付録 2.7.4-28 最終投与後 90 日までに発現した重篤な有害事象の一覧

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=0001, AN=101266, Gender=F, Race=White, Age=59 Years, Rel Day of Study Medication Discontinuance†=175									
101266	Chemotherapy Washout	99	Hyperbilirubinaemia	1.81 Months	4	Y	N	Discontinued	Resolved
		121	Influenza	1.86 Weeks	2	Y	N	None	Resolved
Study Number=3475-002, Site Number=0007, AN=100603, Gender=M, Race=White, Age=44 Years, Rel Day of Study Medication Discontinuance†=360									
100603	Chemotherapy Washout	106	Constipation	6.8 Months	3	Y	N	N/A	Resolved
Study Number=3475-002, Site Number=0008, AN=100141, Gender=M, Race=White, Age=69 Years, Rel Day of Study Medication Discontinuance†=23									
100141	Chemotherapy Washout	33	Pulmonary embolism	4 Days	3	Y	N	None	Resolved
Study Number=3475-002, Site Number=0011, AN=100111, Gender=F, Race=White, Age=69 Years, Rel Day of Study Medication Discontinuance†=127									
100111	Chemotherapy Washout	18	Renal failure acute	6 Days	4	Y	Y	Discontinued	Resolved
Study Number=3475-002, Site Number=0012, AN=101870, Gender=F, Race=White, Age=74 Years, Rel Day of Study Medication Discontinuance†=152									
101870	Treatment Cycle 5	137	Chronic obstructive pulmonary disease	3 Days	3	Y	N	None	Resolved
Study Number=3475-002, Site Number=0018, AN=101852, Gender=M, Race=White, Age=56 Years, Rel Day of Study Medication Discontinuance†=22									
101852	Extended Safety Follow-up	63	Subdural haematoma	4 Days	5	Y	N	None	Fatal

C Confidential

付録 2.7.4-28 最終投与後 90 日までに発現した重篤な有害事象の一覧
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
Control									
Study Number=3475-002, Site Number=0018, AN=101862, Gender=M, Race=Asian, Age=71 Years, Rel Day of Study Medication Discontinuance†=1									
101862	Safety Follow-up	14	Pulmonary embolism	1.29 Weeks	3	Y	N	None	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	4	Dehydration	4 Days	3	Y	Y	None	Resolved
	Safety Follow-up	128	Lobar pneumonia	3.86 Weeks	2	Y	N	None	Resolved
		128	Transient ischaemic attack	2 Days	2	Y	N	None	Resolved
Study Number=3475-002, Site Number=0025, AN=101884, Gender=M, Race=White, Age=52 Years, Rel Day of Study Medication Discontinuance†=41									
101884	Safety Follow-up	57	Tumour haemorrhage	Continuing	3	Y	N	None	Not Resolved
		65	Pneumonia	5 Days	5	Y	N	None	Fatal
Study Number=3475-002, Site Number=0025, AN=102133, Gender=M, Race=White, Age=37 Years, Rel Day of Study Medication Discontinuance†=35									
102133	Safety Follow-up	59	Death	23 Hours	5	Y	N	Discontinued	Fatal
Study Number=3475-002, Site Number=0027, AN=101832, Gender=M, Race=White, Age=46 Years, Rel Day of Study Medication Discontinuance†=50									
101832	Safety Follow-up	71	Ataxia	Continuing	3	Y	N	None	Not Resolved
Study Number=3475-002, Site Number=0028, AN=101503, Gender=F, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=232									
101503	Chemotherapy Washout	116	Hypocalcaemia	2 Days	3	Y	Y	None	Resolved

C Confidential

付録 2.7.4-28 最終投与後 90 日までに発現した重篤な有害事象の一覧

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
Control									
Study Number=3475-002, Site Number=0028, AN=101845, Gender=F, Race=White, Age=55 Years, Rel Day of Study Medication Discontinuance†=29									
101845	Treatment Cycle 1	7	Dyspnoea	Continuing	4	Y	N	None	Not Resolved
	Safety Follow-up	33	Sepsis	3.14 Weeks	4	Y	N	None	Resolved
Study Number=3475-002, Site Number=0029, AN=100668, Gender=M, Race=American Indian Or Alaska Native, Age=46 Years, Rel Day of Study Medication Discontinuance†=168									
100668	Treatment Cycle 1	9	Respiratory syncytial virus infection	4 Days	3	Y	N	None	Resolved
Study Number=3475-002, Site Number=0029, AN=101876, Gender=M, Race=American Indian Or Alaska Native, Age=72 Years, Rel Day of Study Medication Discontinuance†=5									
101876	Safety Follow-up	8	Alanine aminotransferase	Continuing	1	Y	N	None	Not Resolved
		8	Aspartate aminotransferase increased	Continuing	1	Y	N	None	Not Resolved
		8	Back pain	Continuing	2	Y	N	None	Not Resolved
		8	Blood bilirubin increased	Continuing	2	Y	N	None	Not Resolved
		8	Hepatitis	Continuing	1	Y	N	None	Not Resolved
Study Number=3475-002, Site Number=0033, AN=100068, Gender=F, Race=White, Age=42 Years, Rel Day of Study Medication Discontinuance†=222									
100068	Treatment Cycle 4	95	Rectal haemorrhage	4 Days	2	Y	N	N/A	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=101207, Gender=M, Race=White, Age=62 Years, Rel Day of Study Medication Discontinuance†=230									
101207	Treatment Cycle 2	56	Pain in extremity	6.31 Months	3	Y	N	None	Sequelae

C Confidential

付録 2.7.4-28 最終投与後 90 日までに発現した重篤な有害事象の一覧
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
Control									
Study Number=3475-002, Site Number=0036, AN=101210, Gender=F, Race=White, Age=69 Years, Rel Day of Study Medication Discontinuance†=489									
101210	Treatment Cycle 8	215	Sepsis	1.14 Weeks	4	Y	N	Discontinued	Resolved
Study Number=3475-002, Site Number=0053, AN=101215, Gender=M, Race=White, Age=57 Years, Rel Day of Study Medication Discontinuance†=57									
101215	Safety Follow-up	57	Dyspnoea	Continuing	4	Y	N	Discontinued	Not Resolved
		57	Haemoptysis	Continuing	3	Y	N	Discontinued	Not Resolved
Study Number=3475-002, Site Number=0054, AN=100059, Gender=M, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance†=64									
100059	Treatment Cycle 1	2	Sepsis	1 Weeks	4	Y	N	None	Resolved
	Extended Safety Follow-up	104	Small intestinal obstruction	4 Days	3	Y	N	None	Resolved
Study Number=3475-002, Site Number=0054, AN=101254, Gender=F, Race=Black Or African American, Age=65 Years, Rel Day of Study Medication Discontinuance†=22									
101254	Safety Follow-up	17	Abdominal pain	2 Days	3	Y	N	None	Resolved
		30	Dyspnoea	3 Days	3	Y	N	None	Resolved
	Extended Safety Follow-up	37	Enterocolitis infectious	3 Days	3	Y	N	None	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	Bacteraemia	6 Days	3	Y	Y	Interrupted	Resolved
		18	Neutrophil count decreased	5 Days	4	Y	Y	Reduced	Resolved
		18	Platelet count decreased	18.42 Hours	4	Y	Y	Interrupted	Resolved
	Safety Follow-up	71	Anaemia	1.14 Weeks	3	Y	Y	N/A	Resolved
		71	Confusional state	2 Days	2	Y	Y	N/A	Resolved

C Confidential

付録 2.7.4-28 最終投与後 90 日までに発現した重篤な有害事象の一覧
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
Control									
Study Number=3475-002, Site Number=0058, AN=101282, Gender=M, Race=White, Age=55 Years, Rel Day of Study Medication Discontinuance†=50									
101282	Safety Follow-up	71	Nausea	2 Days	3	Y	Y	N/A	Resolved
		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=0060, AN=101230, Gender=M, Race=American Indian Or Alaska Native, Age=73 Years, Rel Day of Study Medication Discontinuance†=64									
101230	Treatment Cycle 1	18	Urinary tract infection	3 Days	3	Y	N	None	Resolved
Study Number=3475-002, Site Number=0061, AN=101201, Gender=M, Race=White, Age=65 Years, Rel Day of Study Medication Discontinuance†=204									
101201	Chemotherapy Washout	60	Femur fracture	1.31 Months	2	Y	N	N/A	Resolved
Study Number=3475-002, Site Number=0061, AN=102118, Gender=M, Race=White, Age=80 Years, Rel Day of Study Medication Discontinuance†=15									
102118	Treatment Cycle 1	2	Colitis	1.31 Months	3	Y	N	Discontinued	Resolved
Study Number=3475-002, Site Number=0062, AN=100130, Gender=F, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance†=154									
100130	Treatment Cycle 1	18	Dehydration	1 Weeks	2	Y	N	Reduced	Resolved
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	18	Myocardial infarction	1 Weeks	3	Y	N	None	Resolved
	Treatment Cycle 3	71	Hypotension	2 Days	3	Y	N	Interrupted	Resolved
Study Number=3475-002, Site Number=0073, AN=101880, Gender=M, Race=White, Age=60 Years, Rel Day of Study Medication Discontinuance†=5									
101880	Safety Follow-up	24	Pneumonia	Continuing	3	Y	N	N/A	Resolving

