付録 2.7.4-40 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 試験パート B3（APaT 集団）

	MK-3475 10 mg/kg Q3W		MK-3475 10 mg/kg Q2W		Total	
	n	(%)	n	(%)	n	(%)
Patients in population	121		123		244	
with one or more adverse events	21	(17.4)	29	(23.6)	50	(20.5)
with no adverse events	100	(82.6)	94	(76.4)	194	(79.5)
Blood and lymphatic system disorders	**1**	**(0.8)**	**1**	**(0.8)**	**2**	**(0.8)**
Anaemia	0	(0.0)	1	(0.8)	1	(0.4)
Thrombocytopenia	1	(0.8)	0	(0.0)	1	(0.4)
Endocrine disorders	**2**	**(1.7)**	**1**	**(0.8)**	**3**	**(1.2)**
Hyperthyroidism	1	(0.8)	1	(0.8)	2	(0.8)
Hypothyroidism	1	(0.8)	0	(0.0)	1	(0.4)
Eye disorders	**1**	**(0.8)**	**1**	**(0.8)**	**2**	**(0.8)**
Retinal tear	0	(0.0)	1	(0.8)	1	(0.4)
Vision blurred	1	(0.8)	0	(0.0)	1	(0.4)
Gastrointestinal disorders	**4**	**(3.3)**	**6**	**(4.9)**	**10**	**(4.1)**
Abdominal pain	1	(0.8)	0	(0.0)	1	(0.4)
Colitis	1	(0.8)	2	(1.6)	3	(1.2)
Diarrhoea	1	(0.8)	2	(1.6)	3	(1.2)
Dry mouth	1	(0.8)	0	(0.0)	1	(0.4)
Glossitis	1	(0.8)	0	(0.0)	1	(0.4)
Nausea	1	(0.8)	2	(1.6)	3	(1.2)
Vomiting	1	(0.8)	2	(1.6)	3	(1.2)
General disorders and administration site conditions	**2**	**(1.7)**	**5**	**(4.1)**	**7**	**(2.9)**
Asthenia	0	(0.0)	1	(0.8)	1	(0.4)
Chest discomfort	0	(0.0)	1	(0.8)	1	(0.4)
Fatigue	0	(0.0)	2	(1.6)	2	(0.8)
Inflammation	0	(0.0)	1	(0.8)	1	(0.4)
Mucosal inflammation	1	(0.8)	0	(0.0)	1	(0.4)
Oedema peripheral	1	(0.8)	1	(0.8)	2	(0.8)
Pain	0	(0.0)	1	(0.8)	1	(0.4)
Hepatobiliary disorders	**1**	**(0.8)**	**0**	**(0.0)**	**1**	**(0.4)**
Autoimmune hepatitis	1	(0.8)	0	(0.0)	1	(0.4)
Infections and infestations	**1**	**(0.8)**	**7**	**(5.7)**	**8**	**(3.3)**
Pneumonia	0	(0.0)	2	(1.6)	2	(0.8)

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付録 2.7.4-40 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 試験パート B3（APaT 集団）（続き）

	MK-3475 10 mg/kg Q3W		MK-3475 10 mg/kg Q2W		Total	
	n	(%)	n	(%)	n	(%)
Infections and infestations	**1**	**(0.8)**	**7**	**(5.7)**	**8**	**(3.3)**
Sepsis	0	(0.0)	1	(0.8)	1	(0.4)
Upper respiratory tract infection	0	(0.0)	3	(2.4)	3	(1.2)
Urinary tract infection	1	(0.8)	2	(1.6)	3	(1.2)
Injury, poisoning and procedural complications	**2**	**(1.7)**	**1**	**(0.8)**	**3**	**(1.2)**
Infusion related reaction	2	(1.7)	1	(0.8)	3	(1.2)
Investigations	**2**	**(1.7)**	**2**	**(1.6)**	**4**	**(1.6)**
Alanine aminotransferase increased	1	(0.8)	1	(0.8)	2	(0.8)
Aspartate aminotransferase increased	0	(0.0)	1	(0.8)	1	(0.4)
Blood alkaline phosphatase increased	0	(0.0)	1	(0.8)	1	(0.4)
Blood creatinine increased	1	(0.8)	0	(0.0)	1	(0.4)
Transaminases increased	0	(0.0)	1	(0.8)	1	(0.4)
Metabolism and nutrition disorders	**2**	**(1.7)**	**4**	**(3.3)**	**6**	**(2.5)**
Dehydration	0	(0.0)	1	(0.8)	1	(0.4)
Failure to thrive	0	(0.0)	1	(0.8)	1	(0.4)
Hypokalaemia	1	(0.8)	0	(0.0)	1	(0.4)
Hyponatraemia	1	(0.8)	3	(2.4)	4	(1.6)
Musculoskeletal and connective tissue disorders	**1**	**(0.8)**	**5**	**(4.1)**	**6**	**(2.5)**
Arthralgia	1	(0.8)	2	(1.6)	3	(1.2)
Back pain	0	(0.0)	1	(0.8)	1	(0.4)
Muscle spasms	0	(0.0)	1	(0.8)	1	(0.4)
Myalgia	1	(0.8)	0	(0.0)	1	(0.4)
Polyarthritis	0	(0.0)	1	(0.8)	1	(0.4)
Nervous system disorders	**2**	**(1.7)**	**1**	**(0.8)**	**3**	**(1.2)**
Cerebrovascular accident	1	(0.8)	0	(0.0)	1	(0.4)
Neuropathy peripheral	1	(0.8)	0	(0.0)	1	(0.4)
Syncope	0	(0.0)	1	(0.8)	1	(0.4)
Renal and urinary disorders	**0**	**(0.0)**	**1**	**(0.8)**	**1**	**(0.4)**
Renal failure acute	0	(0.0)	1	(0.8)	1	(0.4)

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付録 2.7.4-40 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 試験パート B3（APaT 集団）（続き）

	MK-3475 10 mg/kg Q3W		MK-3475 10 mg/kg Q2W		Total	
	n	(%)	n	(%)	n	(%)
Respiratory, thoracic and mediastinal disorders	**1**	**(0.8)**	**2**	**(1.6)**	**3**	**(1.2)**
Cough	0	(0.0)	1	(0.8)	1	(0.4)
Dyspnoea	0	(0.0)	1	(0.8)	1	(0.4)
Pneumonitis	1	(0.8)	0	(0.0)	1	(0.4)
Skin and subcutaneous tissue disorders	**3**	**(2.5)**	**1**	**(0.8)**	**4**	**(1.6)**
Rash	1	(0.8)	0	(0.0)	1	(0.4)
Rash generalised	1	(0.8)	0	(0.0)	1	(0.4)
Rash maculo-papular	1	(0.8)	1	(0.8)	2	(0.8)
Vascular disorders	**0**	**(0.0)**	**1**	**(0.8)**	**1**	**(0.4)**
Hypotension	0	(0.0)	1	(0.8)	1	(0.4)

Every patient 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' not related to the drug is excluded.
(Database Cutoff Date: [redacted]

Data Source: [資料5.3.5.2.1.2: P001V02]

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付録 2.7.4-41 休薬に至った有害事象の一覧

001 試験パート B3（APaT 集団）

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
Trial Number=3475-001, Site Number=0001, Subject ID=001248, Gender=F, Race=White, Age=74 Years, Rel Day of Study Medication Discontinuance†=										
001248	Treatment Cycle 6	127	Blood creatinine increased	1.14 Weeks	Moderate	2		Y	Interrupted	Resolved
Trial Number=3475-001, Site Number=0001, Subject ID=001436, Gender=M, Race=White, Age=65 Years, Rel Day of Study Medication Discontinuance†=										
001436	Treatment Cycle 5	106	Hypothyroidism	Continuing	Moderate	2		Y	Interrupted	Not Resolved
Trial Number=3475-001, Site Number=0008, Subject ID=001295, Gender=F, Race=White, Age=56 Years, Rel Day of Study Medication Discontinuance†=22										
001295	Safety Follow-up	43	Alanine aminotransferase increased	Continuing	Severe	3		N	Interrupted	Not Resolved
Trial Number=3475-001, Site Number=0010, Subject ID=001217, Gender=F, Race=White, Age=86 Years, Rel Day of Study Medication Discontinuance†=168										
001217	Treatment Cycle 4	67	Cerebrovascular accident	1 Days	Severe	3	Y	N	Interrupted	Resolved
	Treatment Cycle 6	147	Urinary tract infection	4 Days	Severe	3	Y	N	Interrupted	Resolved
Trial Number=3475-001, Site Number=0011, Subject ID=001327, Gender=M, Race=White, Age=67 Years, Rel Day of Study Medication Discontinuance†=141										
001327	Treatment Cycle 2	31	Vision blurred	2.46 Months	Moderate	2		Y	Interrupted	Resolved
	Treatment Cycle 3	80	Colitis	Continuing	Mild	1	Y	N	Interrupted	Not Resolved
		92	Nausea	Continuing	Moderate	2	Y	N	Interrupted	Not Resolved
		92	Vomiting	3 Days	Moderate	2	Y	N	Interrupted	Resolved
	Treatment Cycle 4	119	Hypokalaemia	3 Days	Severe	3	Y	N	Interrupted	Resolved

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付録 2.7.4-41 休薬に至った有害事象の一覧

001 試験パート B3（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=0011, Subject ID=001358, Gender=F, Race=White, Age=60 Years, Rel Day of Study Medication Discontinuance†=43										
001358	Safety Follow-up	48	Oedema peripheral	Continuing	Moderate	2		N	Interrupted	Not Resolved
Trial Number=3475-001, Site Number=0011, Subject ID=001372, Gender=M, Race=White, Age=53 Years, Rel Day of Study Medication Discontinuance†=208										
001372	Treatment Cycle 1	1	Infusion related reaction	1 Days	Mild	1		Y	Interrupted	Resolved
Trial Number=3475-001, Site Number=0011, Subject ID=001383, Gender=M, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=176										
001383	Treatment Cycle 1	8	Rash maculo-papular	2.57 Weeks	Moderate	2		Y	Interrupted	Resolved
Trial Number=3475-001, Site Number=0011, Subject ID=001441, Gender=F, Race=White, Age=68 Years, Rel Day of Study Medication Discontinuance†=										
001441	Treatment Cycle 7	148	Neuropathy peripheral	3.14 Weeks	Moderate	2		Y	Interrupted	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 11	247	Hyponatraemia	2 Days	Severe	3		Y	Interrupted	Resolved
Trial Number=3475-001, Site Number=0018, Subject ID=001385, Gender=M, Race=White, Age=81 Years, Rel Day of Study Medication Discontinuance†=										
001385	Treatment Cycle 2	20	Arthralgia	7.62 Months	Mild	1		Y	Interrupted	Resolved
		20	Myalgia	7.62 Months	Mild	1		Y	Interrupted	Resolved
Trial Number=3475-001, Site Number=0018, Subject ID=001410, Gender=F, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance†=63										
001410	Treatment Cycle 2	33	Rash generalised	1.14 Weeks	Severe	3		Y	Interrupted	Resolved
		41	Rash generalised	2 Weeks	Moderate	2		Y	Interrupted	Resolved

