorder	Continuing	3	N	Y	Discontinued	Not Resolved
Trial Number=3475-006, Site Number=0002, Subject ID=366309, Gender=M, Race=White, Age=62 Years, Rel Day of Study Medication Discontinuance†=1									
366309	Safety Follow-up	5	Cardiac failure congestive	23 Hours	5	Y	N	Discontinued	Fatal
Trial Number=3475-006, Site Number=0102, Subject ID=364417, Gender=F, Race=White, Age=47 Years, Rel Day of Study Medication Discontinuance†=1									
364417	Safety Follow-up	4	Intracranial tumour haemorrhage	1.58 Months	3	Y	N	Discontinued	Sequelae
Trial Number=3475-006, Site Number=0102, Subject ID=368067, Gender=M, Race=White, Age=54 Years, Rel Day of Study Medication Discontinuance†=168									
368067	Safety Follow-up	174	Diarrhoea	Continuing	2	N	N	Discontinued	Not Resolved
Trial Number=3475-006, Site Number=0309, Subject ID=366971, Gender=M, Race=White, Age=79 Years, Rel Day of Study Medication Discontinuance†=1									
366971	Safety Follow-up	29	Hepatitis	1.08 Months	3	Y	Y	Discontinued	Resolved
		29	Pneumonitis	3.88 Months	3	Y	Y	Discontinued	Resolved
Trial Number=3475-006, Site Number=0501, Subject ID=362675, Gender=F, Race=White, Age=51 Years, Rel Day of Study Medication Discontinuance†=22									
362675	Safety Follow-up	23	Soft tissue infection	1.29 Weeks	5	Y	N	Discontinued	Fatal

C Confidential

付録 2.7.4-53 治験薬の投与中止に至った有害事象の一覧
006 試験（APaT 集団）（続き）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q3W									
Trial Number=3475-006, Site Number=0602, Subject ID=361473, Gender=M, Race=White, Age=71 Years, Rel Day of Study Medication Discontinuance†=67									
361473	Treatment Cycle 4	67	Anaphylactoid reaction	3 Days	3	Y	Y	Discontinued	Resolved
Trial Number=3475-006, Site Number=0605, Subject ID=360314, Gender=F, Race=White, Age=67 Years, Rel Day of Study Medication Discontinuance†=244									
360314	Safety Follow-up	254	Depression	2.73 Months	3	Y	N	Discontinued	Resolved
Trial Number=3475-006, Site Number=0605, Subject ID=362662, Gender=F, Race=White, Age=38 Years, Rel Day of Study Medication Discontinuance†=232									
362662	Safety Follow-up	233	Oesophagitis	Continuing	3	Y	Y	Discontinued	Resolving
Trial Number=3475-006, Site Number=0605, Subject ID=363218, Gender=M, Race=White, Age=75 Years, Rel Day of Study Medication Discontinuance†=190									
363218	Safety Follow-up	215	Renal failure	Continuing	3	Y	Y	Discontinued	Not Resolved
Trial Number=3475-006, Site Number=0605, Subject ID=366256, Gender=M, Race=White, Age=58 Years, Rel Day of Study Medication Discontinuance†=21									
366256	Treatment Cycle 1	6	Cough	4.47 Months	1	Y	Y	Discontinued	Resolved
	Treatment Cycle 2	21	Thrombocytopenia	Continuing	4	Y	Y	Discontinued	Not Resolved
Trial Number=3475-006, Site Number=0611, Subject ID=364561, Gender=M, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=20									
364561	Treatment Cycle 1	17	Autoimmune hepatitis	3.12 Months	3	Y	Y	Discontinued	Resolved
Trial Number=3475-006, Site Number=0611, Subject ID=365059, Gender=M, Race=White, Age=80 Years, Rel Day of Study Medication Discontinuance†=99									
365059	Safety Follow-up	108	Lung infection	2.14 Weeks	4	Y	N	Discontinued	Fatal
		108	Pulmonary embolism	Continuing	4	Y	N	Discontinued	Not Resolved
Trial Number=3475-006, Site Number=0701, Subject ID=360019, Gender=M, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=64									

C Confidential

付録 2.7.4-53 治験薬の投与中止に至った有害事象の一覧
006 試験（APaT 集団）（続き）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q3W									
Trial Number=3475-006, Site Number=0701, Subject ID=360019, Gender=M, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=64									
360019	Treatment Cycle 3	57	Colitis	3.94 Months	3	Y	Y	Discontinued	Resolved
Trial Number=3475-006, Site Number=0706, Subject ID=367820, Gender=M, Race=White, Age=74 Years, Rel Day of Study Medication Discontinuance†=1									
367820	Safety Follow-up	8	Cardiac failure	4.14 Weeks	5	Y	N	Discontinued	Fatal
Trial Number=3475-006, Site Number=1400, Subject ID=366877, Gender=F, Race=White, Age=53 Years, Rel Day of Study Medication Discontinuance†=1									
366877	Safety Follow-up	15	Metastases to central nervous system	Continuing	1	Y	N	Discontinued	Not Resolved
Trial Number=3475-006, Site Number=1500, Subject ID=363996, Gender=M, Race=White, Age=42 Years, Rel Day of Study Medication Discontinuance†=22									
363996	Safety Follow-up	37	Colitis	1.64 Months	2	Y	Y	Discontinued	Resolved
Trial Number=3475-006, Site Number=1506, Subject ID=364200, Gender=M, Race=White, Age=68 Years, Rel Day of Study Medication Discontinuance†=21									
364200	Treatment Cycle 1	7	Dyspnoea	Continuing	3	Y	N	Discontinued	Not Resolved
Trial Number=3475-006, Site Number=1601, Subject ID=364335, Gender=M, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance†=45									
364335	Treatment Cycle 2	41	Colitis	1.41 Months	4	Y	Y	Discontinued	Resolved
Trial Number=3475-006, Site Number=1707, Subject ID=364658, Gender=M, Race=White, Age=58 Years, Rel Day of Study Medication Discontinuance†=1									
364658	Safety Follow-up	22	Drug-induced liver injury	3.71 Weeks	4	Y	Y	Discontinued	Resolved
		28	Guillain-Barre syndrome	3.15 Months	4	Y	Y	Discontinued	Sequelae
Trial Number=3475-006, Site Number=1804, Subject ID=364357, Gender=F, Race=White, Age=57 Years, Rel Day of Study Medication Discontinuance†=182									
364357	Treatment Cycle 6	115	Arthralgia	Continuing	2	N	Y	Discontinued	Not Resolved

C Confidential

付録 2.7.4-53 治験薬の投与中止に至った有害事象の一覧

006 試験（APaT 集団）（続き）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q3W									
Trial Number=3475-006, Site Number=1807, Subject ID=365454, Gender=F, Race=White, Age=59 Years, Rel Day of Study Medication Discontinuance†=141									
365454	Treatment Cycle 5	137	Salivary gland disorder	Continuing	2	N	Y	Discontinued	Not Resolved
Trial Number=3475-006, Site Number=1812, Subject ID=362552, Gender=M, Race=White, Age=87 Years, Rel Day of Study Medication Discontinuance†=22									
362552	Safety Follow-up	43	Completed suicide	1 Seconds	5	Y	N	Discontinued	Fatal
Trial Number=3475-006, Site Number=1815, Subject ID=360878, Gender=M, Race=White, Age=78 Years, Rel Day of Study Medication Discontinuance†=63									
360878	Treatment Cycle 3	46	Colitis	6.34 Months	4	Y	Y	Discontinued	Resolved
Trial Number=3475-006, Site Number=1816, Subject ID=364466, Gender=M, Race=White, Age=71 Years, Rel Day of Study Medication Discontinuance†=250									
364466	Treatment Cycle 11	209	Vitiligo	Continuing	2	N	Y	Discontinued	Not Resolved
	Safety Follow-up	259	Colitis	3.86 Weeks	3	N	Y	Discontinued	Resolved
Trial Number=3475-006, Site Number=1820, Subject ID=360662, Gender=M, Race=White, Age=55 Years, Rel Day of Study Medication Discontinuance†=1									
360662	Safety Follow-up	9	Metastases to central nervous system	Continuing	3	Y	N	Discontinued	Not Resolved
Trial Number=3475-006, Site Number=1823, Subject ID=362113, Gender=F, Race=White, Age=64 Years, Rel Day of Study Medication Discontinuance†=85									
362113	Safety Follow-up	106	Type 1 diabetes mellitus	Continuing	4	Y	Y	Discontinued	Not Resolved
Trial Number=3475-006, Site Number=1823, Subject ID=366042, Gender=M, Race=White, Age=54 Years, Rel Day of Study Medication Discontinuance†=211									
366042	Treatment Cycle 8	169	Lipase increased	Continuing	3	N	Y	Discontinued	Not Resolved
Trial Number=3475-006, Site Number=1900, Subject ID=362844, Gender=M, Race=White, Age=81 Years, Rel Day of Study Medication Discontinuance†=22									
362844	Safety Follow-up	43	Polyneuropathy	Continuing	2	N	Y	Discontinued	Not Resolved