C Confidential

付録 2.7.4-28 最終投与後 90 日までに発現した重篤な有害事象の一覧
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
Control									
Study Number=3475-002, Site Number=0073, AN=101880, Gender=M, Race=White, Age=60 Years, Rel Day of Study Medication Discontinuance†=5									
101880	Safety Follow-up	24	Thrombocytopenia	Continuing	1	Y	Y	Discontinued	Not Resolved
Study Number=3475-002, Site Number=0080, AN=100328, Gender=M, Race=White, Age=52 Years, Rel Day of Study Medication Discontinuance†=22									
100328	Treatment Cycle 1	5	Lymphoedema	2.71 Weeks	3	Y	N	None	Resolved
		16	Generalised oedema	1.91 Months	3	Y	N	None	Fatal
Study Number=3475-002, Site Number=0080, AN=100906, Gender=F, Race=White, Age=47 Years, Rel Day of Study Medication Discontinuance†=53									
100906	Treatment Cycle 1	22	Febrile neutropenia	6 Days	3	Y	N	None	Resolved
	Treatment Cycle 2	33	Pyrexia	6 Days	3	Y	Y	Reduced	Resolved
		52	Anaemia	2.43 Weeks	3	Y	N	None	Resolved
	Safety Follow-up	57	General physical health deterioration	1.71 Weeks	5	Y	N	Discontinued	Fatal
Study Number=3475-002, Site Number=0080, AN=100924, Gender=M, Race=White, Age=80 Years, Rel Day of Study Medication Discontinuance†=1									
100924	Extended Safety Follow-up	41	Atypical pneumonia	3.71 Weeks	5	Y	N	Discontinued	Fatal
Study Number=3475-002, Site Number=0081, AN=100103, Gender=M, Race=White, Age=78 Years, Rel Day of Study Medication Discontinuance†=1									
100103	Safety Follow-up	6	General physical health deterioration	4 Days	5	Y	N	Discontinued	Fatal
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=100640, Gender=M, Race=White, Age=42 Years, Rel Day of Study Medication Discontinuance†=64									

C Confidential

付録 2.7.4-28 最終投与後 90 日までに発現した重篤な有害事象の一覧
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
Control									
Study Number=3475-002, Site Number=0082, AN=100640, Gender=M, Race=White, Age=42 Years, Rel Day of Study Medication Discontinuance†=64									
100640	Safety Follow-up	71	Nausea	4 Days	2	Y	Y	None	Resolved
		71	Vomiting	4 Days	2	Y	Y	None	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	Chemotherapy Washout	169	Ascites	2.66 Months	3	Y	N	N/A	Resolved
Study Number=3475-002, Site Number=0087, AN=100912, Gender=F, Race=White, Age=45 Years, Rel Day of Study Medication Discontinuance†=1									
100912	Safety Follow-up	5	General physical health deterioration	1.87 Months	5	Y	N	N/A	Fatal
Study Number=3475-002, Site Number=0088, AN=100659, Gender=M, Race=White, Age=58 Years, Rel Day of Study Medication Discontinuance†=23									
100659	Treatment Cycle 1	14	Leukopenia	4 Days	4	Y	Y	Reduced	Resolved
		15	Neutropenia	3 Days	4	Y	Y	Reduced	Resolved
	Safety Follow-up	29	Neutropenia	2.14 Weeks	4	Y	Y	Reduced	Resolved
		50	Leukopenia	2.29 Weeks	1	Y	Y	None	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	7	Soft tissue infection	2.1 Months	3	Y	Y	Discontinued	Resolved
		62	Erysipelas	3 Weeks	3	Y	N	N/A	Resolved
Study Number=3475-002, Site Number=0090, AN=100914, Gender=F, Race=White, Age=31 Years, Rel Day of Study Medication Discontinuance†=1									
100914	Safety Follow-up	3	Thrombocytopenia	Unknown	4	Y	Y	Discontinued	Unknown

C Confidential

付録 2.7.4-28 最終投与後 90 日までに発現した重篤な有害事象の一覧

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
Control									
Study Number=3475-002, Site Number=0090, AN=100914, Gender=F, Race=White, Age=31 Years, Rel Day of Study Medication Discontinuance†=1									
100914	Extended Safety Follow-up	62	Death	23 Hours	5	Y	N	N/A	Fatal
Study Number=3475-002, Site Number=0101, AN=100069, Gender=F, Race=White, Age=56 Years, Rel Day of Study Medication Discontinuance†=61									
100069	Safety Follow-up	77	Myoclonus	5 Days	1	Y	N	Discontinued	Resolved
Study Number=3475-002, Site Number=0101, AN=101253, Gender=M, Race=White, Age=74 Years, Rel Day of Study Medication Discontinuance†=313									
101253	Treatment Cycle 6	146	Diarrhoea	4 Days	2	Y	N	None	Resolved
Study Number=3475-002, Site Number=0101, AN=102129, Gender=M, Race=White, Age=42 Years, Rel Day of Study Medication Discontinuance†=5									
102129	Treatment Cycle 1	5	Haemorrhage intracranial	3.14 Weeks	5	Y	N	Discontinued	Fatal
Study Number=3475-002, Site Number=0103, AN=101827, Gender=F, Race=White, Age=64 Years, Rel Day of Study Medication Discontinuance†=71									
101827	Safety Follow-up	87	Epistaxis	1 Weeks	3	Y	N	None	Resolved
Study Number=3475-002, Site Number=0112, AN=100610, Gender=M, Race=White, Age=33 Years, Rel Day of Study Medication Discontinuance†=97									
100610	Chemotherapy Washout	55	Dyspnoea	Continuing	3	Y	N	N/A	Not Resolved
Study Number=3475-002, Site Number=0112, AN=100632, Gender=M, Race=White, Age=53 Years, Rel Day of Study Medication Discontinuance†=92									
100632	Chemotherapy Washout	28	Tumour pain	Continuing	3	Y	N	N/A	Not Resolved

C Confidential

付録 2.7.4-28 最終投与後 90 日までに発現した重篤な有害事象の一覧

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
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=0130, AN=101872, Gender=M, Race=White, Age=72 Years, Rel Day of Study Medication Discontinuance†=85									
101872	Chemotherapy Washout	114	Pyrexia	1 Weeks	1	Y	Y	None	Resolved
Study Number=3475-002, Site Number=0140, AN=100670, Gender=M, Race=White, Age=63 Years, Rel Day of Study Medication Discontinuance†=22									
100670	Safety Follow-up	17	Anaemia	4 Days	3	Y	Y	None	Resolved
		17	Platelet count decreased	Continuing	4	Y	Y	None	Not Resolved
Study Number=3475-002, Site Number=0141, AN=101809, Gender=M, Race=White, Age=74 Years, Rel Day of Study Medication Discontinuance†=5									
101809	Safety Follow-up	32	Infection	1.15 Months	2	Y	N	N/A	Resolved
Study Number=3475-002, Site Number=0142, AN=101859, Gender=F, Race=White, Age=72 Years, Rel Day of Study Medication Discontinuance†=282									
101859	Treatment Cycle 1	11	Pneumonia	4 Days	3	Y	Y	None	Resolved
Study Number=3475-002, Site Number=0142, AN=101877, Gender=M, Race=White, Age=63 Years, Rel Day of Study Medication Discontinuance†=77									
101877	Safety Follow-up	99	Intracranial tumour haemorrhage	1 Weeks	2	Y	N	None	Resolved
Study Number=3475-002, Site Number=0143, AN=102113, Gender=M, Race=White, Age=57 Years, Rel Day of Study Medication Discontinuance†=185									
102113	Treatment Cycle 1	27	Viral upper respiratory tract infection	2 Days	3	Y	N	None	Resolved
	Chemotherapy Washout	57	Pneumonia	1.14 Weeks	3	Y	N	None	Resolved

C Confidential

付録 2.7.4-28 最終投与後 90 日までに発現した重篤な有害事象の一覧

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
Control									
Study Number=3475-002, Site Number=0151, AN=101803, Gender=M, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance†=150									
101803	Safety Follow-up	165	Cellulitis	4 Days	3	Y	N	None	Resolved
Study Number=3475-002, Site Number=0153, AN=101232, Gender=M, Race=White, Age=67 Years, Rel Day of Study Medication Discontinuance†=64									
101232	Safety Follow-up	82	Syncope	1.29 Weeks	3	Y	N	N/A	Resolved
		83	Erysipelas	1.14 Weeks	3	Y	N	N/A	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 2	32	Febrile neutropenia	1.43 Weeks	3	Y	Y	None	Resolved
Study Number=3475-002, Site Number=0184, AN=102140, Gender=F, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance†=22									
102140	Treatment Cycle 1	17	Nausea	2.14 Weeks	3	Y	Y	None	Resolved
	Safety Follow-up	32	Pulmonary embolism	2 Days	5	Y	N	Discontinued	Fatal
Study Number=3475-002, Site Number=0189, AN=100646, Gender=M, Race=White, Age=52 Years, Rel Day of Study Medication Discontinuance†=149									
100646	Treatment Cycle 1	10	Pulmonary embolism	1.87 Months	3	Y	N	None	Sequelae
		11	Deep vein thrombosis	1.77 Months	2	Y	N	None	Resolved
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	102	Cholecystitis	5 Days	3	Y	N	None	Resolved
Study Number=3475-002, Site Number=0001, AN=100688, Gender=F, Race=White, Age=54 Years, Rel Day of Study Medication Discontinuance†=90									