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付録 2.7.4-41 休薬に至った有害事象の一覧

001 試験パート B3（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=0019, Subject ID=001251, Gender=M, Race=White, Age=71 Years, Rel Day of Study Medication Discontinuance†=363										
001251	Treatment Cycle 8	161	Dry mouth	2.27 Months	Moderate	2		Y	Interrupted	Resolved
		161	Glossitis	2.27 Months	Moderate	2		Y	Interrupted	Resolved
	Treatment Cycle 11	250	Mucosal inflammation	3.14 Weeks	Moderate	2		Y	Interrupted	Resolved
Trial Number=3475-001, Site Number=0020, Subject ID=001257, Gender=M, Race=White, Age=75 Years, Rel Day of Study Medication Discontinuance†=379										
001257	Treatment Cycle 12	246	Rash	1.86 Weeks	Moderate	2		Y	Interrupted	Resolved
Trial Number=3475-001, Site Number=0020, Subject ID=001320, Gender=F, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=										
001320	Treatment Cycle 1	22	Thrombocytopenia	2 Days	Moderate	2	Y	Y	Interrupted	Resolved
Trial Number=3475-001, Site Number=0020, Subject ID=001417, Gender=M, Race=White, Age=59 Years, Rel Day of Study Medication Discontinuance†=43										
001417	Treatment Cycle 1	8	Diarrhoea	2 Days	Moderate	2		Y	Interrupted	Resolved
Trial Number=3475-001, Site Number=0020, Subject ID=001439, Gender=M, Race=White, Age=82 Years, Rel Day of Study Medication Discontinuance†=20										
001439	Safety Follow-up	22	Autoimmune hepatitis	2.2 Months	Moderate	2		Y	Interrupted	Resolved
Trial Number=3475-001, Site Number=0021, Subject ID=001408, Gender=M, Race=White, Age=38 Years, Rel Day of Study Medication Discontinuance†=										
001408	Treatment Cycle 9	176	Abdominal pain	2.14 Weeks	Mild	1		Y	Interrupted	Resolved
Trial Number=3475-001, Site Number=0021, Subject ID=001412, Gender=M, Race=White, Age=57 Years, Rel Day of Study Medication Discontinuance†=										
001412	Treatment Cycle 2	37	Hyperthyroidism	4 Weeks	Severe	3	Y	Y	Interrupted	Resolved

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付録 2.7.4-41 休薬に至った有害事象の一覧

001 試験パート B3（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=0023, Subject ID=001345, Gender=F, Race=White, Age=45 Years, Rel Day of Study Medication Discontinuance†=148										
001345	Treatment Cycle 2	22	Infusion related reaction	1 Days	Moderate	2		Y	Interrupted	Resolved
MK-3475 10 mg/kg Q2W										
Trial Number=3475-001, Site Number=0001, Subject ID=001209, Gender=M, Race=White, Age=69 Years, Rel Day of Study Medication Discontinuance†=										
001209	Treatment Cycle 13	182	Hyponatraemia	4 Days	Severe	3	Y	Y	Interrupted	Resolved
	Treatment Cycle 19	282	Dyspnoea	Continuing	Mild	1		N	Interrupted	Not Resolved
Trial Number=3475-001, Site Number=0001, Subject ID=001218, Gender=M, Race=White, Age=47 Years, Rel Day of Study Medication Discontinuance†=183										
001218	Treatment Cycle 7	103	Colitis	4 Weeks	Moderate	2		Y	Interrupted	Resolved
	Treatment Cycle 9	161	Inflammation	2.14 Weeks	Moderate	2		N	Interrupted	Resolved
		161	Oedema peripheral	2.29 Weeks	Moderate	2		N	Interrupted	Resolved
Trial Number=3475-001, Site Number=0001, Subject ID=001238, Gender=M, Race=White, Age=36 Years, Rel Day of Study Medication Discontinuance†=155										
001238	Treatment Cycle 2	15	Back pain	1 Days	Moderate	2		Y	Interrupted	Resolved
Trial Number=3475-001, Site Number=0002, Subject ID=001234, Gender=M, Race=White, Age=82 Years, Rel Day of Study Medication Discontinuance†=42										
001234	Treatment Cycle 2	15	Muscle spasms	1 Days	Mild	1		Y	Interrupted	Resolved
Trial Number=3475-001, Site Number=0008, Subject ID=001303, Gender=F, Race=White, Age=79 Years, Rel Day of Study Medication Discontinuance†=										
001303	Treatment Cycle 17	229	Upper respiratory tract infection	1.57 Weeks	Severe	3	Y	N	Interrupted	Resolved

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付録 2.7.4-41 休薬に至った有害事象の一覧

001 試験パート B3（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=0008, Subject ID=001305, Gender=F, Race=White, Age=62 Years, Rel Day of Study Medication Discontinuance†=1										
001305	Safety Follow-up	13	Urinary tract infection	3 Days	Severe	3	Y	N	Interrupted	Resolved
Trial Number=3475-001, Site Number=0008, Subject ID=001321, Gender=M, Race=White, Age=78 Years, Rel Day of Study Medication Discontinuance†=										
001321	Treatment Cycle 12	161	Anaemia	1.14 Weeks	Severe	4	Y	N	Interrupted	Resolved
Trial Number=3475-001, Site Number=0010, Subject ID=001201, Gender=M, Race=Asian, Age=74 Years, Rel Day of Study Medication Discontinuance†=										
001201	Treatment Cycle 3	39	Pneumonia	2.43 Weeks	Severe	3	Y	N	Interrupted	Resolved
		44	Renal failure acute	1.71 Weeks	Severe	3	Y	N	Interrupted	Resolved
		44	Sepsis	1.71 Weeks	Severe	3	Y	N	Interrupted	Resolved
		56	Pneumonia	2.29 Weeks	Moderate	2		N	Interrupted	Resolved
	Treatment Cycle 23	343	Hyperthyroidism	2.56 Months	Moderate	2		Y	Interrupted	Resolved
Trial Number=3475-001, Site Number=0010, Subject ID=001215, Gender=F, Race=White, Age=56 Years, Rel Day of Study Medication Discontinuance†=29										
001215	Safety Follow-up	36	Cough	1.22 Months	Severe	3	Y	Y	Interrupted	Resolved
		36	Dehydration	1.22 Months	Severe	3	Y	Y	Interrupted	Resolved
		36	Failure to thrive	1.22 Months	Severe	3	Y	Y	Interrupted	Resolved
Trial Number=3475-001, Site Number=0010, Subject ID=001277, Gender=M, Race=White, Age=52 Years, Rel Day of Study Medication Discontinuance†=14										
001277	Treatment Cycle 1	3	Fatigue	Continuing	Moderate	2		Y	Interrupted	Not Resolved
	Safety Follow-up	29	Nausea	Continuing	Moderate	2		Y	Interrupted	Not Resolved
		29	Vomiting	Continuing	Moderate	2		Y	Interrupted	Not Resolved

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付録 2.7.4-41 休薬に至った有害事象の一覧

001 試験パート B3（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=0010, Subject ID=001328, Gender=M, Race=White, Age=67 Years, Rel Day of Study Medication Discontinuance†=153										
001328	Safety Follow-up	179	Syncope	3 Days	Severe	3	Y	N	Interrupted	Resolved
Trial Number=3475-001, Site Number=0011, Subject ID=001340, Gender=M, Race=White, Age=62 Years, Rel Day of Study Medication Discontinuance†=83										
001340	Safety Follow-up	95	Colitis	1.45 Months	Severe	3	Y	Y	Interrupted	Resolved
Trial Number=3475-001, Site Number=0011, Subject ID=001397, Gender=F, Race=White, Age=57 Years, Rel Day of Study Medication Discontinuance†=										
001397	Treatment Cycle 1	15	Rash maculo-papular	1.14 Weeks	Moderate	2		Y	Interrupted	Resolved
Trial Number=3475-001, Site Number=0011, Subject ID=001451, Gender=M, Race=White, Age=28 Years, Rel Day of Study Medication Discontinuance†=										
001451	Treatment Cycle 13	182	Diarrhoea	2 Days	Severe	3	Y	N	Interrupted	Resolved
Trial Number=3475-001, Site Number=0015, Subject ID=001267, Gender=M, Race=White, Age=50 Years, Rel Day of Study Medication Discontinuance†=										
001267	Treatment Cycle 13	186	Alanine aminotransferase increased	2.57 Weeks	Mild	1		N	Interrupted	Resolved
		186	Aspartate aminotransferase increased	2.57 Weeks	Mild	1		N	Interrupted	Resolved
		186	Blood alkaline phosphatase increased	2.57 Weeks	Severe	3		N	Interrupted	Resolved
		195	Hypotension	1.29 Weeks	Severe	3	Y	N	Interrupted	Resolved
Trial Number=3475-001, Site Number=0015, Subject ID=001285, Gender=M, Race=White, Age=38 Years, Rel Day of Study Medication Discontinuance†=										
001285	Treatment Cycle 9	125	Diarrhoea	3 Days	Moderate	2	Y	Y	Interrupted	Resolved

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付録 2.7.4-41 休薬に至った有害事象の一覧

001 試験パート B3（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=0015, Subject ID=001285, Gender=M, Race=White, Age=38 Years, Rel Day of Study Medication Discontinuance†=										
001285	Treatment Cycle 9	131	Diarrhoea	1.71 Weeks	Moderate	2		Y	Interrupted	Resolved
Trial Number=3475-001, Site Number=0018, Subject ID=001227, Gender=M, Race=White, Age=53 Years, Rel Day of Study Medication Discontinuance†=										
001227	Treatment Cycle 16	228	Pneumonia	2 Weeks	Severe	3	Y	N	Interrupted	Resolved
Trial Number=3475-001, Site Number=0018, Subject ID=001308, Gender=F, Race=White, Age=38 Years, Rel Day of Study Medication Discontinuance†=165										
001308	Treatment Cycle 2	13	Arthralgia	1.38 Months	Moderate	2		Y	Interrupted	Resolved
Trial Number=3475-001, Site Number=0018, Subject ID=001325, Gender=M, Race=White, Age=84 Years, Rel Day of Study Medication Discontinuance†=71										
001325	Treatment Cycle 1	15	Hyponatraemia	1.14 Weeks	Severe	3		N	Interrupted	Resolved
Trial Number=3475-001, Site Number=0018, Subject ID=001398, Gender=M, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance†=										
001398	Treatment Cycle 7	98	Pain	1 Days	Severe	3		Y	Interrupted	Resolved
	Treatment Cycle 10	140	Arthralgia	4.14 Weeks	Moderate	2		Y	Interrupted	Resolved
		140	Pain	4.14 Weeks	Severe	3		Y	Interrupted	Resolved
		141	Asthenia	3 Days	Severe	3	Y	Y	Interrupted	Resolved
		141	Nausea	3 Days	Severe	3	Y	Y	Interrupted	Resolved
		141	Vomiting	3 Days	Severe	3	Y	Y	Interrupted	Resolved
		144	Asthenia	3.57 Weeks	Moderate	2		Y	Interrupted	Resolved
Trial Number=3475-001, Site Number=0018, Subject ID=001432, Gender=M, Race=White, Age=75 Years, Rel Day of Study Medication Discontinuance†=44										
001432	Safety Follow-up	58	Hyponatraemia	Continuing	Severe	3		N	Interrupted	Not Resolved

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付録 2.7.4-41 休薬に至った有害事象の一覧

001 試験パート B3（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=0019, Subject ID=001291, Gender=F, Race=White, Age=67 Years, Rel Day of Study Medication Discontinuance†=										
001291	Treatment Cycle 1	9	Upper respiratory tract infection	4 Weeks	Mild	1		N	Interrupted	Resolved
Trial Number=3475-001, Site Number=0020, Subject ID=001239, Gender=M, Race=White, Age=78 Years, Rel Day of Study Medication Discontinuance†=										
001239	Treatment Cycle 14	190	Retinal tear	1.05 Months	Moderate	2		N	Interrupted	Resolved
	Treatment Cycle 21	307	Upper respiratory tract infection	2.14 Months	Moderate	2		N	Interrupted	Resolved
Trial Number=3475-001, Site Number=0020, Subject ID=001322, Gender=M, Race=White, Age=29 Years, Rel Day of Study Medication Discontinuance†=										
001322	Treatment Cycle 21	295	Transaminases increased	4.14 Weeks	Mild	1		Y	Interrupted	Resolved
Trial Number=3475-001, Site Number=0020, Subject ID=001377, Gender=M, Race=White, Age=35 Years, Rel Day of Study Medication Discontinuance†=182										
001377	Treatment Cycle 10	151	Polyarthritis	1.43 Weeks	Mild	1	Y	Y	Interrupted	Resolved
Trial Number=3475-001, Site Number=0020, Subject ID=001433, Gender=M, Race=White, Age=74 Years, Rel Day of Study Medication Discontinuance†=35										
001433	Treatment Cycle 2	28	Urinary tract infection	Continuing	Moderate	2		Y	Interrupted	Not Resolved
Trial Number=3475-001, Site Number=0021, Subject ID=001423, Gender=M, Race=White, Age=52 Years, Rel Day of Study Medication Discontinuance†=71										
001423	Treatment Cycle 5	58	Chest discomfort	1 Days	Moderate	2		Y	Interrupted	Resolved
Trial Number=3475-001, Site Number=0023, Subject ID=001306, Gender=F, Race=White, Age=52 Years, Rel Day of Study Medication Discontinuance†=210										
001306	Treatment Cycle 2	14	Infusion related reaction	1 Days	Moderate	2		Y	Interrupted	Resolved
Trial Number=3475-001, Site Number=0030, Subject ID=001207, Gender=M, Race=White, Age=82 Years, Rel Day of Study Medication Discontinuance†=154										

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付録 2.7.4-41 休薬に至った有害事象の一覧

001 試験パート B3（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=0030, Subject ID=001207, Gender=M, Race=White, Age=82 Years, Rel Day of Study Medication Discontinuance†=154										
001207	Safety Follow-up	168	Fatigue	Continuing	Severe	3		Y	Interrupted	Not Resolved

†Relative Day of Study Medication Discontinuance is defined as the day of the last recorded dose of study medication for the patient 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' not related to the drug is excluded.