C Confidential

付録 2.7.4-53 治験薬の投与中止に至った有害事象の一覧

006 試験（APaT 集団）（続き）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q3W									
Trial Number=3475-006, Site Number=1900, Subject ID=363703, Gender=F, Race=White, Age=74 Years, Rel Day of Study Medication Discontinuance†=1									
363703	Safety Follow-up	13	Optic neuritis	3.52 Months	2	N	Y	Discontinued	Sequelae

†Relative Day of Study Medication Discontinuance is defined as the day of the last recorded dose of study medication for the subject relative to the start of study medication.

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.

Grades are based on NCI CTCAE version 4.0..

MedDRA preferred terms 'Malignant neoplasm progression' and 'Neoplasm progression' not related to the drug are excluded.

AEs were followed 30 days after last dose of study treatment

(Database Cutoff Date: 03SEP2014).

Data Source: [資料5.3.5.1.2: P006V01]

C Confidential

付録 2.7.4-54 休薬に至った有害事象（いずれかの投与群で発現割合 0%超）
001 試験+002 試験+006 試験（APaT 集団）

	MK-3475 2 mg/kg Q3W		MK-3475 10 mg/kg Q3W		MK-3475 10 mg/kg Q2W		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	340		769		458		1,567	
with one or more adverse events	57	(16.8)	145	(18.9)	108	(23.6)	310	(19.8)
with no adverse events	283	(83.2)	624	(81.1)	350	(76.4)	1,257	(80.2)
Blood and lymphatic system disorders	**6**	**(1.8)**	**6**	**(0.8)**	**4**	**(0.9)**	**16**	**(1.0)**
Anaemia	5	(1.5)	4	(0.5)	4	(0.9)	13	(0.8)
Neutropenia	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)
Thrombocytopenia	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.1)
Cardiac disorders	**0**	**(0.0)**	**3**	**(0.4)**	**4**	**(0.9)**	**7**	**(0.4)**
Angina unstable	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Atrial fibrillation	0	(0.0)	0	(0.0)	2	(0.4)	2	(0.1)
Atrial thrombosis	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Cardiac failure	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Cardiac failure congestive	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Pericardial effusion	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Ear and labyrinth disorders	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.2)**	**1**	**(0.1)**
Deafness	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Endocrine disorders	**1**	**(0.3)**	**10**	**(1.3)**	**8**	**(1.7)**	**19**	**(1.2)**
Adrenal insufficiency	0	(0.0)	2	(0.3)	1	(0.2)	3	(0.2)
Hyperthyroidism	0	(0.0)	2	(0.3)	2	(0.4)	4	(0.3)
Hypophysitis	1	(0.3)	2	(0.3)	0	(0.0)	3	(0.2)
Hypopituitarism	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Hypothyroidism	0	(0.0)	4	(0.5)	4	(0.9)	8	(0.5)
Thyroiditis	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Eye disorders	**0**	**(0.0)**	**6**	**(0.8)**	**2**	**(0.4)**	**8**	**(0.5)**
Eye irritation	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Eyelash discolouration	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Iritis	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Papilloedema	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Retinal tear	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Uveitis	0	(0.0)	2	(0.3)	1	(0.2)	3	(0.2)
Vision blurred	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)

C Confidential

付録 2.7.4-54 休薬に至った有害事象（いずれかの投与群で発現割合 0%超）
001 試験+002 試験+006 試験（APaT 集団）（続き）

	MK-3475 2 mg/kg Q3W		MK-3475 10 mg/kg Q3W		MK-3475 10 mg/kg Q2W		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Gastrointestinal disorders	**10**	**(2.9)**	**27**	**(3.5)**	**23**	**(5.0)**	**60**	**(3.8)**
Abdominal pain	1	(0.3)	3	(0.4)	0	(0.0)	4	(0.3)
Abdominal pain lower	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Abdominal pain upper	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Colitis	3	(0.9)	3	(0.4)	2	(0.4)	8	(0.5)
Constipation	1	(0.3)	0	(0.0)	1	(0.2)	2	(0.1)
Diarrhoea	3	(0.9)	14	(1.8)	10	(2.2)	27	(1.7)
Dry mouth	0	(0.0)	1	(0.1)	1	(0.2)	2	(0.1)
Dysphagia	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)
Gastric disorder	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Gastritis	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Gastrointestinal disorder	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Gastrointestinal haemorrhage	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Glossitis	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Intestinal obstruction	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Intussusception	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Nausea	0	(0.0)	2	(0.3)	6	(1.3)	8	(0.5)
Pancreatitis	1	(0.3)	2	(0.3)	0	(0.0)	3	(0.2)
Rectal haemorrhage	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Small intestinal obstruction	1	(0.3)	1	(0.1)	0	(0.0)	2	(0.1)
Small intestinal perforation	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)
Stomatitis	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Vomiting	0	(0.0)	2	(0.3)	2	(0.4)	4	(0.3)
General disorders and administration site conditions	**6**	**(1.8)**	**16**	**(2.1)**	**16**	**(3.5)**	**38**	**(2.4)**
Adverse drug reaction	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Asthenia	0	(0.0)	2	(0.3)	1	(0.2)	3	(0.2)
Chest discomfort	0	(0.0)	1	(0.1)	1	(0.2)	2	(0.1)
Chills	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)
Fatigue	4	(1.2)	2	(0.3)	4	(0.9)	10	(0.6)
Feeling hot	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Generalised oedema	0	(0.0)	0	(0.0)	2	(0.4)	2	(0.1)
Inflammation	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Influenza like illness	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)

C Confidential

付録 2.7.4-54 休薬に至った有害事象（いずれかの投与群で発現割合 0%超）
001 試験+002 試験+006 試験（APaT 集団）（続き）

	MK-3475 2 mg/kg Q3W		MK-3475 10 mg/kg Q3W		MK-3475 10 mg/kg Q2W		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
General disorders and administration site conditions	**6**	**(1.8)**	**16**	**(2.1)**	**16**	**(3.5)**	**38**	**(2.4)**
Infusion site extravasation	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Injection site extravasation	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Malaise	0	(0.0)	2	(0.3)	2	(0.4)	4	(0.3)
Mucosal inflammation	2	(0.6)	2	(0.3)	0	(0.0)	4	(0.3)
Nodule	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Oedema	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Oedema peripheral	0	(0.0)	2	(0.3)	2	(0.4)	4	(0.3)
Pain	0	(0.0)	1	(0.1)	1	(0.2)	2	(0.1)
Pyrexia	2	(0.6)	3	(0.4)	0	(0.0)	5	(0.3)
Systemic inflammatory response syndrome	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Hepatobiliary disorders	**4**	**(1.2)**	**6**	**(0.8)**	**2**	**(0.4)**	**12**	**(0.8)**
Autoimmune hepatitis	2	(0.6)	1	(0.1)	0	(0.0)	3	(0.2)
Cholecystitis	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Cholestasis	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Drug-induced liver injury	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Hepatitis	1	(0.3)	1	(0.1)	1	(0.2)	3	(0.2)
Hepatomegaly	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)
Hyperbilirubinaemia	0	(0.0)	1	(0.1)	1	(0.2)	2	(0.1)
Immune system disorders	**0**	**(0.0)**	**3**	**(0.4)**	**0**	**(0.0)**	**3**	**(0.2)**
Hypersensitivity	0	(0.0)	3	(0.4)	0	(0.0)	3	(0.2)
Infections and infestations	**7**	**(2.1)**	**18**	**(2.3)**	**16**	**(3.5)**	**41**	**(2.6)**
Appendicitis perforated	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Bronchitis	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Catheter site infection	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)
Cellulitis	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.1)
Conjunctivitis	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Diverticulitis	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.1)
Erysipelas	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Lower respiratory tract infection	0	(0.0)	1	(0.1)	1	(0.2)	2	(0.1)