C Confidential

付録 2.7.4-28 最終投与後 90 日までに発現した重篤な有害事象の一覧
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 2 mg/kg Q3W									
Study Number=3475-002, Site Number=0001, AN=100688, Gender=F, Race=White, Age=54 Years, Rel Day of Study Medication Discontinuance†=90									
100688	Safety Follow-up	97	Metastases to central nervous system	2 Days	2	Y	N	None	Resolved
Study Number=3475-002, Site Number=0007, AN=100315, Gender=F, Race=White, Age=74 Years, Rel Day of Study Medication Discontinuance†=1									
100315	Safety Follow-up	14	Dizziness	4 Days	3	Y	N	None	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	Extended Safety Follow-up	272	Pneumonia	1.43 Weeks	3	Y	N	N/A	Resolved
Study Number=3475-002, Site Number=0008, AN=101521, Gender=F, Race=White, Age=61 Years, Rel Day of Study Medication Discontinuance†=106									
101521	Treatment Cycle 3	46	Pulmonary embolism	4 Days	3	Y	N	None	Resolved
Study Number=3475-002, Site Number=0010, AN=100677, Gender=F, Race=White, Age=76 Years, Rel Day of Study Medication Discontinuance†=252									
100677	Treatment Cycle 4	63	Pyrexia	2 Days	2	Y	N	None	Resolved
	Treatment Cycle 5	104	Clostridium difficile colitis	3.29 Weeks	3	Y	N	None	Resolved
Study Number=3475-002, Site Number=0012, AN=100908, Gender=M, Race=White, Age=43 Years, Rel Day of Study Medication Discontinuance†=90									
100908	Treatment Cycle 4	69	Malabsorption	Continuing	3	Y	N	None	Not Resolved
Study Number=3475-002, Site Number=0012, AN=101244, Gender=M, Race=White, Age=72 Years, Rel Day of Study Medication Discontinuance†=									
101244	Treatment Cycle 10	233	Skin infection	1.71 Months	3	Y	N	None	Resolved
Study Number=3475-002, Site Number=0012, AN=101284, Gender=M, Race=White, Age=75 Years, Rel Day of Study Medication Discontinuance†=43									

C Confidential

付録 2.7.4-28 最終投与後 90 日までに発現した重篤な有害事象の一覧
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 2 mg/kg Q3W									
Study Number=3475-002, Site Number=0012, AN=101284, Gender=M, Race=White, Age=75 Years, Rel Day of Study Medication Discontinuance†=43									
101284	Treatment Cycle 2 Safety Follow-up	32 50	Dehydration Soft tissue infection	5 Days Continuing	3 2	Y Y	N N	None Interrupted	Resolved Not Resolved
Study Number=3475-002, Site Number=0016, AN=100634, Gender=M, Race=White, Age=62 Years, Rel Day of Study Medication Discontinuance†=43									
100634	Safety Follow-up	61	Dehydration	5 Days	3	Y	N	None	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=0019, AN=101847, Gender=M, Race=White, Age=64 Years, Rel Day of Study Medication Discontinuance†=									
101847	Treatment Cycle 1	4	Hypotension	3 Days	3	Y	N	N/A	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 19	Pneumonia Pulmonary embolism	Continuing Continuing	2 3	Y Y	N N	Interrupted Discontinued	Resolving Resolving
Study Number=3475-002, Site Number=0024, AN=101516, Gender=M, Race=White, Age=29 Years, Rel Day of Study Medication Discontinuance†=43									
101516	Safety Follow-up	49	Partial seizures	1 Weeks	1	Y	N	N/A	Resolved
Study Number=3475-002, Site Number=0025, AN=101226, Gender=F, Race=White, Age=76 Years, Rel Day of Study Medication Discontinuance†=169									
101226	Treatment Cycle 2	32	Basal cell carcinoma	1.31 Months	1	Y	N	None	Resolved
Study Number=3475-002, Site Number=0025, AN=102139, Gender=F, Race=White, Age=23 Years, Rel Day of Study Medication Discontinuance†=1									

C Confidential

付録 2.7.4-28 最終投与後 90 日までに発現した重篤な有害事象の一覧
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 2 mg/kg Q3W									
Study Number=3475-002, Site Number=0025, AN=102139, Gender=F, Race=White, Age=23 Years, Rel Day of Study Medication Discontinuance†=1									
102139	Safety Follow-up	12	Abdominal pain	3.14 Weeks	3	Y	N	None	Resolved
Study Number=3475-002, Site Number=0027, AN=100326, Gender=M, Race=White, Age=55 Years, Rel Day of Study Medication Discontinuance†=64									
100326	Treatment Cycle 3	54	Angina pectoris	1.43 Weeks	2	Y	N	None	Resolved
	Safety Follow-up	90	Cough	2 Days	2	Y	N	None	Resolved
	Extended Safety Follow-up	96	Vomiting	1 Weeks	3	Y	N	None	Resolved
Study Number=3475-002, Site Number=0031, AN=100071, Gender=M, Race=White, Age=71 Years, Rel Day of Study Medication Discontinuance†=260									
100071	Treatment Cycle 12	247	Viral infection	1.43 Weeks	3	Y	N	None	Resolved
Study Number=3475-002, Site Number=0031, AN=101267, Gender=M, Race=White, Age=40 Years, Rel Day of Study Medication Discontinuance†=126									
101267	Treatment Cycle 7	126	Paraesthesia	2.86 Weeks	4	Y	N	None	Sequelae
Study Number=3475-002, Site Number=0031, AN=101270, Gender=M, Race=White, Age=77 Years, Rel Day of Study Medication Discontinuance†=85									
101270	Safety Follow-up	104	Generalised oedema	4.63 Months	4	Y	Y	Discontinued	Resolved
	Extended Safety Follow-up	136	Hyperglycaemia	2 Days	3	Y	N	N/A	Resolved
Study Number=3475-002, Site Number=0033, AN=100013, Gender=F, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=156									
100013	Safety Follow-up	163	Syncope	3 Days	3	Y	N	None	Resolved
Study Number=3475-002, Site Number=0033, AN=100043, Gender=F, Race=White, Age=40 Years, Rel Day of Study Medication Discontinuance†=22									

C Confidential

付録 2.7.4-28 最終投与後 90 日までに発現した重篤な有害事象の一覧

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 2 mg/kg Q3W									
Study Number=3475-002, Site Number=0033, AN=100043, Gender=F, Race=White, Age=40 Years, Rel Day of Study Medication Discontinuance†=22									
100043	Treatment Cycle 1	14	Nausea	Continuing	3	Y	N	None	Not Resolved
	Safety Follow-up	35	Confusional state	1.86 Weeks	3	Y	N	None	Resolved
		35	Dehydration	1.86 Weeks	3	Y	N	None	Resolved
		35	Encephalopathy	1.86 Weeks	3	Y	N	None	Resolved
		35	Fall	1.86 Weeks	3	Y	N	None	Resolved
		35	Vomiting	1.86 Weeks	3	Y	N	None	Resolved
Study Number=3475-002, Site Number=0033, AN=101213, Gender=M, Race=White, Age=62 Years, Rel Day of Study Medication Discontinuance†=									
101213	Treatment Cycle 17	360	Rib fracture	3 Days	3	Y	N	None	Resolved
Study Number=3475-002, Site Number=0034, AN=100025, Gender=M, Race=White, Age=53 Years, Rel Day of Study Medication Discontinuance†=186									
100025	Treatment Cycle 2	34	Haemoptysis	3 Days	3	Y	N	None	Resolved
	Treatment Cycle 9	174	Haemoptysis	3 Days	1	Y	N	None	Resolved
Study Number=3475-002, Site Number=0034, AN=101258, Gender=F, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance†=									
101258	Treatment Cycle 6	132	Adrenocortical insufficiency acute	4 Days	3	Y	N	None	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
	Safety Follow-up	113	Sepsis	4.14 Weeks	3	Y	N	N/A	Resolved
	Extended Safety Follow-up	154	Abdominal pain	1.43 Weeks	3	Y	N	N/A	Sequelae

C Confidential

付録 2.7.4-28 最終投与後 90 日までに発現した重篤な有害事象の一覧

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 2 mg/kg Q3W									
Study Number=3475-002, Site Number=0036, AN=101229, Gender=M, Race=Black Or African American, Age=60 Years, Rel Day of Study Medication Discontinuance†=125									
101229	Extended Safety Follow-up	163	Haemothorax	4 Days	5	Y	N	N/A	Fatal
Study Number=3475-002, Site Number=0042, AN=101846, Gender=F, Race=White, Age=55 Years, Rel Day of Study Medication Discontinuance†=22									
101846	Safety Follow-up	32	Mental status changes	1.43 Weeks	3	Y	N	N/A	Resolved
		32	Renal failure acute	Unknown	2	Y	N	None	Unknown
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
	Extended Safety Follow-up	104	Dyspnoea	Continuing	3	Y	N	None	Not Resolved
Study Number=3475-002, Site Number=0054, AN=100092, Gender=M, Race=White, Age=78 Years, Rel Day of Study Medication Discontinuance†=104									
100092	Safety Follow-up	118	Anaemia	6 Days	3	Y	N	None	Resolved
Study Number=3475-002, Site Number=0054, AN=100140, Gender=F, Race=White, Age=65 Years, Rel Day of Study Medication Discontinuance†=									
100140	Treatment Cycle 4	86	Cholecystitis	3.14 Weeks	3	Y	N	None	Resolved
Study Number=3475-002, Site Number=0054, AN=101278, Gender=M, Race=White, Age=73 Years, Rel Day of Study Medication Discontinuance†=									