(Database Cutoff Date: [redacted]

Data Source: [資料5.3.5.2.1.2: P001V02]

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付録 2.7.4-42 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 試験パート B2+D（APaT 集団）

	Ipi-naïve 2 mg/kg Q3W		Ipi-naïve 10 mg/kg Q3W		Ipi-exposed 2 mg/kg Q3W		Ipi-exposed 10 mg/kg Q3W	
	n	(%)	n	(%)	n	(%)	n	(%)
Patients in population	51		52		89		84	
with one or more adverse events	2	(3.9)	5	(9.6)	5	(5.6)	10	(11.9)
with no adverse events	49	(96.1)	47	(90.4)	84	(94.4)	74	(88.1)
Blood and lymphatic system disorders	**1**	**(2.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**
Thrombocytopenia	1	(2.0)	0	(0.0)	0	(0.0)	0	(0.0)
Endocrine disorders	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(1.1)**	**0**	**(0.0)**
Hyperthyroidism	0	(0.0)	0	(0.0)	1	(1.1)	0	(0.0)
Hypophysitis	0	(0.0)	0	(0.0)	1	(1.1)	0	(0.0)
Gastrointestinal disorders	**0**	**(0.0)**	**2**	**(3.8)**	**0**	**(0.0)**	**2**	**(2.4)**
Abdominal pain	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.2)
Colitis	0	(0.0)	1	(1.9)	0	(0.0)	0	(0.0)
Pancreatitis	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.2)
Retroperitoneal haemorrhage	0	(0.0)	1	(1.9)	0	(0.0)	0	(0.0)
General disorders and administration site conditions	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(1.1)**	**1**	**(1.2)**
Gait disturbance	0	(0.0)	0	(0.0)	1	(1.1)	0	(0.0)
Pain	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.2)
Hepatobiliary disorders	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(1.1)**	**0**	**(0.0)**
Autoimmune hepatitis	0	(0.0)	0	(0.0)	1	(1.1)	0	(0.0)
Immune system disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(1.2)**
Autoimmune disorder	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.2)
Metabolism and nutrition disorders	**1**	**(2.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(1.2)**
Hypoglycaemia	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.2)
Insulin resistant diabetes	1	(2.0)	0	(0.0)	0	(0.0)	0	(0.0)

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付録 2.7.4-42 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 試験パート B2+D（APaT 集団）（続き）

	Total	
	n	(%)
Patients in population	276	
with one or more adverse events	22	(8.0)
with no adverse events	254	(92.0)
Blood and lymphatic system disorders	**1**	**(0.4)**
Thrombocytopenia	1	(0.4)
Endocrine disorders	**1**	**(0.4)**
Hyperthyroidism	1	(0.4)
Hypophysitis	1	(0.4)
Gastrointestinal disorders	**4**	**(1.4)**
Abdominal pain	1	(0.4)
Colitis	1	(0.4)
Pancreatitis	1	(0.4)
Retroperitoneal haemorrhage	1	(0.4)
General disorders and administration site conditions	**2**	**(0.7)**
Gait disturbance	1	(0.4)
Pain	1	(0.4)
Hepatobiliary disorders	**1**	**(0.4)**
Autoimmune hepatitis	1	(0.4)
Immune system disorders	**1**	**(0.4)**
Autoimmune disorder	1	(0.4)
Metabolism and nutrition disorders	**2**	**(0.7)**
Hypoglycaemia	1	(0.4)
Insulin resistant diabetes	1	(0.4)

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付録 2.7.4-42 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 試験パート B2+D（APaT 集団）（続き）

	Ipi-naïve 2 mg/kg Q3W		Ipi-naïve 10 mg/kg Q3W		Ipi-exposed 2 mg/kg Q3W		Ipi-exposed 10 mg/kg Q3W	
	n	(%)	n	(%)	n	(%)	n	(%)
Musculoskeletal and connective tissue disorders	**0**	**(0.0)**	**3**	**(5.8)**	**0**	**(0.0)**	**2**	**(2.4)**
Arthralgia	0	(0.0)	1	(1.9)	0	(0.0)	0	(0.0)
Back pain	0	(0.0)	1	(1.9)	0	(0.0)	0	(0.0)
Myositis	0	(0.0)	1	(1.9)	0	(0.0)	0	(0.0)
Pain in extremity	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.2)
Tenosynovitis	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.2)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**2**	**(2.4)**
Metastases to central nervous system	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.2)
Metastases to meninges	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.2)
Nervous system disorders	**1**	**(2.0)**	**0**	**(0.0)**	**2**	**(2.2)**	**0**	**(0.0)**
Cerebrovascular accident	1	(2.0)	0	(0.0)	0	(0.0)	0	(0.0)
Hemiparesis	0	(0.0)	0	(0.0)	1	(1.1)	0	(0.0)
Partial seizures	0	(0.0)	0	(0.0)	1	(1.1)	0	(0.0)
Skin and subcutaneous tissue disorders	**0**	**(0.0)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(1.2)**
Skin lesion	0	(0.0)	0	(0.0)	0	(0.0)	1	(1.2)

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付録 2.7.4-42 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 試験パート B2+D（APaT 集団）（続き）

	Total	
	n	(%)
Musculoskeletal and connective tissue disorders	**5**	**(1.8)**
Arthralgia	1	(0.4)
Back pain	1	(0.4)
Myositis	1	(0.4)
Pain in extremity	1	(0.4)
Tenosynovitis	1	(0.4)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**2**	**(0.7)**
Metastases to central nervous system	1	(0.4)
Metastases to meninges	1	(0.4)
Nervous system disorders	**3**	**(1.1)**
Cerebrovascular accident	1	(0.4)
Hemiparesis	1	(0.4)
Partial seizures	1	(0.4)
Skin and subcutaneous tissue disorders	**1**	**(0.4)**
Skin lesion	1	(0.4)

Every patient 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' not related to the drug is excluded.
(Database Cutoff Date [redacted]

Data Source: [資料5.3.5.2.1.2: P001V02]

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付録 2.7.4-43 治験薬の投与中止に至った有害事象の一覧

001 試験パート B2+D（APaT 集団）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 2 mg/kg Q3W									
Trial Number=3475-001, Site Number=0011, Subject ID=000520, Gender=M, Race=White, Age=58 Years, Rel Day of Study Medication Discontinuance†=44									
000520	Safety Follow-up	58	Cerebrovascular accident	1.86 Weeks	2	Y	N	Discontinued	Resolved
		69	Thrombocytopenia	Continuing	4	Y	N	Discontinued	Not Resolved
Trial Number=3475-001, Site Number=0012, Subject ID=000259, Gender=M, Race=White, Age=65 Years, Rel Day of Study Medication Discontinuance†=190									
000259	Safety Follow-up	197	Partial seizures	Continuing	1	Y	Y	Discontinued	Not Resolved
Trial Number=3475-001, Site Number=0012, Subject ID=000389, Gender=F, Race=White, Age=68 Years, Rel Day of Study Medication Discontinuance†=22									
000389	Safety Follow-up	40	Hyperthyroidism	6.08 Months	2	Y	Y	Discontinued	Resolved
		40	Hypophysitis	3.32 Months	2	Y	Y	Discontinued	Resolved
Trial Number=3475-001, Site Number=0015, Subject ID=000336, Gender=M, Race=White, Age=58 Years, Rel Day of Study Medication Discontinuance†=1									
000336	Safety Follow-up	22	Autoimmune hepatitis	1.08 Months	4	Y	Y	Discontinued	Resolved
Trial Number=3475-001, Site Number=0020, Subject ID=000325, Gender=F, Race=White, Age=67 Years, Rel Day of Study Medication Discontinuance†=106									
000325	Treatment Cycle 4	106	Gait disturbance	Continuing	2		N	Discontinued	Not Resolved
Trial Number=3475-001, Site Number=0021, Subject ID=000493, Gender=M, Race=White, Age=71 Years, Rel Day of Study Medication Discontinuance†=190									
000493	Safety Follow-up	208	Insulin resistant diabetes	1.08 Months	3	Y	Y	Discontinued	Resolved
Trial Number=3475-001, Site Number=0023, Subject ID=000276, Gender=F, Race=White, Age=52 Years, Rel Day of Study Medication Discontinuance†=43									
000276	Safety Follow-up	69	Hemiparesis	3.32 Months	2		N	Discontinued	Resolved

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付録 2.7.4-43 治験薬の投与中止に至った有害事象の一覧

001 試験パート B2+D（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=3475-001, Site Number=0002, Subject ID=000395, Gender=M, Race=White, Age=68 Years, Rel Day of Study Medication Discontinuance†=64									
000395	Safety Follow-up	76	Pancreatitis	Continuing	3	Y	Y	Discontinued	Not Resolved
Trial Number=3475-001, Site Number=0012, Subject ID=000386, Gender=F, Race=White, Age=30 Years, Rel Day of Study Medication Discontinuance†=1									
000386	Safety Follow-up	10	Metastases to meninges	Continuing	3	Y	N	Discontinued	Not Resolved
Trial Number=3475-001, Site Number=0015, Subject ID=000355, Gender=M, Race=White, Age=76 Years, Rel Day of Study Medication Discontinuance†=113									
000355	Treatment Cycle 2	37	Pain	5 Days	3	Y	N	Discontinued	Resolved
Trial Number=3475-001, Site Number=0015, Subject ID=000360, Gender=M, Race=White, Age=62 Years, Rel Day of Study Medication Discontinuance†=1									
000360	Safety Follow-up	7	Hypoglycaemia	1.29 Weeks	3	Y	N	Discontinued	Resolved
Trial Number=3475-001, Site Number=0015, Subject ID=000455, Gender=F, Race=White, Age=45 Years, Rel Day of Study Medication Discontinuance†=228									
000455	Safety Follow-up	254	Retroperitoneal haemorrhage	5 Days	2	Y	N	Discontinued	Resolved
Trial Number=3475-001, Site Number=0016, Subject ID=000327, Gender=F, Race=White, Age=48 Years, Rel Day of Study Medication Discontinuance†=358									
000327	Safety Follow-up	359	Autoimmune disorder	Continuing	2		Y	Discontinued	Not Resolved
Trial Number=3475-001, Site Number=0019, Subject ID=000351, Gender=F, Race=White, Age=53 Years, Rel Day of Study Medication Discontinuance†=83									
000351	Safety Follow-up	84	Pain in extremity	Continuing	2		N	Discontinued	Not Resolved
Trial Number=3475-001, Site Number=0019, Subject ID=000381, Gender=M, Race=White, Age=73 Years, Rel Day of Study Medication Discontinuance†=188									
000381	Safety Follow-up	190	Tenosynovitis	Continuing	1		Y	Discontinued	Not Resolved

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付録 2.7.4-43 治験薬の投与中止に至った有害事象の一覧

001 試験パート B2+D（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=3475-001, Site Number=0020, Subject ID=000321, Gender=F, Race=Asian, Age=67 Years, Rel Day of Study Medication Discontinuance†=63									
000321	Treatment Cycle 1	14	Abdominal pain	Continuing	2		N	Discontinued	Not Resolved
Trial Number=3475-001, Site Number=0020, Subject ID=000393, Gender=M, Race=White, Age=77 Years, Rel Day of Study Medication Discontinuance†=50									
000393	Safety Follow-up	66	Skin lesion	2.29 Weeks	1		N	Discontinued	Resolved
Trial Number=3475-001, Site Number=0020, Subject ID=000546, Gender=F, Race=White, Age=53 Years, Rel Day of Study Medication Discontinuance†=65									
000546	Safety Follow-up	95	Back pain	Continuing	2		N	Discontinued	Not Resolved
Trial Number=3475-001, Site Number=0021, Subject ID=000378, Gender=M, Race=White, Age=64 Years, Rel Day of Study Medication Discontinuance†=42									
000378	Treatment Cycle 2	33	Metastases to central nervous system	Continuing	3		N	Discontinued	Not Resolved
Trial Number=3475-001, Site Number=0021, Subject ID=000476, Gender=M, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance†=295									
000476	Safety Follow-up	296	Colitis	1.35 Months	2	Y	Y	Discontinued	Resolved
Trial Number=3475-001, Site Number=0023, Subject ID=000494, Gender=F, Race=White, Age=71 Years, Rel Day of Study Medication Discontinuance†=316									
000494	Safety Follow-up	323	Arthralgia	Continuing	2		Y	Discontinued	Not Resolved
Trial Number=3475-001, Site Number=0024, Subject ID=000482, Gender=M, Race=White, Age=49 Years, Rel Day of Study Medication Discontinuance†=570									

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付録 2.7.4-43 治験薬の投与中止に至った有害事象の一覧

001 試験パート B2+D（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=3475-001, Site Number=0024, Subject ID=000482, Gender=M, Race=White, Age=49 Years, Rel Day of Study Medication Discontinuance†=570									
000482	Treatment Cycle 22	459	Myositis	Continuing	2		Y	Discontinued	Not 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..