C Confidential

付録 2.7.4-54 休薬に至った有害事象（いずれかの投与群で発現割合 0%超）
001 試験+002 試験+006 試験（APaT 集団）（続き）

	MK-3475 2 mg/kg Q3W		MK-3475 10 mg/kg Q3W		MK-3475 10 mg/kg Q2W		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Infections and infestations	**7**	**(2.1)**	**18**	**(2.3)**	**16**	**(3.5)**	**41**	**(2.6)**
Nasopharyngitis	0	(0.0)	3	(0.4)	0	(0.0)	3	(0.2)
Pelvic abscess	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Pneumonia	1	(0.3)	0	(0.0)	3	(0.7)	4	(0.3)
Pneumonia klebsiella	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Respiratory tract infection viral	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Sepsis	0	(0.0)	2	(0.3)	1	(0.2)	3	(0.2)
Skin infection	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)
Soft tissue infection	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)
Tuberculosis	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Upper respiratory tract infection	2	(0.6)	1	(0.1)	7	(1.5)	10	(0.6)
Urinary tract infection	1	(0.3)	2	(0.3)	4	(0.9)	7	(0.4)
Viral infection	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Injury, poisoning and procedural complications	**1**	**(0.3)**	**8**	**(1.0)**	**1**	**(0.2)**	**10**	**(0.6)**
Infusion related reaction	0	(0.0)	7	(0.9)	1	(0.2)	8	(0.5)
Procedural pain	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Radiation injury	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)
Investigations	**6**	**(1.8)**	**15**	**(2.0)**	**14**	**(3.1)**	**35**	**(2.2)**
Alanine aminotransferase increased	2	(0.6)	7	(0.9)	5	(1.1)	14	(0.9)
Amylase increased	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Aspartate aminotransferase increased	3	(0.9)	6	(0.8)	5	(1.1)	14	(0.9)
Bilirubin conjugated increased	0	(0.0)	1	(0.1)	1	(0.2)	2	(0.1)
Blood alkaline phosphatase increased	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Blood bilirubin increased	3	(0.9)	3	(0.4)	2	(0.4)	8	(0.5)
Blood corticotrophin decreased	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)

C Confidential

付録 2.7.4-54 休薬に至った有害事象（いずれかの投与群で発現割合 0%超）
001 試験+002 試験+006 試験（APaT 集団）（続き）

	MK-3475 2 mg/kg Q3W		MK-3475 10 mg/kg Q3W		MK-3475 10 mg/kg Q2W		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Investigations	**6**	**(1.8)**	**15**	**(2.0)**	**14**	**(3.1)**	**35**	**(2.2)**
Blood cortisol decreased	1	(0.3)	0	(0.0)	1	(0.2)	2	(0.1)
Blood creatinine increased	0	(0.0)	3	(0.4)	1	(0.2)	4	(0.3)
Blood testosterone decreased	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)
C-reactive protein increased	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Cardiac murmur functional	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Gamma-glutamyltransferase increased	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Haemoglobin decreased	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Liver function test abnormal	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Transaminases increased	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Weight decreased	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Metabolism and nutrition disorders	**5**	**(1.5)**	**10**	**(1.3)**	**12**	**(2.6)**	**27**	**(1.7)**
Decreased appetite	0	(0.0)	0	(0.0)	3	(0.7)	3	(0.2)
Dehydration	1	(0.3)	2	(0.3)	2	(0.4)	5	(0.3)
Diabetes mellitus	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)
Failure to thrive	0	(0.0)	1	(0.1)	1	(0.2)	2	(0.1)
Hypermagnesaemia	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Hyperphosphataemia	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Hypertriglyceridaemia	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Hyperuricaemia	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)
Hypoalbuminaemia	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Hypokalaemia	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Hyponatraemia	1	(0.3)	4	(0.5)	5	(1.1)	10	(0.6)
Hypophosphataemia	0	(0.0)	0	(0.0)	2	(0.4)	2	(0.1)
Lactic acidosis	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)
Metabolic disorder	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Musculoskeletal and connective tissue disorders	**6**	**(1.8)**	**8**	**(1.0)**	**15**	**(3.3)**	**29**	**(1.9)**
Arthralgia	3	(0.9)	3	(0.4)	5	(1.1)	11	(0.7)

C Confidential

付録 2.7.4-54 休薬に至った有害事象（いずれかの投与群で発現割合 0%超）
001 試験+002 試験+006 試験（APaT 集団）（続き）

	MK-3475 2 mg/kg Q3W		MK-3475 10 mg/kg Q3W		MK-3475 10 mg/kg Q2W		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Musculoskeletal and connective tissue disorders	**6**	**(1.8)**	**8**	**(1.0)**	**15**	**(3.3)**	**29**	**(1.9)**
Arthritis	0	(0.0)	2	(0.3)	1	(0.2)	3	(0.2)
Arthropathy	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Back pain	0	(0.0)	2	(0.3)	3	(0.7)	5	(0.3)
Chondrocalcinosis pyrophosphate	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Muscle spasms	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Muscular weakness	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)
Musculoskeletal pain	1	(0.3)	1	(0.1)	0	(0.0)	2	(0.1)
Myalgia	1	(0.3)	2	(0.3)	1	(0.2)	4	(0.3)
Myositis	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Pathological fracture	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Polyarthritis	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Spinal osteoarthritis	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**2**	**(0.6)**	**1**	**(0.1)**	**1**	**(0.2)**	**4**	**(0.3)**
Metastases to central nervous system	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)
Metastatic malignant melanoma	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Oncologic complication	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)
Tumour haemorrhage	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Nervous system disorders	**3**	**(0.9)**	**11**	**(1.4)**	**5**	**(1.1)**	**19**	**(1.2)**
Aphasia	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Cerebrovascular accident	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Cognitive disorder	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)
Convulsion	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Epilepsy	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Headache	1	(0.3)	0	(0.0)	1	(0.2)	2	(0.1)
Hydrocephalus	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Ischaemic stroke	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Memory impairment	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Meningitis noninfective	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Myasthenic syndrome	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)

C Confidential

付録 2.7.4-54 休薬に至った有害事象（いずれかの投与群で発現割合 0%超）
001 試験+002 試験+006 試験（APaT 集団）（続き）

	MK-3475 2 mg/kg Q3W		MK-3475 10 mg/kg Q3W		MK-3475 10 mg/kg Q2W		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Nervous system disorders	**3**	**(0.9)**	**11**	**(1.4)**	**5**	**(1.1)**	**19**	**(1.2)**
Neuralgia	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Neuropathy peripheral	1	(0.3)	1	(0.1)	0	(0.0)	2	(0.1)
Normal pressure hydrocephalus	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Peripheral motor neuropathy	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Polyneuropathy	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Syncope	0	(0.0)	1	(0.1)	1	(0.2)	2	(0.1)
Psychiatric disorders	**0**	**(0.0)**	**2**	**(0.3)**	**1**	**(0.2)**	**3**	**(0.2)**
Anxiety	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Confusional state	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.1)
Insomnia	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Renal and urinary disorders	**2**	**(0.6)**	**5**	**(0.7)**	**2**	**(0.4)**	**9**	**(0.6)**
Renal failure	1	(0.3)	3	(0.4)	0	(0.0)	4	(0.3)
Renal failure acute	0	(0.0)	0	(0.0)	2	(0.4)	2	(0.1)
Renal failure chronic	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Tubulointerstitial nephritis	1	(0.3)	2	(0.3)	0	(0.0)	3	(0.2)
Respiratory, thoracic and mediastinal disorders	**8**	**(2.4)**	**17**	**(2.2)**	**12**	**(2.6)**	**37**	**(2.4)**
Bronchiectasis	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)
Cough	2	(0.6)	1	(0.1)	2	(0.4)	5	(0.3)
Dyspnoea	1	(0.3)	6	(0.8)	2	(0.4)	9	(0.6)
Haemoptysis	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.1)
Laryngeal inflammation	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)
Nasal congestion	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Pleural effusion	1	(0.3)	0	(0.0)	1	(0.2)	2	(0.1)
Pneumonitis	1	(0.3)	6	(0.8)	4	(0.9)	11	(0.7)
Productive cough	0	(0.0)	0	(0.0)	2	(0.4)	2	(0.1)
Pulmonary embolism	0	(0.0)	4	(0.5)	1	(0.2)	5	(0.3)
Pulmonary oedema	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Pulmonary thrombosis	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Respiratory failure	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)