C Confidential

付録 2.7.4-28 最終投与後 90 日までに発現した重篤な有害事象の一覧
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 2 mg/kg Q3W									
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 3	49	Pleural effusion	4 Days	3	Y	N	None	Resolved
	Treatment Cycle 4	85	Rash maculo-papular	1.86 Weeks	3	Y	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0054, AN=101865, Gender=F, Race=Black Or African American, Age=82 Years, Rel Day of Study Medication Discontinuance†=51									
101865	Treatment Cycle 1	11	Pericardial effusion	4 Days	3	Y	Y	None	Resolved
	Safety Follow-up	74	Anaemia	Continuing	3	Y	N	None	Not 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 15	308	Gastrointestinal pain	3.09 Months	3	Y	N	None	Resolved
Study Number=3475-002, Site Number=0061, AN=101810, Gender=M, Race=Asian, Age=72 Years, Rel Day of Study Medication Discontinuance†=1									
101810	Safety Follow-up	6	Mental status changes	2.86 Weeks	5	Y	N	None	Fatal
Study Number=3475-002, Site Number=0061, AN=101858, Gender=F, Race=White, Age=74 Years, Rel Day of Study Medication Discontinuance†=21									
101858	Treatment Cycle 1	4	Cellulitis	6 Days	3	Y	N	None	Resolved
		4	Deep vein thrombosis	6 Days	3	Y	N	None	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
		69	Metastases to lymph nodes	Continuing	1	Y	N	N/A	Not Resolved
Study Number=3475-002, Site Number=0080, AN=100617, Gender=M, Race=White, Age=65 Years, Rel Day of Study Medication Discontinuance†=216									
100617	Treatment Cycle 2	22	Pneumonia	1.29 Weeks	3	Y	N	None	Resolved

C Confidential

付録 2.7.4-28 最終投与後 90 日までに発現した重篤な有害事象の一覧
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 2 mg/kg Q3W									
Study Number=3475-002, Site Number=0080, AN=100617, Gender=M, Race=White, Age=65 Years, Rel Day of Study Medication Discontinuance†=216									
100617	Treatment Cycle 7	140	Device dislocation	2.86 Weeks	3	Y	N	None	Resolved
	Treatment Cycle 10	202	Dyspnoea exertional	4 Days	3	Y	N	None	Sequelae
	Safety Follow-up	231	General physical health deterioration	3.35 Months	5	Y	N	Discontinued	Fatal
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
		232	Anaemia	1.41 Months	3	Y	N	None	Sequelae
Study Number=3475-002, Site Number=0080, AN=100922, Gender=F, Race=White, Age=58 Years, Rel Day of Study Medication Discontinuance†=128									
100922	Safety Follow-up	148	Cerebrovascular accident	Continuing	3	Y	N	None	Not Resolved
	Extended Safety Follow-up	161	Haemorrhagic infarction	23 Hours	5	Y	N	None	Fatal
Study Number=3475-002, Site Number=0081, AN=100031, Gender=M, Race=White, Age=55 Years, Rel Day of Study Medication Discontinuance†=22									
100031	Treatment Cycle 1	16	Metastases to central nervous system	3.43 Weeks	4	Y	N	None	Resolved
Study Number=3475-002, Site Number=0081, AN=101820, Gender=M, Race=White, Age=63 Years, Rel Day of Study Medication Discontinuance†=1									
101820	Safety Follow-up	19	Hepatic failure	3 Days	5	Y	N	Discontinued	Fatal
Study Number=3475-002, Site Number=0082, AN=100636, Gender=F, Race=White, Age=61 Years, Rel Day of Study Medication Discontinuance†=60									
100636	Treatment Cycle 1	11	Oedema	1.91 Months	3	Y	N	Discontinued	Resolved
	Treatment Cycle 2	37	Postrenal failure	1 Weeks	3	Y	N	None	Resolved
	Treatment Cycle 3	53	Malaise	2.29 Weeks	3	Y	N	None	Resolved

C Confidential

付録 2.7.4-28 最終投与後 90 日までに発現した重篤な有害事象の一覧
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 2 mg/kg Q3W									
Study Number=3475-002, Site Number=0082, AN=100639, Gender=M, Race=White, Age=76 Years, Rel Day of Study Medication Discontinuance†=246									
100639	Extended Safety Follow-up	288	Aplasia	1.43 Weeks	4	Y	N	N/A	Resolved
Study Number=3475-002, Site Number=0082, AN=100679, Gender=F, Race=White, Age=73 Years, Rel Day of Study Medication Discontinuance†=77									
100679	Safety Follow-up	84	Ileus	2.29 Weeks	3	Y	N	None	Resolved
Study Number=3475-002, Site Number=0087, AN=102107, Gender=M, Race=White, Age=34 Years, Rel Day of Study Medication Discontinuance†=70									
102107	Treatment Cycle 1	11	Wound infection	2.76 Months	3	Y	N	None	Unknown
		15	Partial seizures	1 Weeks	3	Y	N	None	Resolved
	Treatment Cycle 2	41	Generalised oedema	1.77 Months	5	Y	N	Discontinued	Fatal
	Safety Follow-up	75	Delirium	5 Days	3	Y	N	None	Resolved
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
		147	Syncope	2 Minutes	3	Y	N	None	Resolved
Study Number=3475-002, Site Number=0088, AN=101866, Gender=M, Race=White, Age=65 Years, Rel Day of Study Medication Discontinuance†=43									
101866	Treatment Cycle 2	22	Anaemia	Continuing	3	Y	Y	None	Not Resolved
		36	Erysipelas	Continuing	3	Y	N	None	Not Resolved
		36	Tumour pain	Continuing	3	Y	N	None	Not Resolved
		37	Hydronephrosis	Continuing	2	Y	N	Discontinued	Not Resolved
Study Number=3475-002, Site Number=0090, AN=100309, Gender=F, Race=White, Age=59 Years, Rel Day of Study Medication Discontinuance†=43									

C Confidential

付録 2.7.4-28 最終投与後 90 日までに発現した重篤な有害事象の一覧
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 2 mg/kg Q3W									
Study Number=3475-002, Site Number=0090, AN=100309, Gender=F, Race=White, Age=59 Years, Rel Day of Study Medication Discontinuance†=43									
100309	Safety Follow-up	48	Generalised oedema	1.48 Months	3	Y	Y	Discontinued	Resolved
Study Number=3475-002, Site Number=0090, AN=101830, Gender=F, Race=White, Age=51 Years, Rel Day of Study Medication Discontinuance†=50									
101830	Safety Follow-up	71	Death	23 Hours	5	Y	N	None	Fatal
Study Number=3475-002, Site Number=0091, AN=100138, Gender=M, Race=White, Age=74 Years, Rel Day of Study Medication Discontinuance†=253									
100138	Treatment Cycle 3	46	Bronchitis	1.31 Months	3	Y	N	None	Resolved
Study Number=3475-002, Site Number=0091, AN=100678, Gender=M, Race=White, Age=49 Years, Rel Day of Study Medication Discontinuance†=106									
100678	Treatment Cycle 2	36	Constipation	4 Days	2	Y	N	None	Resolved
		39	Vomiting	Continuing	3	Y	N	None	Not Resolved
Study Number=3475-002, Site Number=0100, AN=100607, Gender=M, Race=White, Age=67 Years, Rel Day of Study Medication Discontinuance†=153									
100607	Safety Follow-up	163	Pyrexia	1 Weeks	1	Y	N	None	Resolved
		174	Pyrexia	2 Weeks	1	Y	N	None	Resolved
	Extended Safety Follow-up	210	Pyrexia	3 Weeks	1	Y	N	None	Resolved
Study Number=3475-002, Site Number=0100, AN=102105, Gender=M, Race=White, Age=75 Years, Rel Day of Study Medication Discontinuance†=1									
102105	Safety Follow-up	2	Dyspnoea	Continuing	4	Y	Y	None	Not Resolved
		2	Pelvic pain	Continuing	3	Y	Y	None	Not Resolved
		2	Upper gastrointestinal haemorrhage	Continuing	3	Y	Y	None	Not Resolved
		5	Death	1 Days	5	Y	Y	Discontinued	Fatal

C Confidential

付録 2.7.4-28 最終投与後 90 日までに発現した重篤な有害事象の一覧
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 2 mg/kg Q3W									
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	71	Diabetes mellitus	2 Weeks	3	Y	N	Interrupted	Resolved
	Treatment Cycle 4	106	Anaemia	3 Days	2	Y	N	None	Resolved
	Safety Follow-up	118	Septic shock	4 Days	5	Y	N	Discontinued	Fatal
Study Number=3475-002, Site Number=0103, AN=102117, Gender=F, Race=White, Age=50 Years, Rel Day of Study Medication Discontinuance†=22									
102117	Treatment Cycle 1	1	Intestinal obstruction	1.31 Months	5	Y	N	N/A	Fatal
Study Number=3475-002, Site Number=0110, AN=102128, Gender=F, Race=White, Age=51 Years, Rel Day of Study Medication Discontinuance†=22									
102128	Treatment Cycle 1	18	Mastitis	Continuing	3	Y	N	None	Not 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	Extended Safety Follow-up	77	Tumour pain	Continuing	3	Y	N	None	Resolving
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=0112, AN=101259, Gender=M, Race=White, Age=75 Years, Rel Day of Study Medication Discontinuance†=									
101259	Treatment Cycle 10	192	Lower limb fracture	3.86 Weeks	3	Y	N	None	Resolved
		198	Phlebitis	3 Weeks	3	Y	N	None	Resolved
Study Number=3475-002, Site Number=0112, AN=101883, Gender=M, Race=White, Age=65 Years, Rel Day of Study Medication Discontinuance†=									
101883	Treatment Cycle 8	170	Poor venous access	6 Days	3	Y	N	None	Resolved