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: [redacted]

Data Source: [資料5.3.5.2.1.2: P001V02]

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付録 2.7.4-44 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 試験パート B3（APaT 集団）

	MK-3475 10 mg/kg Q3W		MK-3475 10 mg/kg Q2W		Total	
	n	(%)	n	(%)	n	(%)
Patients in population	121		123		244	
with one or more adverse events	11	(9.1)	17	(13.8)	28	(11.5)
with no adverse events	110	(90.9)	106	(86.2)	216	(88.5)
Blood and lymphatic system disorders	**0**	**(0.0)**	**1**	**(0.8)**	**1**	**(0.4)**
Anaemia	0	(0.0)	1	(0.8)	1	(0.4)
Cardiac disorders	**1**	**(0.8)**	**2**	**(1.6)**	**3**	**(1.2)**
Atrial fibrillation	0	(0.0)	1	(0.8)	1	(0.4)
Cardiac arrest	1	(0.8)	0	(0.0)	1	(0.4)
Cardiac failure congestive	0	(0.0)	1	(0.8)	1	(0.4)
Gastrointestinal disorders	**3**	**(2.5)**	**3**	**(2.4)**	**6**	**(2.5)**
Abdominal distension	1	(0.8)	0	(0.0)	1	(0.4)
Colitis	1	(0.8)	0	(0.0)	1	(0.4)
Diarrhoea	0	(0.0)	2	(1.6)	2	(0.8)
Enterocolitis	0	(0.0)	1	(0.8)	1	(0.4)
Intussusception	1	(0.8)	0	(0.0)	1	(0.4)
General disorders and administration site conditions	**2**	**(1.7)**	**2**	**(1.6)**	**4**	**(1.6)**
Death	1	(0.8)	1	(0.8)	2	(0.8)
Fatigue	0	(0.0)	1	(0.8)	1	(0.4)
Pain	1	(0.8)	0	(0.0)	1	(0.4)
Hepatobiliary disorders	**0**	**(0.0)**	**1**	**(0.8)**	**1**	**(0.4)**
Hyperbilirubinaemia	0	(0.0)	1	(0.8)	1	(0.4)
Infections and infestations	**0**	**(0.0)**	**1**	**(0.8)**	**1**	**(0.4)**
Localised infection	0	(0.0)	1	(0.8)	1	(0.4)
Urinary tract infection	0	(0.0)	1	(0.8)	1	(0.4)
Metabolism and nutrition disorders	**0**	**(0.0)**	**2**	**(1.6)**	**2**	**(0.8)**
Failure to thrive	0	(0.0)	1	(0.8)	1	(0.4)
Hyponatraemia	0	(0.0)	1	(0.8)	1	(0.4)
Musculoskeletal and connective tissue disorders	**0**	**(0.0)**	**2**	**(1.6)**	**2**	**(0.8)**
Back pain	0	(0.0)	1	(0.8)	1	(0.4)

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付録 2.7.4-44 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 試験パート B3（APaT 集団）（続き）

	MK-3475 10 mg/kg Q3W		MK-3475 10 mg/kg Q2W		Total	
	n	(%)	n	(%)	n	(%)
Musculoskeletal and connective tissue disorders	**0**	**(0.0)**	**2**	**(1.6)**	**2**	**(0.8)**
Musculoskeletal pain	0	(0.0)	1	(0.8)	1	(0.4)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**2**	**(1.7)**	**1**	**(0.8)**	**3**	**(1.2)**
Cancer pain	0	(0.0)	1	(0.8)	1	(0.4)
Tumour necrosis	1	(0.8)	0	(0.0)	1	(0.4)
Tumour pain	1	(0.8)	0	(0.0)	1	(0.4)
Nervous system disorders	**2**	**(1.7)**	**4**	**(3.3)**	**6**	**(2.5)**
Brain oedema	0	(0.0)	1	(0.8)	1	(0.4)
Convulsion	1	(0.8)	1	(0.8)	2	(0.8)
Spinal cord compression	1	(0.8)	1	(0.8)	2	(0.8)
Vasogenic cerebral oedema	0	(0.0)	1	(0.8)	1	(0.4)
Respiratory, thoracic and mediastinal disorders	**1**	**(0.8)**	**2**	**(1.6)**	**3**	**(1.2)**
Dyspnoea	1	(0.8)	1	(0.8)	2	(0.8)
Pneumonitis	0	(0.0)	1	(0.8)	1	(0.4)

Every patient 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' not related to the drug is excluded.
(Database Cutoff Date: [redacted])

Data Source: [資料5.3.5.2.1.2: P001V02]

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付録 2.7.4-45 治験薬の投与中止に至った有害事象の一覧

001 試験パート B3（APaT 集団）

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=0011, Subject ID=001324, Gender=F, Race=White, Age=55 Years, Rel Day of Study Medication Discontinuance†=1										
001324	Safety Follow-up	8	Pain	Continuing	Severe	3	Y	N	Discontinued	Not Resolved
Trial Number=3475-001, Site Number=0011, Subject ID=001372, Gender=M, Race=White, Age=53 Years, Rel Day of Study Medication Discontinuance†=208										
001372	Safety Follow-up	222	Colitis	3.29 Weeks	Severe	3	Y	Y	Discontinued	Resolved
Trial Number=3475-001, Site Number=0011, Subject ID=001450, Gender=M, Race=White, Age=53 Years, Rel Day of Study Medication Discontinuance†=22										
001450	Safety Follow-up	34	Spinal cord compression	2 Days	Severe	3	Y	N	Discontinued	Resolved
Trial Number=3475-001, Site Number=0012, Subject ID=001302, Gender=M, Race=White, Age=79 Years, Rel Day of Study Medication Discontinuance†=22										
001302	Safety Follow-up	25	Death	1 Days		5	Y	N	Discontinued	Fatal
Trial Number=3475-001, Site Number=0018, Subject ID=001410, Gender=F, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance†=63										
001410	Safety Follow-up	68	Dyspnoea	2 Days	Severe	3		N	Discontinued	Resolved
Trial Number=3475-001, Site Number=0019, Subject ID=001442, Gender=F, Race=White, Age=53 Years, Rel Day of Study Medication Discontinuance†=42										
001442	Safety Follow-up	59	Intussusception	1 Weeks	Severe	3	Y	N	Discontinued	Resolved
Trial Number=3475-001, Site Number=0020, Subject ID=001298, Gender=F, Race=White, Age=76 Years, Rel Day of Study Medication Discontinuance†=1										
001298	Safety Follow-up	22	Abdominal distension	4.14 Weeks	Moderate	2		N	Discontinued	Resolved
Trial Number=3475-001, Site Number=0020, Subject ID=001332, Gender=M, Race=White, Age=64 Years, Rel Day of Study Medication Discontinuance†=22										
001332	Safety Follow-up	37	Convulsion	3 Days	Severe	3	Y	N	Discontinued	Resolved

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付録 2.7.4-45 治験薬の投与中止に至った有害事象の一覧

001 試験パート B3（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=001350, Gender=M, Race=White, Age=44 Years, Rel Day of Study Medication Discontinuance†=85										
001350	Treatment Cycle 1	15	Tumour pain	Continuing	Moderate	2		N	Discontinued	Not Resolved
Trial Number=3475-001, Site Number=0020, Subject ID=001417, Gender=M, Race=White, Age=59 Years, Rel Day of Study Medication Discontinuance†=43										
001417	Treatment Cycle 1	36	Tumour necrosis	Continuing	Moderate	2		N	Discontinued	Not Resolved
Trial Number=3475-001, Site Number=0024, Subject ID=001334, Gender=M, Race=White, Age=82 Years, Rel Day of Study Medication Discontinuance†=30										
001334	Safety Follow-up	35	Cardiac arrest	1 Days		5	Y	N	Discontinued	Fatal
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=0008, Subject ID=001283, Gender=M, Race=White, Age=57 Years, Rel Day of Study Medication Discontinuance†=71										
001283	Safety Follow-up	75	Dyspnoea	1.57 Weeks	Severe	4	Y	N	Discontinued	Resolved
Trial Number=3475-001, Site Number=0008, Subject ID=001342, Gender=M, Race=White, Age=76 Years, Rel Day of Study Medication Discontinuance†=30										
001342	Safety Follow-up	44 44	Hyperbilirubinaemia Hyponatraemia	Continuing Continuing	Severe Severe	3 3		Y N	Discontinued Discontinued	Not Resolved Not Resolved
Trial Number=3475-001, Site Number=0010, Subject ID=001328, Gender=M, Race=White, Age=67 Years, Rel Day of Study Medication Discontinuance†=153										
001328	Safety Follow-up	168	Brain oedema	Continuing	Moderate	2		N	Discontinued	Not Resolved

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付録 2.7.4-45 治験薬の投与中止に至った有害事象の一覧

001 試験パート B3（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=0011, Subject ID=001319, Gender=M, Race=White, Age=82 Years, Rel Day of Study Medication Discontinuance†=1										
001319	Safety Follow-up	2	Diarrhoea	Continuing	Moderate	2	Y	N	Discontinued	Not Resolved
Trial Number=3475-001, Site Number=0011, Subject ID=001449, Gender=F, Race=White, Age=74 Years, Rel Day of Study Medication Discontinuance†=1										
001449	Safety Follow-up	3	Cancer pain	Continuing	Severe	3	Y	N	Discontinued	Not Resolved
Trial Number=3475-001, Site Number=0012, Subject ID=001316, Gender=M, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=13										
001316	Safety Follow-up	33	Death	1 Days		5	Y	N	Discontinued	Fatal
Trial Number=3475-001, Site Number=0012, Subject ID=001360, Gender=F, Race=White, Age=75 Years, Rel Day of Study Medication Discontinuance†=41										
001360	Safety Follow-up	57	Failure to thrive	Continuing	Severe	3	Y	N	Discontinued	Not Resolved
		57	Localised infection	Continuing	Severe	3	Y	N	Discontinued	Not Resolved
		57	Urinary tract infection	Continuing	Severe	3	Y	N	Discontinued	Not Resolved
Trial Number=3475-001, Site Number=0013, Subject ID=001259, Gender=F, Race=White, Age=54 Years, Rel Day of Study Medication Discontinuance†=58										
001259	Safety Follow-up	72	Spinal cord compression	Continuing	Severe	3	Y	N	Discontinued	Not Resolved
Trial Number=3475-001, Site Number=0015, Subject ID=001402, Gender=M, Race=White, Age=71 Years, Rel Day of Study Medication Discontinuance†=100										
001402	Safety Follow-up	128	Vasogenic cerebral oedema	Continuing	Moderate	2		N	Discontinued	Not Resolved
Trial Number=3475-001, Site Number=0015, Subject ID=001426, Gender=M, Race=White, Age=59 Years, Rel Day of Study Medication Discontinuance†=29										
001426	Safety Follow-up	37	Diarrhoea	3 Days	Severe	3	Y	Y	Discontinued	Resolved