C Confidential

付録 2.7.4-54 休薬に至った有害事象（いずれかの投与群で発現割合 0%超）
001 試験+002 試験+006 試験（APaT 集団）（続き）

	MK-3475 2 mg/kg Q3W		MK-3475 10 mg/kg Q3W		MK-3475 10 mg/kg Q2W		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Skin and subcutaneous tissue disorders	**6**	**(1.8)**	**19**	**(2.5)**	**9**	**(2.0)**	**34**	**(2.2)**
Eczema	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Erythema	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Erythema multiforme	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Lichen planus	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Neutrophilic dermatosis	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)
Night sweats	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Palmar-plantar erythrodysaesthesia syndrome	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)
Penile ulceration	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Pruritus	1	(0.3)	4	(0.5)	1	(0.2)	6	(0.4)
Rash	2	(0.6)	5	(0.7)	3	(0.7)	10	(0.6)
Rash erythematous	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Rash generalised	0	(0.0)	2	(0.3)	1	(0.2)	3	(0.2)
Rash maculo-papular	3	(0.9)	5	(0.7)	2	(0.4)	10	(0.6)
Vitiligo	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Vascular disorders	**0**	**(0.0)**	**2**	**(0.3)**	**2**	**(0.4)**	**4**	**(0.3)**
Aortic stenosis	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Flushing	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Hypertension	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Hypotension	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)

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.
MedDRA preferred terms "Neoplasm Progression", "Malignant Neoplasm Progression" and "Disease Progression" not related to the drug are excluded.
Include all treated subjects in PN001 Part B1, B2, B3, D and all subjects in PN002 treated with Pembrolizumab in the original phase, and all subjects in PN006 treated with Pembrolizumab.
(MK-3475 PN001 Database Cutoff Date: [redacted]
(MK-3475 PN002 Database Cutoff Date: 12MAY2014).
(MK-3475 PN006 Database Cutoff Date: 03SEP2014).

Confidential

付録 2.7.4-55 治験薬の投与中止に至った有害事象（いずれかの投与群で発現割合 0%超）
001 試験+002 試験+006 試験（APaT 集団）

	MK-3475 2 mg/kg Q3W		MK-3475 10 mg/kg Q3W		MK-3475 10 mg/kg Q2W		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	340		769		458		1,567	
with one or more adverse events	28	(8.2)	91	(11.8)	47	(10.3)	166	(10.6)
with no adverse events	312	(91.8)	678	(88.2)	411	(89.7)	1,401	(89.4)
Blood and lymphatic system disorders	**2**	**(0.6)**	**1**	**(0.1)**	**2**	**(0.4)**	**5**	**(0.3)**
Anaemia	1	(0.3)	0	(0.0)	1	(0.2)	2	(0.1)
Haemolytic anaemia	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Thrombocytopenia	1	(0.3)	1	(0.1)	0	(0.0)	2	(0.1)
Cardiac disorders	**0**	**(0.0)**	**4**	**(0.5)**	**4**	**(0.9)**	**8**	**(0.5)**
Acute myocardial infarction	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Atrial fibrillation	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Cardiac arrest	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Cardiac failure	0	(0.0)	1	(0.1)	1	(0.2)	2	(0.1)
Cardiac failure congestive	0	(0.0)	1	(0.1)	1	(0.2)	2	(0.1)
Cardiac ventricular disorder	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Myocardial infarction	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Endocrine disorders	**2**	**(0.6)**	**2**	**(0.3)**	**2**	**(0.4)**	**6**	**(0.4)**
Adrenal insufficiency	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Hyperthyroidism	1	(0.3)	0	(0.0)	1	(0.2)	2	(0.1)
Hypophysitis	2	(0.6)	0	(0.0)	0	(0.0)	2	(0.1)
Hypopituitarism	0	(0.0)	2	(0.3)	0	(0.0)	2	(0.1)
Gastrointestinal disorders	**1**	**(0.3)**	**19**	**(2.5)**	**8**	**(1.7)**	**28**	**(1.8)**
Abdominal distension	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Abdominal pain	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Autoimmune pancreatitis	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Colitis	1	(0.3)	9	(1.2)	3	(0.7)	13	(0.8)
Diarrhoea	0	(0.0)	1	(0.1)	2	(0.4)	3	(0.2)
Enterocolitis	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Gastrointestinal haemorrhage	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Intussusception	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Nausea	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)

C Confidential

付録 2.7.4-55 治験薬の投与中止に至った有害事象（いずれかの投与群で発現割合 0%超）
001 試験+002 試験+006 試験（APaT 集団）（続き）

	MK-3475 2 mg/kg Q3W		MK-3475 10 mg/kg Q3W		MK-3475 10 mg/kg Q2W		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Gastrointestinal disorders	**1**	**(0.3)**	**19**	**(2.5)**	**8**	**(1.7)**	**28**	**(1.8)**
Oesophagitis	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Pancreatitis	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Retroperitoneal haemorrhage	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Salivary gland disorder	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Upper gastrointestinal haemorrhage	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Vomiting	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
General disorders and administration site conditions	**9**	**(2.6)**	**12**	**(1.6)**	**5**	**(1.1)**	**26**	**(1.7)**
Asthenia	1	(0.3)	3	(0.4)	0	(0.0)	4	(0.3)
Death	1	(0.3)	3	(0.4)	2	(0.4)	6	(0.4)
Fatigue	0	(0.0)	1	(0.1)	2	(0.4)	3	(0.2)
Gait disturbance	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)
General physical health deterioration	1	(0.3)	3	(0.4)	1	(0.2)	5	(0.3)
Generalised oedema	3	(0.9)	0	(0.0)	0	(0.0)	3	(0.2)
Oedema	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)
Oedema peripheral	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Pain	1	(0.3)	2	(0.3)	0	(0.0)	3	(0.2)
Hepatobiliary disorders	**2**	**(0.6)**	**5**	**(0.7)**	**3**	**(0.7)**	**10**	**(0.6)**
Autoimmune hepatitis	1	(0.3)	2	(0.3)	1	(0.2)	4	(0.3)
Drug-induced liver injury	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Hepatic failure	1	(0.3)	1	(0.1)	0	(0.0)	2	(0.1)
Hepatic function abnormal	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Hepatitis	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Hyperbilirubinaemia	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Immune system disorders	**0**	**(0.0)**	**2**	**(0.3)**	**1**	**(0.2)**	**3**	**(0.2)**
Anaphylactoid reaction	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Autoimmune disorder	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Drug hypersensitivity	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)

C Confidential

付録 2.7.4-55 治験薬の投与中止に至った有害事象（いずれかの投与群で発現割合 0%超）
001 試験+002 試験+006 試験（APaT 集団）（続き）