C Confidential

付録 2.7.4-28 最終投与後 90 日までに発現した重篤な有害事象の一覧
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 2 mg/kg Q3W									
Study Number=3475-002, Site Number=0113, AN=101850, Gender=F, Race=White, Age=72 Years, Rel Day of Study Medication Discontinuance†=65									
101850	Treatment Cycle 1	2	Large intestinal ulcer	2.1 Months	3	Y	N	None	Resolved
Study Number=3475-002, Site Number=0120, AN=101853, Gender=M, Race=White, Age=21 Years, Rel Day of Study Medication Discontinuance†=1									
101853	Safety Follow-up	11	Constipation	1.29 Weeks	3	Y	N	N/A	Resolved
		28	Hypercalcaemia	6 Days	3	Y	N	Discontinued	Resolved
Study Number=3475-002, Site Number=0140, AN=100006, Gender=M, Race=White, Age=76 Years, Rel Day of Study Medication Discontinuance†=1									
100006	Safety Follow-up	4	Stevens-Johnson syndrome	4.14 Months	3	Y	Y	Discontinued	Resolved
Study Number=3475-002, Site Number=0140, AN=100320, Gender=M, Race=White, Age=53 Years, Rel Day of Study Medication Discontinuance†=63									
100320	Treatment Cycle 2	19	Dyspnoea	1.02 Months	3	Y	N	None	Resolved
Study Number=3475-002, Site Number=0140, AN=100620, Gender=M, Race=White, Age=55 Years, Rel Day of Study Medication Discontinuance†=252									
100620	Treatment Cycle 2	27	Metastatic pain	Continuing	3	Y	N	None	Resolving
	Treatment Cycle 5	103	Vertigo positional	3 Days	3	Y	N	None	Resolved
	Treatment Cycle 9	181	Musculoskeletal pain	1.29 Weeks	3	Y	N	None	Resolved
	Treatment Cycle 12	234	Chest pain	3 Days	3	Y	N	None	Resolved
Study Number=3475-002, Site Number=0140, AN=100902, Gender=F, Race=White, Age=52 Years, Rel Day of Study Medication Discontinuance†=122									
100902	Treatment Cycle 2	33	Spinal cord compression	1.35 Months	3	Y	N	None	Sequelae
	Treatment Cycle 5	122	Eye movement disorder	Continuing	3	Y	N	None	Not Resolved
Study Number=3475-002, Site Number=0140, AN=102127, Gender=M, Race=White, Age=56 Years, Rel Day of Study Medication Discontinuance†=1									

C Confidential

付録 2.7.4-28 最終投与後 90 日までに発現した重篤な有害事象の一覧
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 2 mg/kg Q3W									
Study Number=3475-002, Site Number=0140, AN=102127, Gender=M, Race=White, Age=56 Years, Rel Day of Study Medication Discontinuance†=1									
102127	Safety Follow-up	7	Anaemia	4 Days	4	Y	N	None	Resolved
		7	Epilepsy	Continuing	3	Y	N	None	Not Resolved
Study Number=3475-002, Site Number=0143, AN=100011, Gender=M, Race=White, Age=67 Years, Rel Day of Study Medication Discontinuance†=274									
100011	Treatment Cycle 11	223	Convulsion	15 Minutes	1	Y	N	None	Resolved
Study Number=3475-002, Site Number=0143, AN=101824, Gender=F, Race=White, Age=63 Years, Rel Day of Study Medication Discontinuance†=									
101824	Treatment Cycle 2	24	Skin mass	2.86 Weeks	3	Y	N	None	Resolved
	Treatment Cycle 3	55	Skin infection	4 Days	3	Y	N	None	Resolved
Study Number=3475-002, Site Number=0150, AN=100078, Gender=M, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance†=106									
100078	Treatment Cycle 2	29	Bronchitis	1.86 Weeks	3	Y	N	None	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=0150, AN=101223, Gender=F, Race=White, Age=84 Years, Rel Day of Study Medication Discontinuance†=									
101223	Treatment Cycle 6	111	Diverticulitis	1.43 Weeks	3	Y	N	None	Resolved
	Treatment Cycle 12	249	Diverticulum	3 Days	2	Y	N	None	Resolved
	Treatment Cycle 13	281	Diverticulitis	2 Days	2	Y	N	None	Resolved
	Treatment Cycle 15	322	Chronic obstructive pulmonary disease	2.43 Weeks	2	Y	N	None	Resolved

C Confidential

付録 2.7.4-28 最終投与後 90 日までに発現した重篤な有害事象の一覧

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 2 mg/kg Q3W									
Study Number=3475-002, Site Number=0150, AN=101502, Gender=F, Race=White, Age=60 Years, Rel Day of Study Medication Discontinuance†=42									
101502	Treatment Cycle 2	21	Asthenia	1.43 Weeks	3	Y	N	None	Resolved
Study Number=3475-002, Site Number=0150, AN=101513, Gender=M, Race=White, Age=61 Years, Rel Day of Study Medication Discontinuance†=1									
101513	Safety Follow-up	13	Confusional state	2 Days	3	Y	N	None	Resolved
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 6	135	Chest pain	3 Days	3	Y	Y	None	Resolved
Study Number=3475-002, Site Number=0151, AN=100602, Gender=M, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance†=252									
100602	Safety Follow-up	261	Haematemesis	3 Days	3	Y	N	None	Resolved
Study Number=3475-002, Site Number=0151, AN=101807, Gender=M, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=45									
101807	Treatment Cycle 1 Treatment Cycle 2 Safety Follow-up	14 24 53	Pyrexia Hyponatraemia Death	1.29 Weeks 4 Days 3 Weeks	3 3 5	Y Y Y	N N N	None None None	Resolved Resolved Fatal
Study Number=3475-002, Site Number=0170, AN=101510, Gender=F, Race=White, Age=69 Years, Rel Day of Study Medication Discontinuance†=1									
101510	Treatment Cycle 1	1	Hypophysitis	4.14 Weeks	3	Y	Y	Discontinued	Sequelae
Study Number=3475-002, Site Number=0185, AN=100129, Gender=M, Race=White, Age=77 Years, Rel Day of Study Medication Discontinuance†=203									
100129	Treatment Cycle 4 Treatment Cycle 5	73 134	Cardiogenic shock Intussusception	3 Weeks 2 Weeks	2 1	Y Y	N N	None None	Resolved Resolved

C Confidential

付録 2.7.4-28 最終投与後 90 日までに発現した重篤な有害事象の一覧

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 2 mg/kg Q3W									
Study Number=3475-002, Site Number=0185, AN=101236, Gender=F, Race=White, Age=73 Years, Rel Day of Study Medication Discontinuance†=1									
101236	Safety Follow-up	9	Infectious pleural effusion	4 Days	1	Y	N	N/A	Resolved
		16	Infectious pleural effusion	2.57 Weeks	5	Y	N	Discontinued	Fatal
Study Number=3475-002, Site Number=0189, AN=100656, Gender=F, Race=White, Age=76 Years, Rel Day of Study Medication Discontinuance†=22									
100656	Safety Follow-up	35	Cachexia	1.43 Weeks	5	Y	N	Discontinued	Fatal
MK-3475 10 mg/kg Q3W									
Study Number=3475-002, Site Number=0001, AN=100615, Gender=M, Race=White, Age=72 Years, Rel Day of Study Medication Discontinuance†=21									
100615	Safety Follow-up	35	Upper gastrointestinal haemorrhage	6 Days	5	Y	N	Discontinued	Fatal
Study Number=3475-002, Site Number=0001, AN=100672, Gender=M, Race=White, Age=47 Years, Rel Day of Study Medication Discontinuance†=1									
100672	Safety Follow-up	17	Confusional state	3 Days	1	Y	N	None	Resolved
	Extended Safety Follow-up	36	Muscular weakness	Continuing	3	Y	N	N/A	Not Resolved
Study Number=3475-002, Site Number=0007, AN=100903, Gender=M, Race=White, Age=60 Years, Rel Day of Study Medication Discontinuance†=398									
100903	Treatment Cycle 7	126	Pulmonary thrombosis	4 Days	3	Y	N	None	Sequelae
	Safety Follow-up	406	Procedural pain	Continuing	2	Y	N	Interrupted	Not Resolved
	Extended Safety Follow-up	429	Dehydration	2 Days	3	Y	N	None	Resolved
Study Number=3475-002, Site Number=0007, AN=100905, Gender=F, Race=White, Age=33 Years, Rel Day of Study Medication Discontinuance†=									