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付録 2.7.4-45 治験薬の投与中止に至った有害事象の一覧

001 試験パート B3（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=0018, Subject ID=001308, Gender=F, Race=White, Age=38 Years, Rel Day of Study Medication Discontinuance†=165										
001308	Treatment Cycle 13	165	Enterocolitis	1.86 Weeks	Severe	3	Y	Y	Discontinued	Resolved
Trial Number=3475-001, Site Number=0018, Subject ID=001432, Gender=M, Race=White, Age=75 Years, Rel Day of Study Medication Discontinuance†=44										
001432	Safety Follow-up	59	Anaemia	2 Weeks	Severe	3	Y	N	Discontinued	Resolved
		59	Cardiac failure congestive	Continuing	Severe	3	Y	N	Discontinued	Not Resolved
Trial Number=3475-001, Site Number=0020, Subject ID=001404, Gender=F, Race=White, Age=42 Years, Rel Day of Study Medication Discontinuance†=71										
001404	Treatment Cycle 5	69	Musculoskeletal pain	Continuing	Mild	1		N	Discontinued	Not Resolved
Trial Number=3475-001, Site Number=0020, Subject ID=001433, Gender=M, Race=White, Age=74 Years, Rel Day of Study Medication Discontinuance†=35										
001433	Safety Follow-up	43	Atrial fibrillation	4 Days	Severe	3	Y	N	Discontinued	Resolved
		55	Fatigue	Continuing	Severe	3		N	Discontinued	Not Resolved
Trial Number=3475-001, Site Number=0020, Subject ID=001446, Gender=M, Race=White, Age=59 Years, Rel Day of Study Medication Discontinuance†=1										
001446	Safety Follow-up	10	Convulsion	Continuing	Severe	3		N	Discontinued	Not Resolved
Trial Number=3475-001, Site Number=0021, Subject ID=001363, Gender=M, Race=White, Age=64 Years, Rel Day of Study Medication Discontinuance†=127										

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付録 2.7.4-45 治験薬の投与中止に至った有害事象の一覧

001 試験パート B3（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=0021, Subject ID=001363, Gender=M, Race=White, Age=64 Years, Rel Day of Study Medication Discontinuance†=127										
001363	Treatment Cycle 5	57	Back pain	Continuing	Moderate	2	Y	N	Discontinued	Not Resolved

†Relative Day of Study Medication Discontinuance is defined as the day of the last recorded dose of study medication for the patient 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' not related to the drug is excluded.

(Database Cutoff Date: [redacted]

Data Source: [資料5.3.5.2.1.2: P001V02]

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付録 2.7.4-46 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）
002 試験（APaT 集団）

	Control		MK-3475 2 mg/kg Q3W		MK-3475 10 mg/kg Q3W	
	n	(%)	n	(%)	n	(%)
Subjects in population	171		178		179	
with one or more adverse events	35	(20.5)	23	(12.9)	26	(14.5)
with no adverse events	136	(79.5)	155	(87.1)	153	(85.5)
Blood and lymphatic system disorders	**12**	**(7.0)**	**1**	**(0.6)**	**0**	**(0.0)**
Anaemia	4	(2.3)	1	(0.6)	0	(0.0)
Febrile neutropenia	1	(0.6)	0	(0.0)	0	(0.0)
Granulocytopenia	1	(0.6)	0	(0.0)	0	(0.0)
Leukopenia	4	(2.3)	0	(0.0)	0	(0.0)
Neutropenia	3	(1.8)	0	(0.0)	0	(0.0)
Pancytopenia	1	(0.6)	0	(0.0)	0	(0.0)
Thrombocytopenia	3	(1.8)	0	(0.0)	0	(0.0)
Eye disorders	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.6)**
Iritis	0	(0.0)	0	(0.0)	1	(0.6)
Gastrointestinal disorders	**3**	**(1.8)**	**4**	**(2.2)**	**5**	**(2.8)**
Abdominal distension	1	(0.6)	0	(0.0)	0	(0.0)
Abdominal pain lower	0	(0.0)	0	(0.0)	1	(0.6)
Colitis	0	(0.0)	2	(1.1)	0	(0.0)
Diarrhoea	1	(0.6)	0	(0.0)	3	(1.7)
Dysphagia	0	(0.0)	1	(0.6)	0	(0.0)
Gastric disorder	0	(0.0)	0	(0.0)	1	(0.6)
Gastrointestinal disorder	0	(0.0)	0	(0.0)	1	(0.6)
Gastrointestinal toxicity	1	(0.6)	0	(0.0)	0	(0.0)
Haematochezia	1	(0.6)	0	(0.0)	0	(0.0)
Pancreatitis	0	(0.0)	1	(0.6)	0	(0.0)
Small intestinal perforation	0	(0.0)	1	(0.6)	0	(0.0)
General disorders and administration site conditions	**10**	**(5.8)**	**2**	**(1.1)**	**5**	**(2.8)**
Chest discomfort	0	(0.0)	0	(0.0)	1	(0.6)
Fatigue	7	(4.1)	1	(0.6)	0	(0.0)
Feeling hot	0	(0.0)	0	(0.0)	1	(0.6)
Injection site extravasation	0	(0.0)	0	(0.0)	1	(0.6)
Malaise	1	(0.6)	0	(0.0)	1	(0.6)
Mucosal inflammation	0	(0.0)	1	(0.6)	1	(0.6)
Pyrexia	2	(1.2)	0	(0.0)	1	(0.6)
Hepatobiliary disorders	**0**	**(0.0)**	**1**	**(0.6)**	**1**	**(0.6)**
Autoimmune hepatitis	0	(0.0)	1	(0.6)	0	(0.0)
Cholestasis	0	(0.0)	0	(0.0)	1	(0.6)

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付録 2.7.4-46 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）
002 試験（APaT 集団）（続き）

	Control		MK-3475 2 mg/kg Q3W		MK-3475 10 mg/kg Q3W	
	n	(%)	n	(%)	n	(%)
Infections and infestations	**4**	**(2.3)**	**3**	**(1.7)**	**3**	**(1.7)**
Appendicitis perforated	0	(0.0)	0	(0.0)	1	(0.6)
Bacteraemia	1	(0.6)	0	(0.0)	0	(0.0)
Bronchitis	1	(0.6)	0	(0.0)	0	(0.0)
Conjunctivitis	0	(0.0)	0	(0.0)	1	(0.6)
Infection	1	(0.6)	0	(0.0)	0	(0.0)
Influenza	1	(0.6)	0	(0.0)	0	(0.0)
Pelvic abscess	0	(0.0)	0	(0.0)	1	(0.6)
Pneumonia	0	(0.0)	1	(0.6)	0	(0.0)
Soft tissue infection	0	(0.0)	1	(0.6)	0	(0.0)
Upper respiratory tract infection	0	(0.0)	0	(0.0)	1	(0.6)
Urinary tract infection	0	(0.0)	1	(0.6)	0	(0.0)
Viral infection	1	(0.6)	0	(0.0)	0	(0.0)
Injury, poisoning and procedural complications	**1**	**(0.6)**	**1**	**(0.6)**	**1**	**(0.6)**
Infusion related reaction	1	(0.6)	0	(0.0)	0	(0.0)
Procedural pain	0	(0.0)	0	(0.0)	1	(0.6)
Radiation injury	0	(0.0)	1	(0.6)	0	(0.0)
Investigations	**7**	**(4.1)**	**1**	**(0.6)**	**2**	**(1.1)**
Alanine aminotransferase increased	0	(0.0)	0	(0.0)	1	(0.6)
Aspartate aminotransferase increased	0	(0.0)	1	(0.6)	1	(0.6)
Granulocyte count decreased	1	(0.6)	0	(0.0)	0	(0.0)
Haemoglobin decreased	0	(0.0)	0	(0.0)	1	(0.6)
Lymphocyte count decreased	1	(0.6)	0	(0.0)	0	(0.0)
Neutrophil count decreased	3	(1.8)	0	(0.0)	0	(0.0)
Platelet count decreased	5	(2.9)	0	(0.0)	0	(0.0)
White blood cell count decreased	2	(1.2)	0	(0.0)	0	(0.0)
Metabolism and nutrition disorders	**1**	**(0.6)**	**2**	**(1.1)**	**1**	**(0.6)**
Decreased appetite	1	(0.6)	0	(0.0)	0	(0.0)
Diabetes mellitus	0	(0.0)	1	(0.6)	0	(0.0)
Hyponatraemia	0	(0.0)	0	(0.0)	1	(0.6)
Lactic acidosis	0	(0.0)	1	(0.6)	0	(0.0)
Musculoskeletal and connective tissue disorders	**1**	**(0.6)**	**3**	**(1.7)**	**2**	**(1.1)**
Arthralgia	0	(0.0)	2	(1.1)	0	(0.0)
Back pain	1	(0.6)	0	(0.0)	1	(0.6)

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付録 2.7.4-46 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）
002 試験（APaT 集団）（続き）

	Control		MK-3475 2 mg/kg Q3W		MK-3475 10 mg/kg Q3W	
	n	(%)	n	(%)	n	(%)
Musculoskeletal and connective tissue disorders	**1**	**(0.6)**	**3**	**(1.7)**	**2**	**(1.1)**
Musculoskeletal pain	0	(0.0)	1	(0.6)	1	(0.6)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**0**	**(0.0)**	**1**	**(0.6)**	**0**	**(0.0)**
Oncologic complication	0	(0.0)	1	(0.6)	0	(0.0)
Nervous system disorders	**5**	**(2.9)**	**1**	**(0.6)**	**4**	**(2.2)**
Meningitis noninfective	0	(0.0)	0	(0.0)	1	(0.6)
Myasthenic syndrome	0	(0.0)	0	(0.0)	1	(0.6)
Neuropathy peripheral	2	(1.2)	1	(0.6)	0	(0.0)
Peripheral motor neuropathy	0	(0.0)	0	(0.0)	1	(0.6)
Peripheral sensorimotor neuropathy	1	(0.6)	0	(0.0)	0	(0.0)
Polyneuropathy	2	(1.2)	0	(0.0)	1	(0.6)
Psychiatric disorders	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.6)**
Confusional state	0	(0.0)	0	(0.0)	1	(0.6)
Renal and urinary disorders	**0**	**(0.0)**	**2**	**(1.1)**	**1**	**(0.6)**
Renal failure	0	(0.0)	1	(0.6)	0	(0.0)
Renal failure chronic	0	(0.0)	0	(0.0)	1	(0.6)
Tubulointerstitial nephritis	0	(0.0)	1	(0.6)	1	(0.6)
Respiratory, thoracic and mediastinal disorders	**3**	**(1.8)**	**2**	**(1.1)**	**3**	**(1.7)**
Cough	1	(0.6)	0	(0.0)	0	(0.0)
Dyspnoea	1	(0.6)	0	(0.0)	3	(1.7)
Laryngeal inflammation	0	(0.0)	1	(0.6)	0	(0.0)
Pulmonary embolism	1	(0.6)	0	(0.0)	0	(0.0)
Respiratory failure	0	(0.0)	1	(0.6)	0	(0.0)
Skin and subcutaneous tissue disorders	**1**	**(0.6)**	**2**	**(1.1)**	**3**	**(1.7)**
Erythema multiforme	0	(0.0)	0	(0.0)	1	(0.6)
Hyperhidrosis	1	(0.6)	0	(0.0)	0	(0.0)
Palmar-plantar erythrodysaesthesia syndrome	0	(0.0)	1	(0.6)	0	(0.0)
Pruritus	0	(0.0)	0	(0.0)	1	(0.6)
Rash maculo-papular	0	(0.0)	2	(1.1)	1	(0.6)
Vascular disorders	**2**	**(1.2)**	**0**	**(0.0)**	**1**	**(0.6)**

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付録 2.7.4-46 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）
002 試験（APaT 集団）（続き）

	Control		MK-3475 2 mg/kg Q3W		MK-3475 10 mg/kg Q3W	
	n	(%)	n	(%)	n	(%)
Vascular disorders	**2**	**(1.2)**	**0**	**(0.0)**	**1**	**(0.6)**
Flushing	1	(0.6)	0	(0.0)	1	(0.6)
Hypotension	1	(0.6)	0	(0.0)	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.
MedDRA preferred terms "Neoplasm Progression", "Malignant Neoplasm Progression" and "Disease Progression" not related to the drug are excluded.
(Database Cutoff Date: 12MAY2014).