	MK-3475 2 mg/kg Q3W		MK-3475 10 mg/kg Q3W		MK-3475 10 mg/kg Q2W		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Infections and infestations	**2**	**(0.6)**	**3**	**(0.4)**	**3**	**(0.7)**	**8**	**(0.5)**
Cellulitis	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Encephalitis	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Infectious pleural effusion	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)
Localised infection	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Lung infection	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Pneumonia	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Septic shock	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)
Soft tissue infection	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Urinary tract infection	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Injury, poisoning and procedural complications	**0**	**(0.0)**	**2**	**(0.3)**	**1**	**(0.2)**	**3**	**(0.2)**
Facial bones fracture	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Wound decomposition	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Wound haemorrhage	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Investigations	**0**	**(0.0)**	**3**	**(0.4)**	**0**	**(0.0)**	**3**	**(0.2)**
Alanine aminotransferase increased	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Gamma-glutamyltransferase increased	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Lipase increased	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Metabolism and nutrition disorders	**3**	**(0.9)**	**4**	**(0.5)**	**5**	**(1.1)**	**12**	**(0.8)**
Cachexia	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)
Cell death	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Decreased appetite	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Failure to thrive	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Gout	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Hypercalcaemia	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)
Hypoalbuminaemia	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Hypoglycaemia	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Hyponatraemia	0	(0.0)	1	(0.1)	1	(0.2)	2	(0.1)
Insulin resistant diabetes	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)

C Confidential

付録 2.7.4-55 治験薬の投与中止に至った有害事象（いずれかの投与群で発現割合 0%超）
001 試験+002 試験+006 試験（APaT 集団）（続き）

	MK-3475 2 mg/kg Q3W		MK-3475 10 mg/kg Q3W		MK-3475 10 mg/kg Q2W		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Metabolism and nutrition disorders	**3**	**(0.9)**	**4**	**(0.5)**	**5**	**(1.1)**	**12**	**(0.8)**
Malnutrition	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Type 1 diabetes mellitus	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Musculoskeletal and connective tissue disorders	**1**	**(0.3)**	**9**	**(1.2)**	**4**	**(0.9)**	**14**	**(0.9)**
Arthralgia	0	(0.0)	3	(0.4)	0	(0.0)	3	(0.2)
Back pain	0	(0.0)	2	(0.3)	1	(0.2)	3	(0.2)
Musculoskeletal pain	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Myopathy	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Myositis	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Neck pain	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)
Pain in extremity	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Rhabdomyolysis	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Sjogren's syndrome	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Tenosynovitis	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**0**	**(0.0)**	**8**	**(1.0)**	**4**	**(0.9)**	**12**	**(0.8)**
Cancer pain	0	(0.0)	1	(0.1)	1	(0.2)	2	(0.1)
Intracranial tumour haemorrhage	0	(0.0)	1	(0.1)	1	(0.2)	2	(0.1)
Lymphangiosis carcinomatosa	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Metastases to central nervous system	0	(0.0)	3	(0.4)	0	(0.0)	3	(0.2)
Metastases to meninges	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Metastatic malignant melanoma	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Tumour necrosis	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Tumour pain	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Nervous system disorders	**4**	**(1.2)**	**7**	**(0.9)**	**7**	**(1.5)**	**18**	**(1.1)**
Brain oedema	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Cerebrovascular accident	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)

C Confidential

付録 2.7.4-55 治験薬の投与中止に至った有害事象（いずれかの投与群で発現割合 0%超）
001 試験+002 試験+006 試験（APaT 集団）（続き）

	MK-3475 2 mg/kg Q3W		MK-3475 10 mg/kg Q3W		MK-3475 10 mg/kg Q2W		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Nervous system disorders	**4**	**(1.2)**	**7**	**(0.9)**	**7**	**(1.5)**	**18**	**(1.1)**
Cognitive disorder	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Convulsion	0	(0.0)	1	(0.1)	1	(0.2)	2	(0.1)
Epilepsy	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Guillain-Barre syndrome	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Haemorrhage intracranial	1	(0.3)	1	(0.1)	0	(0.0)	2	(0.1)
Hemiparesis	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)
Migraine	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Optic neuritis	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Partial seizures	1	(0.3)	0	(0.0)	1	(0.2)	2	(0.1)
Peripheral sensory neuropathy	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Polyneuropathy	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Spinal cord compression	0	(0.0)	1	(0.1)	1	(0.2)	2	(0.1)
Vasogenic cerebral oedema	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Psychiatric disorders	**0**	**(0.0)**	**2**	**(0.3)**	**0**	**(0.0)**	**2**	**(0.1)**
Completed suicide	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Depression	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Renal and urinary disorders	**1**	**(0.3)**	**1**	**(0.1)**	**2**	**(0.4)**	**4**	**(0.3)**
Hydronephrosis	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)
Renal failure	0	(0.0)	1	(0.1)	1	(0.2)	2	(0.1)
Renal failure acute	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Respiratory, thoracic and mediastinal disorders	**1**	**(0.3)**	**13**	**(1.7)**	**5**	**(1.1)**	**19**	**(1.2)**
Cough	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Dyspnoea	0	(0.0)	5	(0.7)	1	(0.2)	6	(0.4)
Interstitial lung disease	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Pleural effusion	0	(0.0)	1	(0.1)	1	(0.2)	2	(0.1)
Pneumonitis	0	(0.0)	5	(0.7)	3	(0.7)	8	(0.5)
Pneumothorax	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Pulmonary embolism	1	(0.3)	1	(0.1)	0	(0.0)	2	(0.1)
Respiratory failure	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)

C Confidential

付録 2.7.4-55 治験薬の投与中止に至った有害事象（いずれかの投与群で発現割合 0%超）
001 試験+002 試験+006 試験（APaT 集団）（続き）

	MK-3475 2 mg/kg Q3W		MK-3475 10 mg/kg Q3W		MK-3475 10 mg/kg Q2W		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Skin and subcutaneous tissue disorders	**1**	**(0.3)**	**2**	**(0.3)**	**1**	**(0.2)**	**4**	**(0.3)**
Psoriasis	0	(0.0)	0	(0.0)	1	(0.2)	1	(0.1)
Skin lesion	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Stevens-Johnson syndrome	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)
Vitiligo	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)

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.
MedDRA preferred terms "Neoplasm Progression", "Malignant Neoplasm Progression" and "Disease Progression" not related to the drug are excluded.
Include all treated subjects in PN001 Part B1, B2, B3, D and all subjects in PN002 treated with Pembrolizumab in the original phase, and all subjects in PN006 treated with Pembrolizumab
(MK-3475 PN001 Database Cutoff Date: [redacted]).
(MK-3475 PN002 Database Cutoff Date: 12MAY2014).
(MK-3475 PN006 Database Cutoff Date: 03SEP2014).

Confidential

付録 2.7.4-56 休薬に至った有害事象（発現割合 0%超）
041 試験（APaT 集団）

	Subjects With Advanced Melanoma	
	n	(%)
Subjects in population	42	
with one or more adverse events	9	(21.4)
with no adverse events	33	(78.6)
Endocrine disorders	**2**	**(4.8)**
Hypophysitis	1	(2.4)
Hypothyroidism	1	(2.4)
Gastrointestinal disorders	**3**	**(7.1)**
Abdominal pain	1	(2.4)
Colitis	2	(4.8)
Diarrhoea	1	(2.4)
Gastritis	1	(2.4)
General disorders and administration site conditions	**1**	**(2.4)**
Influenza like illness	1	(2.4)
Hepatobiliary disorders	**1**	**(2.4)**
Bile duct obstruction	1	(2.4)
Investigations	**2**	**(4.8)**
Alanine aminotransferase increased	1	(2.4)
Aspartate aminotransferase increased	1	(2.4)
Thyroid function test abnormal	1	(2.4)

C Confidential

付録 2.7.4-56 休薬に至った有害事象（発現割合 0%超）
041 試験（APaT 集団）（続き）

	Subjects With Advanced Melanoma	
	n	(%)
Skin and subcutaneous tissue disorders	**1**	**(2.4)**
Drug eruption	1	(2.4)

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.
MedDRA preferred terms "Neoplasm Progression", "Malignant Neoplasm Progression" and "Disease Progression" not related to the drug are excluded.
Adverse event terms are from MedDRA Version 18.0.
(Data Cutoff Date: [redacted].