C Confidential

付録 2.7.4-28 最終投与後 90 日までに発現した重篤な有害事象の一覧
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=0007, AN=100905, Gender=F, Race=White, Age=33 Years, Rel Day of Study Medication Discontinuance†=									
100905	Treatment Cycle 9	177	Meningitis noninfective	2.14 Months	3	Y	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0007, AN=101222, Gender=F, Race=White, Age=60 Years, Rel Day of Study Medication Discontinuance†=1									
101222	Safety Follow-up	13	Asthenia	Continuing	3	Y	N	Discontinued	Not Resolved
Study Number=3475-002, Site Number=0007, AN=101823, Gender=M, Race=White, Age=55 Years, Rel Day of Study Medication Discontinuance†=22									
101823	Safety Follow-up	32	Renal failure	6 Days	3	Y	N	None	Sequelae
Study Number=3475-002, Site Number=0007, AN=101825, Gender=M, Race=White, Age=80 Years, Rel Day of Study Medication Discontinuance†=									
101825	Treatment Cycle 2	20	Infusion site extravasation	2 Hours	1	Y	N	None	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	Pneumonitis	2 Days	2	Y	Y	Discontinued	Resolved
Study Number=3475-002, Site Number=0011, AN=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
Study Number=3475-002, Site Number=0012, AN=101279, Gender=M, Race=White, Age=68 Years, Rel Day of Study Medication Discontinuance†=87									
101279	Treatment Cycle 1	1	Hypersensitivity	5 Days	2	Y	N	None	Resolved
	Safety Follow-up	93	Neck pain	2.14 Weeks	3	Y	N	None	Resolved
		109	Pneumonia aspiration	1.14 Weeks	3	Y	N	None	Resolved
Study Number=3475-002, Site Number=0016, AN=100040, Gender=M, Race=White, Age=76 Years, Rel Day of Study Medication Discontinuance†=1									

C Confidential

付録 2.7.4-28 最終投与後 90 日までに発現した重篤な有害事象の一覧
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=0016, AN=100040, Gender=M, Race=White, Age=76 Years, Rel Day of Study Medication Discontinuance†=1									
100040	Safety Follow-up	14	Hyponatraemia	2 Weeks	4	Y	Y	Discontinued	Resolved
Study Number=3475-002, Site Number=0016, AN=100612, Gender=M, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance†=63									
100612	Treatment Cycle 3	41	Pyrexia	3 Days	2	Y	N	None	Resolved
Study Number=3475-002, Site Number=0016, AN=101821, Gender=M, Race=White, Age=74 Years, Rel Day of Study Medication Discontinuance†=1									
101821	Safety Follow-up	9	Arthralgia	Continuing		Y	Y	None	Not Resolved
		9	Fatigue	Continuing		Y	N	N/A	Not Resolved
		9	Pyrexia	Continuing		Y	Y	None	Not Resolved
		14	Candida infection	Continuing	3	Y	N	N/A	Resolving
Study Number=3475-002, Site Number=0017, AN=101815, Gender=M, Race=White, Age=37 Years, Rel Day of Study Medication Discontinuance†=									
101815	Treatment Cycle 6	107	Herpes zoster	Continuing	3	Y	N	None	Resolving
Study Number=3475-002, Site Number=0018, AN=101520, Gender=F, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=61									
101520	Treatment Cycle 3	43	Sciatica	5 Days	3	Y	N	N/A	Resolved
Study Number=3475-002, Site Number=0025, AN=102125, Gender=F, Race=White, Age=59 Years, Rel Day of Study Medication Discontinuance†=22									
102125	Treatment Cycle 1	5	Pain	1.86 Weeks	3	Y	N	None	Resolved
	Safety Follow-up	25	Lumbar radiculopathy	6 Days	3	Y	N	None	Resolved
Study Number=3475-002, Site Number=0027, AN=101273, Gender=M, Race=White, Age=48 Years, Rel Day of Study Medication Discontinuance†=									
101273	Treatment Cycle 6	127	Arthralgia	2.86 Weeks	3	Y	Y	Reduced	Resolved

C Confidential

付録 2.7.4-28 最終投与後 90 日までに発現した重篤な有害事象の一覧
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=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=0029, AN=101233, Gender=M, Race=White, Age=74 Years, Rel Day of Study Medication Discontinuance†=									
101233	Treatment Cycle 11	215	Hyperparathyroidism	2.68 Hours	2	Y	N	None	Resolved
Study Number=3475-002, Site Number=0032, AN=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
Study Number=3475-002, Site Number=0033, AN=100609, Gender=M, Race=White, Age=43 Years, Rel Day of Study Medication Discontinuance†=									
100609	Treatment Cycle 3	50	Hemiparesis	4 Days	2	Y	N	None	Resolved
Study Number=3475-002, Site Number=0033, AN=100663, Gender=F, Race=White, Age=33 Years, Rel Day of Study Medication Discontinuance†=64									
100663	Treatment Cycle 2	33	Ileus	4 Days	2	Y	N	N/A	Resolved
Study Number=3475-002, Site Number=0033, AN=101504, Gender=F, Race=White, Age=43 Years, Rel Day of Study Medication Discontinuance†=112									
101504	Treatment Cycle 1	8	Hypoxia	2.29 Weeks	2	Y	N	None	Resolved
		20	Dyspnoea	Continuing	3	Y	N	None	Not Resolved
	Safety Follow-up	122	Cardiac ventricular disorder	1.71 Weeks	3	Y	N	Discontinued	Sequelae
Study Number=3475-002, Site Number=0046, AN=102136, Gender=M, Race=White, Age=62 Years, Rel Day of Study Medication Discontinuance†=1									

C Confidential

付録 2.7.4-28 最終投与後 90 日までに発現した重篤な有害事象の一覧

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=0046, AN=102136, Gender=M, Race=White, Age=62 Years, Rel Day of Study Medication Discontinuance†=1									
102136	Safety Follow-up	7	Pleural effusion	Continuing	3	Y	N	None	Not Resolved
		7	Pulmonary embolism	Continuing	3	Y	N	N/A	Not Resolved
		20	Deep vein thrombosis	Continuing	2	Y	N	None	Not Resolved
Study Number=3475-002, Site Number=0053, AN=101848, Gender=F, Race=White, Age=83 Years, Rel Day of Study Medication Discontinuance†=64									
101848	Safety Follow-up	72	General physical health deterioration	Continuing	4	Y	N	Discontinued	Not Resolved
Study Number=3475-002, Site Number=0070, AN=100108, Gender=M, Race=White, Age=51 Years, Rel Day of Study Medication Discontinuance†=148									
100108	Extended Safety Follow-up	213	Colitis	2.23 Months	3	Y	N	N/A	Resolved
Study Number=3475-002, Site Number=0070, AN=101856, Gender=M, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=1									
101856	Safety Follow-up	2	Abdominal pain	2.71 Weeks	2	Y	N	None	Resolved
Study Number=3475-002, Site Number=0077, AN=100690, Gender=M, Race=White, Age=61 Years, Rel Day of Study Medication Discontinuance†=106									
100690	Extended Safety Follow-up	167	Odynophagia	4.29 Weeks	3	Y	N	N/A	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
	Safety Follow-up	28	Hypopituitarism	Continuing	3	Y	Y	Discontinued	Not Resolved
Study Number=3475-002, Site Number=0080, AN=100909, Gender=F, Race=White, Age=49 Years, Rel Day of Study Medication Discontinuance†=1									

C Confidential

付録 2.7.4-28 最終投与後 90 日までに発現した重篤な有害事象の一覧

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=0080, AN=100909, Gender=F, Race=White, Age=49 Years, Rel Day of Study Medication Discontinuance†=1									
100909	Safety Follow-up	19	General physical health deterioration	6 Days	5	Y	N	Discontinued	Fatal
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	8	Autoimmune hepatitis	Continuing	3	Y	Y	Discontinued	Resolving
		13	Iritis	1.02 Months	3	Y	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0080, AN=101813, Gender=F, Race=White, Age=49 Years, Rel Day of Study Medication Discontinuance†=1									
101813	Safety Follow-up	9	General physical health deterioration	1 Days	5	Y	N	Discontinued	Fatal
Study Number=3475-002, Site Number=0080, AN=102131, Gender=M, Race=White, Age=63 Years, Rel Day of Study Medication Discontinuance†=1									
102131	Safety Follow-up	22	Hepatic failure	2 Days	5	Y	N	Discontinued	Fatal
Study Number=3475-002, Site Number=0081, AN=100052, Gender=M, Race=White, Age=53 Years, Rel Day of Study Medication Discontinuance†=106									
100052	Treatment Cycle 4	81	General physical health deterioration	2 Days	3	Y	N	None	Resolved
Study Number=3475-002, Site Number=0081, AN=100628, Gender=F, Race=White, Age=71 Years, Rel Day of Study Medication Discontinuance†=64									
100628	Treatment Cycle 1	18	Spinal fracture	3.43 Weeks	3	Y	N	None	Sequelae
	Safety Follow-up	85	Death	1 Days	5	Y	N	Discontinued	Fatal
Study Number=3475-002, Site Number=0081, AN=101834, Gender=M, Race=White, Age=74 Years, Rel Day of Study Medication Discontinuance†=148									
101834	Treatment Cycle 4	84	Salmonellosis	1.43 Weeks	2	Y	N	None	Resolved
	Safety Follow-up	153	Spondylolisthesis	3 Days	3	Y	N	None	Sequelae
		158	Cardiac failure	2.57 Weeks	3	Y	N	None	Resolved