Data Source: [資料5.3.5.1.1: P002V01]

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付録 2.7.4-47 休薬に至った有害事象の一覧

002 試験（APaT 集団）

AN	Epoch	Rel Day of Onset	Adverse Event	Duration	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
Control									
Study Number=3475-002, Site Number=0008, AN=100141, Gender=M, Race=White, Age=69 Years, Rel Day of Study Medication Discontinuance†=23									
100141	Treatment Cycle 2	23	Thrombocytopenia	Continuing	2	N	Y	Interrupted	Not Resolved
Study Number=3475-002, Site Number=0016, AN=100021, Gender=M, Race=White, Age=44 Years, Rel Day of Study Medication Discontinuance†=211									
100021	Treatment Cycle 3	43	Fatigue	Continuing	2	N	Y	Interrupted	Not Resolved
	Treatment Cycle 4	64	Neuropathy peripheral	Continuing	2	N	N	Interrupted	Not Resolved
		85	Hyperhidrosis	Continuing	1	N	N	Interrupted	Not Resolved
		85	Pulmonary embolism	1.22 Months	3	N	N	Interrupted	Resolved
Study Number=3475-002, Site Number=0016, AN=100038, Gender=F, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance†=									
100038	Treatment Cycle 6	165	Viral infection	1.43 Weeks	1	N	N	Interrupted	Resolved
Study Number=3475-002, Site Number=0016, AN=100085, Gender=M, Race=White, Age=56 Years, Rel Day of Study Medication Discontinuance†=190									
100085	Treatment Cycle 2	22	Platelet count decreased	2.99 Months	3	N	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0018, AN=100604, Gender=M, Race=White, Age=65 Years, Rel Day of Study Medication Discontinuance†=146									
100604	Treatment Cycle 3	59	Neuropathy peripheral	7.1 Months	2	N	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0018, AN=102119, Gender=M, Race=White, Age=61 Years, Rel Day of Study Medication Discontinuance†=90									
102119	Treatment Cycle 1	27	Febrile neutropenia	1 Weeks	4	Y	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0019, AN=100074, Gender=M, Race=White, Age=87 Years, Rel Day of Study Medication Discontinuance†=102									
100074	Treatment Cycle 1	20	White blood cell count decreased	2.14 Weeks	3	N	Y	Interrupted	Resolved

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AN	Epoch	Rel Day of Onset	Adverse Event	Duration	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
Control									
Study Number=3475-002, Site Number=0019, AN=100324, Gender=M, Race=White, Age=65 Years, Rel Day of Study Medication Discontinuance†=152									
100324	Treatment Cycle 1	20	Lymphocyte count decreased	4 Weeks	3	N	Y	Interrupted	Resolved
		20	Platelet count decreased	6 Days	2	N	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0021, AN=102141, Gender=F, Race=White, Age=67 Years, Rel Day of Study Medication Discontinuance†=29									
102141	Treatment Cycle 1	19	Thrombocytopenia	1.29 Weeks	1	N	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0025, AN=101281, Gender=F, Race=White, Age=29 Years, Rel Day of Study Medication Discontinuance†=281									
101281	Treatment Cycle 1	22	Neutropenia	3 Weeks	2	N	Y	Interrupted	Resolved
	Treatment Cycle 5	127	Neutropenia	1.14 Weeks	2	N	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0033, AN=101805, Gender=F, Race=White, Age=80 Years, Rel Day of Study Medication Discontinuance†=120									
101805	Chemotherapy Washout	42	Haematochezia	2.14 Weeks	3	Y	N	Interrupted	Sequelae
Study Number=3475-002, Site Number=0036, AN=100004, Gender=M, Race=White, Age=76 Years, Rel Day of Study Medication Discontinuance†=									
100004	Treatment Cycle 3	43	Peripheral sensorimotor neuropathy	Continuing	2	N	Y	Interrupted	Not Resolved
Study Number=3475-002, Site Number=0046, AN=101260, Gender=F, Race=White, Age=57 Years, Rel Day of Study Medication Discontinuance†=54									
101260	Treatment Cycle 1	29	Neutrophil count decreased	3.14 Weeks	4	N	Y	Interrupted	Resolved
		29	Platelet count decreased	1 Weeks	3	N	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0052, AN=100144, Gender=M, Race=White, Age=62 Years, Rel Day of Study Medication Discontinuance†=									
100144	Treatment Cycle 2	41	Neutrophil count decreased	1.14 Weeks	2	N	Y	Interrupted	Resolved

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AN	Epoch	Rel Day of Onset	Adverse Event	Duration	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
Control									
Study Number=3475-002, Site Number=0052, AN=100144, Gender=M, Race=White, Age=62 Years, Rel Day of Study Medication Discontinuance†=									
100144	Treatment Cycle 2	41	Platelet count decreased	1.14 Weeks	2	N	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0058, AN=101282, Gender=M, Race=White, Age=55 Years, Rel Day of Study Medication Discontinuance†=50									
101282	Treatment Cycle 1	18	Anaemia	5 Days	3	N	Y	Interrupted	Resolved
		18	Bacteraemia	6 Days	3	Y	Y	Interrupted	Resolved
		18	Platelet count decreased	18.42 Hours	4	Y	Y	Interrupted	Resolved
	Safety Follow-up	71	Neutrophil count decreased	5 Days	3	Y	Y	Interrupted	Resolved
		71	White blood cell count decreased	1.14 Weeks	3	Y	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0059, AN=100122, Gender=F, Race=White, Age=58 Years, Rel Day of Study Medication Discontinuance†=									
100122	Treatment Cycle 4	81	Bronchitis	1 Weeks	1	N	N	Interrupted	Resolved
		82	Influenza	1 Weeks	1	N	N	Interrupted	Resolved
Study Number=3475-002, Site Number=0060, AN=100093, Gender=M, Race=White, Age=47 Years, Rel Day of Study Medication Discontinuance†=64									
100093	Treatment Cycle 1	1	Infusion related reaction	37 Minutes	2	N	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0061, AN=100314, Gender=M, Race=White, Age=51 Years, Rel Day of Study Medication Discontinuance†=243									
100314	Treatment Cycle 1	14	Leukopenia	2 Weeks	3	N	Y	Interrupted	Resolved
		14	Neutropenia	2 Weeks	3	N	Y	Interrupted	Resolved
	Chemotherapy Washout	43	Leukopenia	1.71 Weeks	3	N	Y	Interrupted	Resolved
		43	Neutropenia	1.71 Weeks	2	N	Y	Interrupted	Resolved

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AN	Epoch	Rel Day of Onset	Adverse Event	Duration	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
Control									
Study Number=3475-002, Site Number=0067, AN=101276, Gender=M, Race=White, Age=84 Years, Rel Day of Study Medication Discontinuance†=213									
101276	Treatment Cycle 1	15	Granulocyte count decreased	4 Days	3	N	Y	Interrupted	Resolved
		26	Diarrhoea	3.86 Weeks	2	N	N	Interrupted	Resolved
	Treatment Cycle 3	71	Hypotension	2 Days	3	Y	N	Interrupted	Resolved
Study Number=3475-002, Site Number=0080, AN=100924, Gender=M, Race=White, Age=80 Years, Rel Day of Study Medication Discontinuance†=1									
100924	Safety Follow-up	21	Granulocytopenia	2 Weeks	4	N	Y	Interrupted	Resolved
		21	Leukopenia	2 Weeks	3	N	Y	Interrupted	Resolved
		21	Thrombocytopenia	6 Days	3	N	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0082, AN=100083, Gender=M, Race=White, Age=63 Years, Rel Day of Study Medication Discontinuance†=									
100083	Treatment Cycle 3	64	Anaemia	1.29 Weeks	3	Y	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0082, AN=100920, Gender=M, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance†=218									
100920	Treatment Cycle 1	1	Malaise	1 Hours	2	N	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0083, AN=100055, Gender=F, Race=White, Age=55 Years, Rel Day of Study Medication Discontinuance†=353									
100055	Treatment Cycle 3	57	Polyneuropathy	Continuing	2	N	Y	Interrupted	Not Resolved
Study Number=3475-002, Site Number=0087, AN=100053, Gender=F, Race=White, Age=56 Years, Rel Day of Study Medication Discontinuance†=196									
100053	Treatment Cycle 1	8	Leukopenia	6.21 Months	2	N	Y	Interrupted	Resolved
		22	Pancytopenia	2.1 Months	1	N	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0087, AN=100618, Gender=M, Race=White, Age=77 Years, Rel Day of Study Medication Discontinuance†=109									

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AN	Epoch	Rel Day of Onset	Adverse Event	Duration	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
Control									
Study Number=3475-002, Site Number=0087, AN=100618, Gender=M, Race=White, Age=77 Years, Rel Day of Study Medication Discontinuance†=109									
100618	Treatment Cycle 1	12	Fatigue	1.94 Months	2	N	Y	Interrupted	Resolved
	Treatment Cycle 3	80	Polyneuropathy	Continuing	1	N	Y	Interrupted	Not Resolved
	Safety Follow-up	111	Fatigue	Continuing	2	N	Y	Interrupted	Not Resolved
Study Number=3475-002, Site Number=0087, AN=102111, Gender=F, Race=White, Age=71 Years, Rel Day of Study Medication Discontinuance†=238									
102111	Treatment Cycle 1	15	Leukopenia	9.03 Months	1	N	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0088, AN=101822, Gender=M, Race=White, Age=50 Years, Rel Day of Study Medication Discontinuance†=115									
101822	Chemotherapy Washout	31	Pyrexia	2 Days	1	N	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0103, AN=101235, Gender=F, Race=White, Age=52 Years, Rel Day of Study Medication Discontinuance†=69									
101235	Treatment Cycle 1	14	Pyrexia	2.29 Weeks	1	N	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0111, AN=101519, Gender=M, Race=White, Age=48 Years, Rel Day of Study Medication Discontinuance†=129									
101519	Treatment Cycle 2	39	Cough	Continuing	2	N	N	Interrupted	Not Resolved
	Chemotherapy Washout	51	Fatigue	Continuing	2	N	N	Interrupted	Not Resolved
		59	Decreased appetite	Continuing	1	N	N	Interrupted	Not Resolved
Study Number=3475-002, Site Number=0112, AN=100685, Gender=F, Race=White, Age=46 Years, Rel Day of Study Medication Discontinuance†=89									
100685	Treatment Cycle 1	22	Anaemia	4.3 Months	3	N	Y	Interrupted	Resolved

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AN	Epoch	Rel Day of Onset	Adverse Event	Duration	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
Control									
Study Number=3475-002, Site Number=0120, AN=100689, Gender=M, Race=White, Age=40 Years, Rel Day of Study Medication Discontinuance†=85									
100689	Safety Follow-up	107	Infection	3.14 Weeks	3	Y	N	Interrupted	Resolved
Study Number=3475-002, Site Number=0150, AN=100009, Gender=F, Race=White, Age=67 Years, Rel Day of Study Medication Discontinuance†=484									
100009	Treatment Cycle 1	14	Neutropenia	1.29 Weeks	3	N	Y	Interrupted	Resolved
	Treatment Cycle 2	43	Neutropenia	1.14 Weeks	3	N	Y	Interrupted	Resolved
	Treatment Cycle 3	64	Anaemia	1.14 Weeks	3	N	Y	Interrupted	Resolved
		64	Neutropenia	1.14 Weeks	3	N	Y	Interrupted	Resolved
	Treatment Cycle 5	106	Gastrointestinal toxicity	1 Weeks	1	N	Y	Interrupted	Resolved
		113	Fatigue	4 Days	2	N	Y	Interrupted	Resolved
	Treatment Cycle 7	141	Neutropenia	1 Weeks	3	N	Y	Interrupted	Resolved
		142	Abdominal distension	1.57 Weeks	2	N	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0150, AN=100016, Gender=M, Race=White, Age=74 Years, Rel Day of Study Medication Discontinuance†=134									
100016	Treatment Cycle 1	1	Back pain	23 Hours	3	N	Y	Interrupted	Resolved
		1	Dyspnoea	23 Hours	1	N	Y	Interrupted	Resolved
		1	Flushing	23 Hours	3	N	Y	Interrupted	Resolved
	Treatment Cycle 3	67	Fatigue	3.14 Weeks	2	N	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0150, AN=100077, Gender=M, Race=White, Age=68 Years, Rel Day of Study Medication Discontinuance†=176									
100077	Safety Follow-up	184	Fatigue	3 Weeks	3	N	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0170, AN=101268, Gender=M, Race=White, Age=78 Years, Rel Day of Study Medication Discontinuance†=197									
101268	Treatment Cycle 5	88	Fatigue	Continuing	2	N	Y	Interrupted	Not Resolved