Data Source: [資料5.3.5.2.3: P041V01]

C Confidential

付録 2.7.4-57 治験薬の投与中止に至った有害事象（発現割合 0%超）

041 試験（APaT 集団）

	Subjects With Advanced Melanoma	
	n	(%)
Subjects in population	42	
with one or more adverse events	6	(14.3)
with no adverse events	36	(85.7)
Endocrine disorders	**1**	**(2.4)**
Hypophysitis	1	(2.4)
General disorders and administration site conditions	**1**	**(2.4)**
Death	1	(2.4)
Infections and infestations	**1**	**(2.4)**
Lung infection	1	(2.4)
Metabolism and nutrition disorders	**2**	**(4.8)**
Hyperglycaemia	1	(2.4)
Marasmus	1	(2.4)
Nervous system disorders	**1**	**(2.4)**
Cerebral haemorrhage	1	(2.4)
Encephalopathy	1	(2.4)
Respiratory, thoracic and mediastinal disorders	**2**	**(4.8)**
Acute respiratory failure	1	(2.4)

C Confidential

付録 2.7.4-57 治験薬の投与中止に至った有害事象（発現割合 0%超）
041 試験（APaT 集団）（続き）

	Subjects With Advanced Melanoma	
	n	(%)
Respiratory, thoracic and mediastinal disorders	**2**	**(4.8)**
Pneumonitis	1	(2.4)

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.
MedDRA preferred terms "Neoplasm Progression", "Malignant Neoplasm Progression" and "Disease Progression" not related to the drug are excluded.
Adverse event terms are from MedDRA Version 18.0.
(Data Cutoff Date: [redacted]

Data Source: [資料5.3.5.2.3: P041V01]

Confidential

付録 2.7.4-58 AEOSI-肺臓炎を発現した患者の一覧

001 試験+002 試験+006 試験（APaT 集団）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 2 mg/kg Q3W										
Trial Number=3475-001, Site Number=0008, Subject ID=000319, Gender=F, Race=White, Age=72 Years, Rel Day of Study Medication Discontinuance†=437										
000319	Treatment Cycle 7	136	Pneumonitis	3.75 Months	Mild	1		Y		Resolved
Trial Number=3475-001, Site Number=0010, Subject ID=000265, Gender=F, Race=White, Age=61 Years, Rel Day of Study Medication Discontinuance†=211										
000265	Treatment Cycle 8	170	Pneumonitis	1.86 Weeks	Severe	3	Y	Y	Interrupted	Resolved
		183	Pneumonitis	4 Weeks	Moderate	2		N	Interrupted	Resolved
	Treatment Cycle 9	211	Pneumonitis	2.57 Weeks	Mild	1		N	N/A	Resolved
	Safety Follow-up	229	Pneumonitis	5.16 Months	Moderate	2	Y	Y	Interrupted	Resolved
Trial Number=3475-001, Site Number=0021, Subject ID=000287, Gender=F, Race=White, Age=59 Years, Rel Day of Study Medication Discontinuance†=										
000287	Treatment Cycle 4	82	Interstitial lung disease	Continuing	Mild	1		Y	N/A	Not Resolved
Trial Number=3475-002, Site Number=0010, Subject ID=101263, Gender=M, Race=White, Age=58 Years, Rel Day of Study Medication Discontinuance†=										
101263	Treatment Cycle 9	170	Pneumonitis	3.57 Weeks		1	N	N	None	Resolved
Trial Number=3475-002, Site Number=0054, Subject ID=100135, Gender=M, Race=White, Age=79 Years, Rel Day of Study Medication Discontinuance†=										
100135	Treatment Cycle 5	125	Pneumonitis	2.79 Months		1	N	N	None	Resolved
Trial Number=3475-002, Site Number=0111, Subject ID=102122, Gender=F, Race=White, Age=75 Years, Rel Day of Study Medication Discontinuance†=113										
102122	Treatment Cycle 4	84	Pneumonitis	Continuing		1	N	Y	None	Not Resolved
MK-3475 10 mg/kg Q3W										

C Confidential

付録 2.7.4-58 AEOSI-肺臓炎を発現した患者の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q3W										
Trial Number=3475-001, Site Number=0001, Subject ID=001240, Gender=F, Race=White, Age=48 Years, Rel Day of Study Medication Discontinuance†=244										
001240	Treatment Cycle 10	195	Pneumonitis	4.14 Weeks	Moderate	2		Y	Interrupted	Resolved
	Treatment Cycle 11	224	Pneumonitis	Continuing	Mild	1		Y	N/A	Not Resolved
Trial Number=3475-001, Site Number=0010, Subject ID=000143, Gender=M, Race=White, Age=77 Years, Rel Day of Study Medication Discontinuance†=										
000143	Treatment Cycle 27	588	Pneumonitis	Continuing	Mild	1		N	Interrupted	Not Resolved
Trial Number=3475-001, Site Number=0011, Subject ID=000171, Gender=F, Race=White, Age=55 Years, Rel Day of Study Medication Discontinuance†=302										
000171	Treatment Cycle 9	169	Pneumonitis	Continuing	Mild	1		Y	N/A	Not Resolved
Trial Number=3475-001, Site Number=0012, Subject ID=000088, Gender=M, Race=White, Age=74 Years, Rel Day of Study Medication Discontinuance†=274										
000088	Treatment Cycle 12	252	Pneumonitis	1.41 Months	Mild	1		Y	N/A	Resolved
	Safety Follow-up	295	Pneumonitis	4.6 Months	Moderate	2		Y	Discontinued	Resolved
Trial Number=3475-001, Site Number=0018, Subject ID=001266, Gender=M, Race=White, Age=37 Years, Rel Day of Study Medication Discontinuance†=										
001266	Treatment Cycle 12	253	Pneumonitis	Continuing	Mild	1		Y	N/A	Not Resolved
Trial Number=3475-001, Site Number=0018, Subject ID=001281, Gender=M, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=										
001281	Treatment Cycle 8	169	Pneumonitis	Continuing	Mild	1		Y	N/A	Not Resolved
Trial Number=3475-001, Site Number=0019, Subject ID=000148, Gender=F, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=										
000148	Treatment Cycle 12	259	Pneumonitis	3.29 Weeks	Mild	1		Y	N/A	Resolved

C Confidential

付録 2.7.4-58 AEOSI-肺臓炎を発現した患者の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q3W										
Trial Number=3475-001, Site Number=0020, Subject ID=000205, Gender=F, Race=White, Age=37 Years, Rel Day of Study Medication Discontinuance†=293										
000205	Safety Follow-up	302	Pneumonitis	1.18 Months	Mild	1		Y	Interrupted	Resolved
Trial Number=3475-001, Site Number=0021, Subject ID=000271, Gender=M, Race=White, Age=61 Years, Rel Day of Study Medication Discontinuance†=										
000271	Treatment Cycle 1	6	Pneumonitis	1.87 Months	Moderate	2		Y	Interrupted	Resolved
	Treatment Cycle 4	62	Pneumonitis	1.41 Months	Mild	1		Y		Resolved
Trial Number=3475-002, Site Number=0010, Subject ID=101857, Gender=M, Race=White, Age=54 Years, Rel Day of Study Medication Discontinuance†=64										
101857	Safety Follow-up	93	Pneumonitis	2 Days		2	Y	Y	Discontinued	Resolved
Trial Number=3475-002, Site Number=0011, Subject ID=100139, Gender=M, Race=White, Age=61 Years, Rel Day of Study Medication Discontinuance†=22										
100139	Safety Follow-up	35	Pneumonitis	3.57 Weeks		3	Y	Y	Discontinued	Resolved
Trial Number=3475-002, Site Number=0032, Subject ID=101271, Gender=F, Race=White, Age=59 Years, Rel Day of Study Medication Discontinuance†=63										
101271	Safety Follow-up	77	Pneumonitis	5 Days		3	Y	Y	Discontinued	Resolved
		82	Pneumonitis	1.58 Months		2	N	N	Discontinued	Resolved
Trial Number=3475-002, Site Number=0180, Subject ID=101272, Gender=F, Race=White, Age=74 Years, Rel Day of Study Medication Discontinuance†=64										
101272	Safety Follow-up	85	Interstitial lung disease	Continuing		3	Y	Y	Discontinued	Resolving
Trial Number=3475-006, Site Number=0007, Subject ID=366702, Gender=M, Race=White, Age=59 Years, Rel Day of Study Medication Discontinuance†=										
366702	Treatment Cycle 12	247	Pneumonitis	2.86 Months		1	N	Y	None	Resolved