C Confidential

付録 2.7.4-28 最終投与後 90 日までに発現した重篤な有害事象の一覧
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=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=0087, AN=100655, Gender=F, Race=White, Age=78 Years, Rel Day of Study Medication Discontinuance†=64									
100655	Treatment Cycle 1	5	Vomiting	3 Days	3	Y	N	None	Resolved
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 7 Treatment Cycle 9	137 176	Osteolysis Erythema multiforme	Continuing Continuing	3 3	Y Y	N Y	None Interrupted	Resolving Not Resolved
Study Number=3475-002, Site Number=0090, AN=100911, Gender=M, Race=White, Age=67 Years, Rel Day of Study Medication Discontinuance†=22									
100911	Safety Follow-up	39	Dyspnoea	1.71 Weeks	5	Y	N	Discontinued	Fatal
Study Number=3475-002, Site Number=0090, AN=101225, Gender=F, Race=White, Age=29 Years, Rel Day of Study Medication Discontinuance†=1									
101225	Safety Follow-up	10	Dyspnoea	5 Days	5	Y	N	Discontinued	Fatal
Study Number=3475-002, Site Number=0101, AN=101804, Gender=F, Race=White, Age=59 Years, Rel Day of Study Medication Discontinuance†=43									
101804	Safety Follow-up	61	Back pain	Continuing	3	Y	N	Discontinued	Not Resolved
Study Number=3475-002, Site Number=0101, AN=101868, Gender=M, Race=White, Age=35 Years, Rel Day of Study Medication Discontinuance†=									
101868	Treatment Cycle 1	11	Superior vena cava syndrome	3.09 Months	3	Y	N	None	Resolved
Study Number=3475-002, Site Number=0102, AN=100305, Gender=M, Race=White, Age=54 Years, Rel Day of Study Medication Discontinuance†=85									
100305	Treatment Cycle 5	85	Anaphylactic reaction	3.5 Hours	4	Y	Y	None	Resolved

C Confidential

付録 2.7.4-28 最終投与後 90 日までに発現した重篤な有害事象の一覧
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=0103, AN=101231, Gender=M, Race=White, Age=58 Years, Rel Day of Study Medication Discontinuance†=43									
101231	Treatment Cycle 1	3	Pyrexia	2.14 Weeks	1	Y	N	None	Resolved
		10	Venous thrombosis	2.14 Weeks	2	Y	N	None	Sequelae
	Treatment Cycle 2	34	Hyponatraemia	1.71 Weeks	3	Y	N	None	Resolved
	Safety Follow-up	67	Groin pain	Continuing	3	Y	N	N/A	Not Resolved
Study Number=3475-002, Site Number=0110, AN=100614, Gender=M, Race=White, Age=29 Years, Rel Day of Study Medication Discontinuance†=103									
100614	Safety Follow-up	110	Abdominal pain	Continuing	3	Y	N	None	Not Resolved
Study Number=3475-002, Site Number=0112, AN=100018, Gender=M, Race=White, Age=49 Years, Rel Day of Study Medication Discontinuance†=60									
100018	Treatment Cycle 3	48	Ascites	Continuing	3	Y	N	N/A	Not Resolved
Study Number=3475-002, Site Number=0112, AN=102106, Gender=M, Race=White, Age=54 Years, Rel Day of Study Medication Discontinuance†=64									
102106	Treatment Cycle 1	10	Dizziness	3.43 Weeks	3	Y	N	None	Resolved
	Treatment Cycle 3	55	Ileus	Continuing	3	Y	N	None	Not 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
	Extended Safety Follow-up	99	Constipation	5 Days	2	Y	N	None	Resolved
Study Number=3475-002, Site Number=0113, AN=102112, Gender=M, Race=White, Age=34 Years, Rel Day of Study Medication Discontinuance†=1									
102112	Safety Follow-up	4	Abdominal pain	1.29 Weeks	2	Y	Y	None	Resolved
		21	Confusional state	Continuing	1	Y	N	None	Not Resolved

Confidential

付録 2.7.4-28 最終投与後 90 日までに発現した重篤な有害事象の一覧

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	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
	Safety Follow-up	108	Adrenocortical insufficiency acute	Continuing	3	Y	N	None	Not Resolved
Study Number=3475-002, Site Number=0140, AN=100010, Gender=F, Race=White, Age=54 Years, Rel Day of Study Medication Discontinuance†=106									
100010	Treatment Cycle 1	11	Dyspnoea	Continuing	3	Y	N	None	Not 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	33	Erysipelas	1.57 Weeks	3	Y	Y	None	Resolved
		43	Peripheral motor neuropathy	2.79 Months	2	Y	Y	Interrupted	Resolved
Study Number=3475-002, Site Number=0150, AN=101501, Gender=M, Race=White, Age=77 Years, Rel Day of Study Medication Discontinuance†=									
101501	Treatment Cycle 21	428	Influenza	6 Days	3	Y	N	None	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

C Confidential

付録 2.7.4-28 最終投与後 90 日までに発現した重篤な有害事象の一覧
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=0150, AN=101808, Gender=F, Race=White, Age=80 Years, Rel Day of Study Medication Discontinuance†=211									
101808	Safety Follow-up	218	Death	1 Days	5	Y	N	Discontinued	Fatal
Study Number=3475-002, Site Number=0150, AN=102101, Gender=M, Race=White, Age=50 Years, Rel Day of Study Medication Discontinuance†=63									
102101	Treatment Cycle 3	58	Abdominal pain	5 Days	3	Y	N	None	Resolved
Study Number=3475-002, Site Number=0151, AN=100002, Gender=F, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance†=212									
100002	Treatment Cycle 2	83	Diarrhoea	9.07 Months	2	Y	Y	None	Resolved
Study Number=3475-002, Site Number=0153, AN=101228, Gender=M, Race=White, Age=85 Years, Rel Day of Study Medication Discontinuance†=									
101228	Treatment Cycle 3	61	Pneumonia	3.86 Weeks	3	Y	N	None	Resolved
	Treatment Cycle 7	144	Diarrhoea	3 Weeks	3	Y	Y	None	Resolved
Study Number=3475-002, Site Number=0170, AN=100622, Gender=M, Race=White, Age=76 Years, Rel Day of Study Medication Discontinuance†=1									
100622	Safety Follow-up	13	Hypopituitarism	1.02 Months	3	Y	Y	Discontinued	Sequelae
Study Number=3475-002, Site Number=0170, AN=100682, Gender=M, Race=White, Age=74 Years, Rel Day of Study Medication Discontinuance†=									
100682	Treatment Cycle 4	78	Urinary tract infection	6 Days	3	Y	N	None	Resolved
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
Study Number=3475-002, Site Number=0180, AN=101272, Gender=F, Race=White, Age=74 Years, Rel Day of Study Medication Discontinuance†=64									

C Confidential

付録 2.7.4-28 最終投与後 90 日までに発現した重篤な有害事象の一覧

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=0180, AN=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
Study Number=3475-002, Site Number=0186, AN=100050, Gender=M, Race=White, Age=76 Years, Rel Day of Study Medication Discontinuance†=172									
100050	Safety Follow-up	188	General physical health deterioration	3.43 Weeks	3	Y	N	None	Sequelae
Study Number=3475-002, Site Number=0189, AN=100321, Gender=M, Race=White, Age=82 Years, Rel Day of Study Medication Discontinuance†=86									
100321	Safety Follow-up	113	Orthostatic hypotension	1.14 Weeks	2	Y	N	None	Resolved
		114	Pneumonia	1.71 Weeks	2	Y	N	None	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]

C Confidential

付録 2.7.4-29 最終投与後 90 日までに発現した重篤な副作用
（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	17	(9.9)	14	(7.9)	20	(11.2)
with no adverse events	154	(90.1)	164	(92.1)	159	(88.8)
Blood and lymphatic system disorders	**8**	**(4.7)**	**1**	**(0.6)**	**0**	**(0.0)**
Anaemia	3	(1.8)	1	(0.6)	0	(0.0)
Febrile neutropenia	2	(1.2)	0	(0.0)	0	(0.0)
Leukopenia	1	(0.6)	0	(0.0)	0	(0.0)
Neutropenia	1	(0.6)	0	(0.0)	0	(0.0)
Thrombocytopenia	2	(1.2)	0	(0.0)	0	(0.0)
Cardiac disorders	**0**	**(0.0)**	**1**	**(0.6)**	**0**	**(0.0)**
Pericardial effusion	0	(0.0)	1	(0.6)	0	(0.0)
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)
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)**	**5**	**(2.8)**	**4**	**(2.2)**
Abdominal pain	0	(0.0)	0	(0.0)	1	(0.6)
Colitis	0	(0.0)	1	(0.6)	0	(0.0)
Diarrhoea	0	(0.0)	0	(0.0)	3	(1.7)
Dysphagia	0	(0.0)	1	(0.6)	0	(0.0)
Nausea	3	(1.8)	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)
Upper gastrointestinal haemorrhage	0	(0.0)	1	(0.6)	0	(0.0)
Vomiting	1	(0.6)	0	(0.0)	0	(0.0)
General disorders and administration site conditions	**2**	**(1.2)**	**4**	**(2.2)**	**1**	**(0.6)**
Chest pain	0	(0.0)	1	(0.6)	0	(0.0)
Death	0	(0.0)	1	(0.6)	0	(0.0)
Generalised oedema	0	(0.0)	2	(1.1)	0	(0.0)
Pyrexia	2	(1.2)	0	(0.0)	1	(0.6)
Hepatobiliary disorders	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.6)**