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AN	Epoch	Rel Day of Onset	Adverse Event	Duration	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 2 mg/kg Q3W									
Study Number=3475-002, Site Number=0001, AN=100094, Gender=M, Race=White, Age=64 Years, Rel Day of Study Medication Discontinuance†=									
100094	Treatment Cycle 5	127	Autoimmune hepatitis	1.28 Months	2	N	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0007, AN=102109, Gender=M, Race=White, Age=75 Years, Rel Day of Study Medication Discontinuance†=212									
102109	Safety Follow-up	233	Neuropathy peripheral	Continuing	2	N	Y	Interrupted	Not Resolved
Study Number=3475-002, Site Number=0012, AN=101284, Gender=M, Race=White, Age=75 Years, Rel Day of Study Medication Discontinuance†=43									
101284	Safety Follow-up	50	Soft tissue infection	Continuing	2	Y	N	Interrupted	Not Resolved
Study Number=3475-002, Site Number=0018, AN=102134, Gender=F, Race=White, Age=73 Years, Rel Day of Study Medication Discontinuance†=1									
102134	Safety Follow-up	22	Urinary tract infection	1.43 Weeks	3	Y	N	Interrupted	Resolved
Study Number=3475-002, Site Number=0021, AN=101251, Gender=F, Race=White, Age=74 Years, Rel Day of Study Medication Discontinuance†=32									
101251	Treatment Cycle 1	19	Pneumonia	Continuing	2	Y	N	Interrupted	Resolving
Study Number=3475-002, Site Number=0028, AN=100671, Gender=F, Race=White, Age=71 Years, Rel Day of Study Medication Discontinuance†=68									
100671	Treatment Cycle 3	61	Lactic acidosis	Continuing	2	N	N	Interrupted	Not Resolved
Study Number=3475-002, Site Number=0031, AN=101219, Gender=M, Race=White, Age=80 Years, Rel Day of Study Medication Discontinuance†=177									
101219	Treatment Cycle 6	143	Mucosal inflammation	1.15 Months	2	N	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0036, AN=100301, Gender=F, Race=White, Age=24 Years, Rel Day of Study Medication Discontinuance†=85									
100301	Treatment Cycle 3	43	Oncologic complication	Continuing	3	Y	N	Interrupted	Not Resolved

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AN	Epoch	Rel Day of Onset	Adverse Event	Duration	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 2 mg/kg Q3W									
Study Number=3475-002, Site Number=0052, AN=100145, Gender=M, Race=White, Age=69 Years, Rel Day of Study Medication Discontinuance†=									
100145	Treatment Cycle 5	101	Radiation injury	24 Hours	3	Y	N	Interrupted	Resolved
Study Number=3475-002, Site Number=0054, AN=100064, Gender=M, Race=White, Age=87 Years, Rel Day of Study Medication Discontinuance†=44									
100064	Safety Follow-up	52	Laryngeal inflammation	4.44 Months	3	Y	Y	Interrupted	Resolved
		70	Dysphagia	Continuing	3	Y	Y	Interrupted	Not Resolved
Study Number=3475-002, Site Number=0054, AN=101278, Gender=M, Race=White, Age=73 Years, Rel Day of Study Medication Discontinuance†=									
101278	Treatment Cycle 4	85	Rash maculo-papular	1.86 Weeks	3	Y	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0061, AN=101204, Gender=F, Race=White, Age=43 Years, Rel Day of Study Medication Discontinuance†=									
101204	Treatment Cycle 7	141	Palmar-plantar erythrodysaesthesia syndrome	1.57 Weeks	2	N	Y	Interrupted	Resolved
		141	Rash maculo-papular	1.57 Weeks	2	N	N	Interrupted	Resolved
Study Number=3475-002, Site Number=0080, AN=100070, Gender=M, Race=White, Age=44 Years, Rel Day of Study Medication Discontinuance†=43									
100070	Safety Follow-up	61	Anaemia	1.71 Weeks	2	Y	N	Interrupted	Resolved
Study Number=3475-002, Site Number=0080, AN=100910, Gender=F, Race=White, Age=36 Years, Rel Day of Study Medication Discontinuance†=274									
100910	Treatment Cycle 10	191	Colitis	1.38 Months	2	Y	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0082, AN=100653, Gender=F, Race=White, Age=63 Years, Rel Day of Study Medication Discontinuance†=									
100653	Treatment Cycle 13	269	Respiratory failure	1.43 Weeks	2	N	Y	Interrupted	Resolved

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AN	Epoch	Rel Day of Onset	Adverse Event	Duration	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 2 mg/kg Q3W									
Study Number=3475-002, Site Number=0088, AN=101285, Gender=F, Race=White, Age=64 Years, Rel Day of Study Medication Discontinuance†=									
101285	Treatment Cycle 6	126	Pancreatitis	1 Weeks	2	Y	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0102, AN=101241, Gender=M, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=106									
101241	Treatment Cycle 3	64	Renal failure	1.86 Weeks	2	N	N	Interrupted	Resolved
		71	Diabetes mellitus	2 Weeks	3	Y	N	Interrupted	Resolved
Study Number=3475-002, Site Number=0112, AN=100084, Gender=M, Race=White, Age=49 Years, Rel Day of Study Medication Discontinuance†=									
100084	Treatment Cycle 2	20	Arthralgia	2.4 Months	3	N	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0112, AN=100923, Gender=F, Race=White, Age=44 Years, Rel Day of Study Medication Discontinuance†=43									
100923	Safety Follow-up	62	Arthralgia	Continuing	2	N	Y	Interrupted	Not Resolved
Study Number=3475-002, Site Number=0112, AN=101216, Gender=M, Race=White, Age=67 Years, Rel Day of Study Medication Discontinuance†=41									
101216	Safety Follow-up	62	Tubulointerstitial nephritis	Continuing	2	Y	Y	Interrupted	Resolving
Study Number=3475-002, Site Number=0113, AN=101869, Gender=M, Race=White, Age=63 Years, Rel Day of Study Medication Discontinuance†=									
101869	Treatment Cycle 2	43	Aspartate aminotransferase increased	1.64 Months	3	N	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0150, AN=100667, Gender=F, Race=White, Age=56 Years, Rel Day of Study Medication Discontinuance†=									
100667	Treatment Cycle 3	55	Small intestinal perforation	1.14 Weeks	3	Y	Y	Interrupted	Resolved
		87	Colitis	1.64 Months	2	Y	N	Interrupted	Resolved
Study Number=3475-002, Site Number=0151, AN=100007, Gender=M, Race=White, Age=65 Years, Rel Day of Study Medication Discontinuance†=									

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AN	Epoch	Rel Day of Onset	Adverse Event	Duration	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 2 mg/kg Q3W									
Study Number=3475-002, Site Number=0151, AN=100007, Gender=M, Race=White, Age=65 Years, Rel Day of Study Medication Discontinuance†=									
100007	Treatment Cycle 15	379	Fatigue	Continuing	2	N	Y	Interrupted	Not Resolved
		379	Musculoskeletal pain	4.4 Months	2	N	Y	Interrupted	Resolved
MK-3475 10 mg/kg Q3W									
Study Number=3475-002, Site Number=0007, AN=100903, Gender=M, Race=White, Age=60 Years, Rel Day of Study Medication Discontinuance†=398									
100903	Safety Follow-up	406	Procedural pain	Continuing	2	Y	N	Interrupted	Not Resolved
Study Number=3475-002, Site Number=0007, AN=100905, Gender=F, Race=White, Age=33 Years, Rel Day of Study Medication Discontinuance†=									
100905	Treatment Cycle 1	1	Feeling hot	1 Hours	1	N	Y	Interrupted	Resolved
		1	Flushing	1 Hours	1	N	Y	Interrupted	Resolved
		1	Pruritus	1 Hours	1	N	Y	Interrupted	Resolved
		1	Pruritus	1 Hours	1	N	Y	Interrupted	Resolved
	Treatment Cycle 9	177	Meningitis noninfective	2.14 Months	3	Y	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0010, AN=101857, Gender=M, Race=White, Age=54 Years, Rel Day of Study Medication Discontinuance†=64									
101857	Safety Follow-up	93	Dyspnoea	2 Days	1	N	Y	Interrupted	Resolved
		93	Malaise	Continuing	1	N	Y	Interrupted	Not Resolved
Study Number=3475-002, Site Number=0016, AN=100647, Gender=F, Race=White, Age=74 Years, Rel Day of Study Medication Discontinuance†=274									
100647	Treatment Cycle 1	1	Abdominal pain lower	3 Hours	2	N	N	Interrupted	Resolved
		1	Chest discomfort	3 Hours	2	N	N	Interrupted	Resolved
		1	Pyrexia	3 Hours	1	N	N	Interrupted	Resolved

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AN	Epoch	Rel Day of Onset	Adverse Event	Duration	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q3W									
Study Number=3475-002, Site Number=0016, AN=100647, Gender=F, Race=White, Age=74 Years, Rel Day of Study Medication Discontinuance†=274									
100647	Treatment Cycle 4	85	Diarrhoea	4 Days	2	N	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0027, AN=101837, Gender=M, Race=White, Age=79 Years, Rel Day of Study Medication Discontinuance†=									
101837	Treatment Cycle 1	18	Conjunctivitis	1.14 Weeks	2	N	N	Interrupted	Resolved
Study Number=3475-002, Site Number=0028, AN=101511, Gender=M, Race=White, Age=65 Years, Rel Day of Study Medication Discontinuance†=43									
101511	Safety Follow-up	64	Hyponatraemia	Continuing	3	Y	N	Interrupted	Not Resolved
Study Number=3475-002, Site Number=0028, AN=102124, Gender=M, Race=White, Age=59 Years, Rel Day of Study Medication Discontinuance†=162									
102124	Treatment Cycle 7	133	Confusional state	2.29 Weeks	2	Y	N	Interrupted	Resolved
Study Number=3475-002, Site Number=0053, AN=101851, Gender=M, Race=White, Age=89 Years, Rel Day of Study Medication Discontinuance†=235									
101851	Treatment Cycle 3	43	Rash maculo-papular	2.2 Months	3	N	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0059, AN=101247, Gender=F, Race=White, Age=60 Years, Rel Day of Study Medication Discontinuance†=64									
101247	Treatment Cycle 1	1 22	Back pain Back pain	15 Minutes 2 Hours	2 2	N N	Y Y	Interrupted Interrupted	Resolved Resolved
Study Number=3475-002, Site Number=0070, AN= , Gender=M, Race=White, Age=68 Years, Rel Day of Study Medication Discontinuance†=43									
101879	Treatment Cycle 2	21	Cholestasis	Continuing	2	N	N	Interrupted	Not Resolved
Study Number=3475-002, Site Number=0080, AN=100674, Gender=M, Race=White, Age=65 Years, Rel Day of Study Medication Discontinuance†=23									
100674	Treatment Cycle 1	15	Gastrointestinal disorder	Continuing	3	Y	N	Interrupted	Not Resolved