C Confidential

付録 2.7.4-58 AEOSI-肺臓炎を発現した患者の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q3W										
Trial Number=3475-006, Site Number=0309, Subject ID=366971, Gender=M, Race=White, Age=79 Years, Rel Day of Study Medication Discontinuance†=1										
366971	Safety Follow-up	29	Pneumonitis	3.88 Months		3	Y	Y	Discontinued	Resolved
Trial Number=3475-006, Site Number=1708, Subject ID=366213, Gender=F, Race=White, Age=67 Years, Rel Day of Study Medication Discontinuance†=309										
366213	Treatment Cycle 8	169	Pneumonitis	4.14 Weeks		2	N	Y	Interrupted	Resolved
Trial Number=3475-006, Site Number=1804, Subject ID=367122, Gender=F, Race=White, Age=89 Years, Rel Day of Study Medication Discontinuance†=190										
367122	Safety Follow-up	209	Pneumonitis	Continuing		2	N	Y	Interrupted	Not Resolved
Trial Number=3475-006, Site Number=1812, Subject ID=362552, Gender=M, Race=White, Age=87 Years, Rel Day of Study Medication Discontinuance†=22										
362552	Safety Follow-up	40	Pneumonitis	Continuing		2	N	N	None	Not Resolved
MK-3475 10 mg/kg Q2W										
Trial Number=3475-001, Site Number=0001, Subject ID=001393, Gender=M, Race=White, Age=55 Years, Rel Day of Study Medication Discontinuance†=71										
001393	Safety Follow-up	83	Pneumonitis	1.57 Weeks	Severe	3	Y	Y	Discontinued	Resolved
Trial Number=3475-001, Site Number=0002, Subject ID=000097, Gender=F, Race=White, Age=62 Years, Rel Day of Study Medication Discontinuance†=										
000097	Treatment Cycle 6	85	Pneumonitis	8.74 Months	Mild	1		Y		Resolved
	Treatment Cycle 21	392	Pneumonitis	2.83 Months	Mild	1		Y	N/A	Resolved
Trial Number=3475-001, Site Number=0003, Subject ID=000066, Gender=M, Race=White, Age=67 Years, Rel Day of Study Medication Discontinuance†=162										

C Confidential

付録 2.7.4-58 AEOSI-肺臓炎を発現した患者の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q2W										
Trial Number=3475-001, Site Number=0003, Subject ID=000066, Gender=M, Race=White, Age=67 Years, Rel Day of Study Medication Discontinuance†=162										
000066	Treatment Cycle 5	71	Pneumonitis	4.14 Weeks	Moderate	2		Y	Interrupted	Resolved
	Treatment Cycle 8	141	Pneumonitis	4.17 Months	Mild	1		Y	Discontinued	Resolved
Trial Number=3475-001, Site Number=0010, Subject ID=000045, Gender=M, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance†=441										
000045	Treatment Cycle 18	252	Pneumonitis	1.84 Months	Moderate	2		Y	Interrupted	Resolved
		308	Pneumonitis	3.71 Months	Mild	1	Y	Y	N/A	Resolved
	Safety Follow-up	463	Pneumonitis	Continuing	Mild	1	Y	Y	Interrupted	Not Resolved
Trial Number=3475-001, Site Number=0010, Subject ID=000051, Gender=M, Race=White, Age=94 Years, Rel Day of Study Medication Discontinuance†=72										
000051	Safety Follow-up	94	Pneumonitis	1 Weeks	Moderate	2		Y	N/A	Resolved
Trial Number=3475-001, Site Number=0015, Subject ID=000038, Gender=F, Race=White, Age=89 Years, Rel Day of Study Medication Discontinuance†=313										
000038	Treatment Cycle 20	291	Pneumonitis	1.14 Weeks	Moderate	2		Y	Interrupted	Resolved
Trial Number=3475-001, Site Number=0021, Subject ID=000076, Gender=M, Race=White, Age=65 Years, Rel Day of Study Medication Discontinuance†=1										
000076	Safety Follow-up	2	Pneumonitis	2.37 Months	Moderate	2		Y	Discontinued	Resolved
Trial Number=3475-006, Site Number=1710, Subject ID=364232, Gender=F, Race=White, Age=34 Years, Rel Day of Study Medication Discontinuance†=121										

C Confidential

付録 2.7.4-58 AEOSI-肺臓炎を発現した患者の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q2W										
Trial Number=3475-006, Site Number=1710, Subject ID=364232, Gender=F, Race=White, Age=34 Years, Rel Day of Study Medication Discontinuance[†]=121										
364232	Treatment Cycle 2	29	Pneumonitis	4.14 Weeks		2	Y	Y	Interrupted	Resolved

[†]Relative Day of Study Medication Discontinuance is defined as the day of the last recorded dose of study medication for the subject relative to the start of study medication.

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.

Grades are based on NCI CTCAE version 4.0.

(MK-3475 PN001 Database Cutoff Date: [redacted].

(MK-3475 PN002 Database Cutoff Date: 12MAY2014).

(MK-3475 PN006 Database Cutoff Date: 03SEP2014).

C Confidential

付録 2.7.4-59 AEOSI-肺臓炎に対する副腎皮質ホルモン剤使用の一覧

001 試験+002 試験+006 試験（APaT 集団）

Subject ID	Med. Start Day	Med. Duration (Days)	Med. Name	Total Daily Dose	Frequency	Route	Prednisone Equiv.† (mg)	Adverse Event for Use	AE Start Day	AE End Day	AE Toxicity Grade
MK-3475 2 mg/kg Q3W											
Trial Number=3475-001, Site Number=0010, Subject ID=000265, Gender=F, Race=White, Age=61 Years, Rel Day of Study Medication Discontinuance‡=211											
000265	182	22	Prednisone	40	QD	Oral Administration	40.00	Pneumonitis	170	182	3
	182	22	Prednisone	40	QD	Oral Administration	40.00	Pneumonitis	183	210	2
	204	2	Prednisone	30	QD	Oral Administration	30.00	Pneumonitis	183	210	2
	206	2	Prednisone	20	QD	Oral Administration	20.00	Pneumonitis	183	210	2
	208	2	Prednisone	10	QD	Oral Administration	10.00	Pneumonitis	183	210	2
	210	1	Prednisone	5	QD	Oral Administration	5.00	Pneumonitis	183	210	2
	229	10	Prednisone	80	QD	Oral Administration	80.00	Pneumonitis	229	385	2
	239	7	Prednisone	70	QD	Oral Administration	70.00	Pneumonitis	229	385	2
	246	8	Prednisone	60	QD	Oral Administration	60.00	Pneumonitis	229	385	2
	254	5	Prednisone	50	QD	Oral Administration	50.00	Pneumonitis	229	385	2
	259	8	Prednisone	40	QD	Oral Administration	40.00	Pneumonitis	229	385	2
	267	16	Prednisone	30	QD	Oral Administration	30.00	Pneumonitis	229	385	2
	283	61	Prednisone	10	QD	Oral Administration	10.00	Pneumonitis	229	385	2
	344	42	Prednisone	20	QD	Oral Administration	20.00	Pneumonitis	229	385	2
MK-3475 10 mg/kg Q3W											