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AN	Epoch	Rel Day of Onset	Adverse Event	Duration	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q3W									
Study Number=3475-002, Site Number=0080, AN=100913, Gender=F, Race=White, Age=53 Years, Rel Day of Study Medication Discontinuance†=1									
100913	Safety Follow-up	13	Iritis	1.02 Months	3	Y	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0083, AN=100042, Gender=F, Race=White, Age=69 Years, Rel Day of Study Medication Discontinuance†=64									
100042	Safety Follow-up	74	Myasthenic syndrome	8.38 Months	3	Y	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0083, AN=100651, Gender=F, Race=White, Age=73 Years, Rel Day of Study Medication Discontinuance†=355									
100651	Treatment Cycle 11	231	Tubulointerstitial nephritis	1.71 Weeks	1	N	N	Interrupted	Resolved
	Treatment Cycle 12	263	Renal failure chronic	1.18 Months	2	N	Y	Interrupted	Sequelae
Study Number=3475-002, Site Number=0088, AN=100080, Gender=M, Race=White, Age=60 Years, Rel Day of Study Medication Discontinuance†=									
100080	Treatment Cycle 9	176	Erythema multiforme	Continuing	3	Y	Y	Interrupted	Not Resolved
		176	Mucosal inflammation	3.19 Months	2	N	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0088, AN=101878, Gender=F, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=									
101878	Treatment Cycle 7	146	Polyneuropathy	Continuing	2	N	N	Interrupted	Not Resolved
Study Number=3475-002, Site Number=0090, AN=100034, Gender=F, Race=White, Age=63 Years, Rel Day of Study Medication Discontinuance†=169									
100034	Safety Follow-up	184	Dyspnoea	2.57 Weeks	2	N	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0113, AN=100090, Gender=F, Race=White, Age=42 Years, Rel Day of Study Medication Discontinuance†=64									
100090	Treatment Cycle 1	9	Gastric disorder	2.53 Months	3	Y	N	Interrupted	Resolved
Study Number=3475-002, Site Number=0120, AN=101811, Gender=F, Race=White, Age=49 Years, Rel Day of Study Medication Discontinuance†=169									

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付録 2.7.4-47 休薬に至った有害事象の一覧

002 試験（APaT 集団）（続き）

AN	Epoch	Rel Day of Onset	Adverse Event	Duration	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q3W									
Study Number=3475-002, Site Number=0120, AN=101811, Gender=F, Race=White, Age=49 Years, Rel Day of Study Medication Discontinuance†=169									
101811	Treatment Cycle 2	29	Diarrhoea	1.48 Months	2	N	Y	Interrupted	Resolved
	Treatment Cycle 3	51	Upper respiratory tract infection	Unknown	2	N	N	Interrupted	Unknown
	Safety Follow-up	183	Dyspnoea	Continuing	3	Y	N	Interrupted	Not Resolved
Study Number=3475-002, Site Number=0130, AN=100919, Gender=F, Race=White, Age=51 Years, Rel Day of Study Medication Discontinuance†=96									
100919	Treatment Cycle 2	42	Diarrhoea	1.08 Months	3	Y	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0140, AN=100635, Gender=F, Race=White, Age=46 Years, Rel Day of Study Medication Discontinuance†=112									
100635	Treatment Cycle 1	22	Alanine aminotransferase increased	1.51 Months	3	Y	Y	Interrupted	Resolved
		22	Aspartate aminotransferase increased	2.27 Months	3	Y	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0141, AN=101861, Gender=F, Race=White, Age=75 Years, Rel Day of Study Medication Discontinuance†=22									
101861	Safety Follow-up	43	Peripheral motor neuropathy	2.79 Months	2	Y	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0150, AN=101802, Gender=F, Race=White, Age=50 Years, Rel Day of Study Medication Discontinuance†=106									
101802	Treatment Cycle 2	23	Musculoskeletal pain	1.51 Months	3	Y	N	Interrupted	Resolved
Study Number=3475-002, Site Number=0161, AN=101265, Gender=M, Race=White, Age=67 Years, Rel Day of Study Medication Discontinuance†=71									
101265	Treatment Cycle 1	20	Haemoglobin decreased	Continuing	3	N	N	Interrupted	Not Resolved
Study Number=3475-002, Site Number=0170, AN=100311, Gender=M, Race=White, Age=33 Years, Rel Day of Study Medication Discontinuance†=									
100311	Treatment Cycle 17	336	Injection site extravasation	2 Days	2	N	Y	Interrupted	Resolved

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付録 2.7.4-47 休薬に至った有害事象の一覧

002 試験（APaT 集団）（続き）

AN	Epoch	Rel Day of Onset	Adverse Event	Duration	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q3W									
Study Number=3475-002, Site Number=0170, AN=100684, Gender=M, Race=White, Age=54 Years, Rel Day of Study Medication Discontinuance†=163									
100684	Treatment Cycle 3	57	Appendicitis perforated	1.29 Weeks	3	Y	N	Interrupted	Resolved
		71	Pelvic abscess	1.71 Weeks	3	Y	N	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.

MedDRA preferred terms "Neoplasm Progression", "Malignant Neoplasm Progression" and "Disease Progression" not related to the drug are excluded.

(Database Cutoff Date: 12MAY2014).

Data Source: [資料5.3.5.1.1: P002V01]

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付録 2.7.4-48 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）
002 試験（APaT 集団）

	Control		MK-3475 2 mg/kg Q3W		MK-3475 10 mg/kg Q3W	
	n	(%)	n	(%)	n	(%)
Subjects in population	171		178		179	
with one or more adverse events	20	(11.7)	18	(10.1)	26	(14.5)
with no adverse events	151	(88.3)	160	(89.9)	153	(85.5)
Blood and lymphatic system disorders	**4**	**(2.3)**	**1**	**(0.6)**	**0**	**(0.0)**
Anaemia	2	(1.2)	1	(0.6)	0	(0.0)
Pancytopenia	1	(0.6)	0	(0.0)	0	(0.0)
Thrombocytopenia	3	(1.8)	0	(0.0)	0	(0.0)
Cardiac disorders	**1**	**(0.6)**	**0**	**(0.0)**	**1**	**(0.6)**
Atrial fibrillation	1	(0.6)	0	(0.0)	0	(0.0)
Cardiac ventricular disorder	0	(0.0)	0	(0.0)	1	(0.6)
Endocrine disorders	**0**	**(0.0)**	**1**	**(0.6)**	**2**	**(1.1)**
Hypophysitis	0	(0.0)	1	(0.6)	0	(0.0)
Hypopituitarism	0	(0.0)	0	(0.0)	2	(1.1)
Gastrointestinal disorders	**2**	**(1.2)**	**0**	**(0.0)**	**4**	**(2.2)**
Colitis	1	(0.6)	0	(0.0)	2	(1.1)
Gingival bleeding	1	(0.6)	0	(0.0)	0	(0.0)
Nausea	0	(0.0)	0	(0.0)	1	(0.6)
Upper gastrointestinal haemorrhage	0	(0.0)	0	(0.0)	1	(0.6)
Vomiting	0	(0.0)	0	(0.0)	1	(0.6)
General disorders and administration site conditions	**5**	**(2.9)**	**7**	**(3.9)**	**9**	**(5.0)**
Asthenia	1	(0.6)	1	(0.6)	3	(1.7)
Death	1	(0.6)	1	(0.6)	2	(1.1)
Fatigue	1	(0.6)	0	(0.0)	1	(0.6)
General physical health deterioration	2	(1.2)	1	(0.6)	3	(1.7)
Generalised oedema	0	(0.0)	3	(1.7)	0	(0.0)
Oedema	0	(0.0)	1	(0.6)	0	(0.0)
Oedema peripheral	0	(0.0)	0	(0.0)	1	(0.6)
Hepatobiliary disorders	**1**	**(0.6)**	**1**	**(0.6)**	**2**	**(1.1)**
Autoimmune hepatitis	0	(0.0)	0	(0.0)	1	(0.6)
Hepatic failure	0	(0.0)	1	(0.6)	1	(0.6)
Hyperbilirubinaemia	1	(0.6)	0	(0.0)	0	(0.0)
Immune system disorders	**1**	**(0.6)**	**0**	**(0.0)**	**0**	**(0.0)**

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付録 2.7.4-48 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）
002 試験（APaT 集団）（続き）

	Control		MK-3475 2 mg/kg Q3W		MK-3475 10 mg/kg Q3W	
	n	(%)	n	(%)	n	(%)
Immune system disorders	**1**	**(0.6)**	**0**	**(0.0)**	**0**	**(0.0)**
Anaphylactic reaction	1	(0.6)	0	(0.0)	0	(0.0)
Infections and infestations	**3**	**(1.8)**	**2**	**(1.1)**	**0**	**(0.0)**
Bacterial sepsis	1	(0.6)	0	(0.0)	0	(0.0)
Infectious pleural effusion	0	(0.0)	1	(0.6)	0	(0.0)
Sepsis	1	(0.6)	0	(0.0)	0	(0.0)
Septic shock	0	(0.0)	1	(0.6)	0	(0.0)
Soft tissue infection	1	(0.6)	0	(0.0)	0	(0.0)
Urosepsis	1	(0.6)	0	(0.0)	0	(0.0)
Investigations	**2**	**(1.2)**	**0**	**(0.0)**	**1**	**(0.6)**
C-reactive protein increased	1	(0.6)	0	(0.0)	0	(0.0)
Gamma-glutamyltransferase increased	0	(0.0)	0	(0.0)	1	(0.6)
Lymphocyte count decreased	1	(0.6)	0	(0.0)	0	(0.0)
Metabolism and nutrition disorders	**0**	**(0.0)**	**2**	**(1.1)**	**2**	**(1.1)**
Cachexia	0	(0.0)	1	(0.6)	0	(0.0)
Cell death	0	(0.0)	0	(0.0)	1	(0.6)
Hypercalcaemia	0	(0.0)	1	(0.6)	0	(0.0)
Hyponatraemia	0	(0.0)	0	(0.0)	1	(0.6)
Musculoskeletal and connective tissue disorders	**0**	**(0.0)**	**1**	**(0.6)**	**1**	**(0.6)**
Back pain	0	(0.0)	0	(0.0)	1	(0.6)
Neck pain	0	(0.0)	1	(0.6)	0	(0.0)
Nervous system disorders	**4**	**(2.3)**	**0**	**(0.0)**	**0**	**(0.0)**
Haemorrhage intracranial	1	(0.6)	0	(0.0)	0	(0.0)
Myoclonus	1	(0.6)	0	(0.0)	0	(0.0)
Neuropathy peripheral	2	(1.2)	0	(0.0)	0	(0.0)
Renal and urinary disorders	**1**	**(0.6)**	**1**	**(0.6)**	**0**	**(0.0)**
Hydronephrosis	0	(0.0)	1	(0.6)	0	(0.0)
Renal failure acute	1	(0.6)	0	(0.0)	0	(0.0)
Respiratory, thoracic and mediastinal disorders	**2**	**(1.2)**	**1**	**(0.6)**	**7**	**(3.9)**
Dyspnoea	1	(0.6)	0	(0.0)	3	(1.7)
Haemoptysis	1	(0.6)	0	(0.0)	0	(0.0)
Interstitial lung disease	0	(0.0)	0	(0.0)	1	(0.6)
Pleural effusion	0	(0.0)	0	(0.0)	1	(0.6)
Pneumonitis	0	(0.0)	0	(0.0)	3	(1.7)

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付録 2.7.4-48 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）

002 試験（APaT 集団）（続き）

	Control		MK-3475 2 mg/kg Q3W		MK-3475 10 mg/kg Q3W	
	n	(%)	n	(%)	n	(%)
Respiratory, thoracic and mediastinal disorders	**2**	**(1.2)**	**1**	**(0.6)**	**7**	**(3.9)**
Pulmonary embolism	1	(0.6)	1	(0.6)	0	(0.0)
Skin and subcutaneous tissue disorders	**1**	**(0.6)**	**1**	**(0.6)**	**0**	**(0.0)**
Alopecia	1	(0.6)	0	(0.0)	0	(0.0)
Stevens-Johnson syndrome	0	(0.0)	1	(0.6)	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.
MedDRA preferred terms "Neoplasm Progression", "Malignant Neoplasm Progression" and "Disease Progression" not related to the drug are excluded.
(Database Cutoff Date: 12MAY2014).

Data Source: [資料5.3.5.1.1: P002V01]

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