C Confidential

付録 2.7.4-59 AEOSI-肺臓炎に対する副腎皮質ホルモン剤使用の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Med. Start Day	Med. Duration (Days)	Med. Name	Total Daily Dose	Frequency	Route	Prednisone Equiv.† (mg)	Adverse Event for Use	AE Start Day	AE End Day	AE Toxicity Grade
Trial Number=3475-001, Site Number=0001, Subject ID=001240, Gender=F, Race=White, Age=48 Years, Rel Day of Study Medication Discontinuance‡=244											
001240	209	.	Prednisone	10	OTHER	Oral Administration	10.00	Pneumonitis	195	223	2
Trial Number=3475-001, Site Number=0012, Subject ID=000088, Gender=M, Race=White, Age=74 Years, Rel Day of Study Medication Discontinuance‡=274											
000088	337	34	Prednisone	60	BID	Oral Administration	60.00	Pneumonitis	295	434	2
	371	21	Prednisone	40	BID	Oral Administration	40.00	Pneumonitis	295	434	2
	392	43	Prednisone	20	BID	Oral Administration	20.00	Pneumonitis	295	434	2
	435	34	Prednisone	4.285	3 TIMES PER WEEK	Oral Administration	4.29	Pneumonitis	295	434	2
Trial Number=3475-002, Site Number=0010, Subject ID=101857, Gender=M, Race=White, Age=54 Years, Rel Day of Study Medication Discontinuance‡=64											
101857	93	14	Prednisone	70	QD	Oral	70.00	Pneumonitis	93	94	2
	107	3	Prednisone	60	QD	Oral	60.00	Pneumonitis	93	94	2
	110	3	Prednisone	50	QD	Oral	50.00	Pneumonitis	93	94	2
	113	3	Prednisone	40	QD	Oral	40.00	Pneumonitis	93	94	2
	116	3	Prednisone	30	QD	Oral	30.00	Pneumonitis	93	94	2
	119	3	Prednisone	20	QD	Oral	20.00	Pneumonitis	93	94	2
	122	3	Prednisone	10	QD	Oral	10.00	Pneumonitis	93	94	2
Trial Number=3475-002, Site Number=0011, Subject ID=100139, Gender=M, Race=White, Age=61 Years, Rel Day of Study Medication Discontinuance‡=22											
100139	45	12	Prednisone	60	QD	Oral	60.00	Pneumonitis	35	59	3

C Confidential

付録 2.7.4-59 AEOSI-肺臓炎に対する副腎皮質ホルモン剤使用の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Med. Start Day	Med. Duration (Days)	Med. Name	Total Daily Dose	Frequency	Route	Prednisone Equiv.† (mg)	Adverse Event for Use	AE Start Day	AE End Day	AE Toxicity Grade
	57	.	Prednisone	20	QD	Oral	20.00	Pneumonitis	35	59	3
Trial Number=3475-002, Site Number=0032, Subject ID=101271, Gender=F, Race=White, Age=59 Years, Rel Day of Study Medication Discontinuance‡=63											
101271	77	1	Methylprednisolone Sodium Succinate	25	ONCE	Intravenous	31.25	Pneumonitis	77	81	3
	77	1	Methylprednisolone Sodium Succinate	25	ONCE	Intravenous	31.25	Pneumonitis	82	129	2
	81	7	Prednisone	100	QD	Oral	100.00	Pneumonitis	77	81	3
	81	7	Prednisone	100	QD	Oral	100.00	Pneumonitis	82	129	2
	88	7	Prednisone	80	QD	Oral	80.00	Pneumonitis	77	81	3
	88	7	Prednisone	80	QD	Oral	80.00	Pneumonitis	82	129	2
	95	7	Prednisone	60	QD	Oral	60.00	Pneumonitis	77	81	3
	95	7	Prednisone	60	QD	Oral	60.00	Pneumonitis	82	129	2
Trial Number=3475-006, Site Number=0309, Subject ID=366971, Gender=M, Race=White, Age=79 Years, Rel Day of Study Medication Discontinuance‡=1											
366971	29	1	Dexamethasone	20	OTHER	Oral	133.40	Pneumonitis	29	146	3
	30	1	Dexamethasone	20	QID	Oral	133.40	Pneumonitis	29	146	3
Trial Number=3475-006, Site Number=1708, Subject ID=366213, Gender=F, Race=White, Age=67 Years, Rel Day of Study Medication Discontinuance‡=309											
366213	172	5	Prednisolone	40	QD	Oral	40.00	Pneumonitis	169	197	2
	177	7	Prednisolone	50	QD	Oral	50.00	Pneumonitis	169	197	2
	184	7	Prednisolone	30	QD	Oral	30.00	Pneumonitis	169	197	2

C Confidential

付録 2.7.4-59 AEOSI-肺臓炎に対する副腎皮質ホルモン剤使用の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Med. Start Day	Med. Duration (Days)	Med. Name	Total Daily Dose	Frequency	Route	Prednisone Equiv.† (mg)	Adverse Event for Use	AE Start Day	AE End Day	AE Toxicity Grade
	191	13	Prednisolone	10	QD	Oral	10.00	Pneumonitis	169	197	2
MK-3475 10 mg/kg Q2W											
Trial Number=3475-001, Site Number=0010, Subject ID=000045, Gender=M, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance‡=441											
000045	281	3	Prednisone	60	QD	Oral Administration	60.00	Pneumonitis	252	307	2
	284	3	Prednisone	40	QD	Oral Administration	40.00	Pneumonitis	252	307	2
	287	3	Prednisone	30	QD	Oral Administration	30.00	Pneumonitis	252	307	2
	290	3	Prednisone	20	QD	Oral Administration	20.00	Pneumonitis	252	307	2
	293	8	Prednisone	10	QD	Oral Administration	10.00	Pneumonitis	252	307	2
	301	7	Prednisone	5	QD	Oral Administration	5.00	Pneumonitis	252	307	2
Trial Number=3475-001, Site Number=0015, Subject ID=000038, Gender=F, Race=White, Age=89 Years, Rel Day of Study Medication Discontinuance‡=313											
000038	292	1	Dexamethasone	10	ONCE	Oral Administration	66.70	Pneumonitis	291	298	2
	292	3	Prednisone	40	ONCE	Oral Administration	40.00	Pneumonitis	291	298	2
	295	2	Prednisone	20	QD	Oral Administration	20.00	Pneumonitis	291	298	2
	297	2	Prednisone	10	QD	Oral Administration	10.00	Pneumonitis	291	298	2
Trial Number=3475-001, Site Number=0021, Subject ID=000076, Gender=M, Race=White, Age=65 Years, Rel Day of Study Medication Discontinuance‡=1											
000076	41	33	Prednisone	30	QD	Oral Administration	30.00	Pneumonitis	2	73	2
Trial Number=3475-006, Site Number=1710, Subject ID=364232, Gender=F, Race=White, Age=34 Years, Rel Day of Study Medication Discontinuance‡=121											

C Confidential

付録 2.7.4-59 AEOSI-肺臓炎に対する副腎皮質ホルモン剤使用の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Med. Start Day	Med. Duration (Days)	Med. Name	Total Daily Dose	Frequency	Route	Prednisone Equiv.† (mg)	Adverse Event for Use	AE Start Day	AE End Day	AE Toxicity Grade
364232	78	4	Dexamethasone	6	QD	Oral	40.02	Pneumonitis	29	57	2
	29	8	Hydrocortisone	800	QID	Intravenous	200.00	Pneumonitis	29	57	2
	38	5	Prednisolone	40	QD	Oral	40.00	Pneumonitis	29	57	2
	43	7	Prednisolone	20	QD	Oral	20.00	Pneumonitis	29	57	2
	50	7	Prednisolone	10	QD	Oral	10.00	Pneumonitis	29	57	2
	57	6	Prednisolone	5	QD	Oral	5.00	Pneumonitis	29	57	2

Med.: Medication.
Equiv.: Equivalent.
AE: Adverse Event.
†: Prednisone equivalent total daily dose.
‡Relative Day of Study Medication Discontinuance is defined as the day of the last recorded dose of study medication for the subject relative to the start of study medication.
AE start date is defined as the start day of the adverse event for the subject relative to the start of study medication.
Grades are based on NCI CTCAE version 4.0.
(MK-3475 PN001 Database Cutoff Date: [redacted]).
(MK-3475 PN002 Database Cutoff Date: 12MAY2014).
(MK-3475 PN006 Database Cutoff Date: 03SEP2014).

C Confidential