C Confidential

付録 2.7.4-29 最終投与後 90 日までに発現した重篤な副作用
（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	(%)
Hepatobiliary disorders	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.6)**
Autoimmune hepatitis	0	(0.0)	0	(0.0)	1	(0.6)
Immune system disorders	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.6)**
Anaphylactic reaction	0	(0.0)	0	(0.0)	1	(0.6)
Infections and infestations	**3**	**(1.8)**	**0**	**(0.0)**	**1**	**(0.6)**
Bacteraemia	1	(0.6)	0	(0.0)	0	(0.0)
Erysipelas	0	(0.0)	0	(0.0)	1	(0.6)
Pneumonia	1	(0.6)	0	(0.0)	0	(0.0)
Soft tissue infection	1	(0.6)	0	(0.0)	0	(0.0)
Investigations	**2**	**(1.2)**	**0**	**(0.0)**	**1**	**(0.6)**
Alanine aminotransferase increased	0	(0.0)	0	(0.0)	1	(0.6)
Aspartate aminotransferase increased	0	(0.0)	0	(0.0)	1	(0.6)
Neutrophil count decreased	1	(0.6)	0	(0.0)	0	(0.0)
Platelet count decreased	2	(1.2)	0	(0.0)	0	(0.0)
White blood cell count decreased	1	(0.6)	0	(0.0)	0	(0.0)
Metabolism and nutrition disorders	**2**	**(1.2)**	**0**	**(0.0)**	**1**	**(0.6)**
Dehydration	1	(0.6)	0	(0.0)	0	(0.0)
Hypocalcaemia	1	(0.6)	0	(0.0)	0	(0.0)
Hyponatraemia	0	(0.0)	0	(0.0)	1	(0.6)
Musculoskeletal and connective tissue disorders	**0**	**(0.0)**	**0**	**(0.0)**	**2**	**(1.1)**
Arthralgia	0	(0.0)	0	(0.0)	2	(1.1)
Nervous system disorders	**0**	**(0.0)**	**0**	**(0.0)**	**3**	**(1.7)**
Meningitis noninfective	0	(0.0)	0	(0.0)	1	(0.6)
Myasthenic syndrome	0	(0.0)	0	(0.0)	1	(0.6)
Peripheral motor neuropathy	0	(0.0)	0	(0.0)	1	(0.6)
Psychiatric disorders	**1**	**(0.6)**	**0**	**(0.0)**	**0**	**(0.0)**
Confusional state	1	(0.6)	0	(0.0)	0	(0.0)
Renal and urinary disorders	**1**	**(0.6)**	**1**	**(0.6)**	**0**	**(0.0)**
Renal failure acute	1	(0.6)	0	(0.0)	0	(0.0)
Tubulointerstitial nephritis	0	(0.0)	1	(0.6)	0	(0.0)

C Confidential

付録 2.7.4-29 最終投与後 90 日までに発現した重篤な副作用
（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	(%)
Reproductive system and breast disorders	**0**	**(0.0)**	**1**	**(0.6)**	**0**	**(0.0)**
Pelvic pain	0	(0.0)	1	(0.6)	0	(0.0)
Respiratory, thoracic and mediastinal disorders	**0**	**(0.0)**	**2**	**(1.1)**	**4**	**(2.2)**
Dyspnoea	0	(0.0)	1	(0.6)	0	(0.0)
Interstitial lung disease	0	(0.0)	0	(0.0)	1	(0.6)
Laryngeal inflammation	0	(0.0)	1	(0.6)	0	(0.0)
Pneumonitis	0	(0.0)	0	(0.0)	3	(1.7)
Skin and subcutaneous tissue disorders	**0**	**(0.0)**	**2**	**(1.1)**	**1**	**(0.6)**
Erythema multiforme	0	(0.0)	0	(0.0)	1	(0.6)
Rash maculo-papular	0	(0.0)	1	(0.6)	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.
(Database Cutoff Date: 12MAY2014).

Data Source: [資料5.3.5.1.1: P002V01]

C Confidential

付録 2.7.4-30 最終投与後 90 日までに発現した重篤な有害事象
（いずれかの投与群で発現割合 0%超）
006 試験（MK-3475 併合）（APaT 集団）

	Control		MK-3475 combined	
	n	(%)	n	(%)
Subjects in population	256		555	
with one or more adverse events	81	(31.6)	148	(26.7)
with no adverse events	175	(68.4)	407	(73.3)
Blood and lymphatic system disorders	**0**	**(0.0)**	**8**	**(1.4)**
Anaemia	0	(0.0)	6	(1.1)
Thrombocytopenia	0	(0.0)	2	(0.4)
Cardiac disorders	**2**	**(0.8)**	**10**	**(1.8)**
Acute coronary syndrome	0	(0.0)	1	(0.2)
Angina unstable	0	(0.0)	1	(0.2)
Atrial fibrillation	0	(0.0)	2	(0.4)
Atrial flutter	1	(0.4)	0	(0.0)
Cardiac failure	0	(0.0)	3	(0.5)
Cardiac failure congestive	0	(0.0)	2	(0.4)
Cardio-respiratory arrest	1	(0.4)	0	(0.0)
Myocardial infarction	0	(0.0)	1	(0.2)
Pericardial effusion	0	(0.0)	1	(0.2)
Endocrine disorders	**5**	**(2.0)**	**5**	**(0.9)**
Adrenal insufficiency	1	(0.4)	2	(0.4)
Hypophysitis	2	(0.8)	1	(0.2)
Hypopituitarism	2	(0.8)	1	(0.2)
Thyroiditis	0	(0.0)	1	(0.2)
Eye disorders	**2**	**(0.8)**	**1**	**(0.2)**
Diplopia	1	(0.4)	0	(0.0)
Glaucoma	0	(0.0)	1	(0.2)
Uveitis	1	(0.4)	0	(0.0)
Gastrointestinal disorders	**36**	**(14.1)**	**33**	**(5.9)**
Abdominal distension	0	(0.0)	1	(0.2)
Abdominal pain	2	(0.8)	2	(0.4)
Abdominal pain lower	0	(0.0)	1	(0.2)
Anal fistula	0	(0.0)	1	(0.2)
Autoimmune pancreatitis	0	(0.0)	1	(0.2)

C Confidential

付録 2.7.4-30 最終投与後 90 日までに発現した重篤な有害事象
（いずれかの投与群で発現割合 0%超）
006 試験（MK-3475 併合）（APaT 集団）（続き）

	Control		MK-3475 combined	
	n	(%)	n	(%)
Gastrointestinal disorders	**36**	**(14.1)**	**33**	**(5.9)**
Colitis	16	(6.3)	10	(1.8)
Constipation	1	(0.4)	0	(0.0)
Diarrhoea	10	(3.9)	12	(2.2)
Enteritis	1	(0.4)	0	(0.0)
Enterocolitis	2	(0.8)	0	(0.0)
Gastritis	0	(0.0)	2	(0.4)
Gastrointestinal haemorrhage	1	(0.4)	1	(0.2)
Gastrooesophageal reflux disease	1	(0.4)	0	(0.0)
Ileus	0	(0.0)	1	(0.2)
Intestinal obstruction	0	(0.0)	2	(0.4)
Intestinal stenosis	1	(0.4)	0	(0.0)
Large intestine perforation	1	(0.4)	0	(0.0)
Lower gastrointestinal haemorrhage	1	(0.4)	0	(0.0)
Nausea	1	(0.4)	0	(0.0)
Oesophagitis	0	(0.0)	1	(0.2)
Pancreatitis	0	(0.0)	1	(0.2)
Small intestinal obstruction	0	(0.0)	1	(0.2)
Stomatitis necrotising	0	(0.0)	1	(0.2)
Vomiting	3	(1.2)	1	(0.2)
General disorders and administration site conditions	**8**	**(3.1)**	**10**	**(1.8)**
Asthenia	0	(0.0)	1	(0.2)
Chest pain	1	(0.4)	0	(0.0)
Death	1	(0.4)	1	(0.2)
Fatigue	0	(0.0)	1	(0.2)
General physical health deterioration	1	(0.4)	2	(0.4)
Generalised oedema	0	(0.0)	1	(0.2)
Malaise	0	(0.0)	2	(0.4)
Pain	1	(0.4)	0	(0.0)
Pyrexia	4	(1.6)	2	(0.4)
Hepatobiliary disorders	**5**	**(2.0)**	**11**	**(2.0)**
Autoimmune hepatitis	1	(0.4)	4	(0.7)
Bile duct obstruction	1	(0.4)	0	(0.0)

Confidential

付録 2.7.4-30 最終投与後 90 日までに発現した重篤な有害事象
（いずれかの投与群で発現割合 0%超）
006 試験（MK-3475 併合）（APaT 集団）（続き）

	Control		MK-3475 combined	
	n	(%)	n	(%)
Hepatobiliary disorders	**5**	**(2.0)**	**11**	**(2.0)**
Cholangitis	1	(0.4)	0	(0.0)
Cholecystitis	0	(0.0)	1	(0.2)
Drug-induced liver injury	0	(0.0)	2	(0.4)
Hepatic function abnormal	0	(0.0)	1	(0.2)
Hepatitis	0	(0.0)	3	(0.5)
Hepatocellular injury	2	(0.8)	0	(0.0)
Hepatotoxicity	1	(0.4)	0	(0.0)
Hyperbilirubinaemia	0	(0.0)	1	(0.2)
Immune system disorders	**0**	**(0.0)**	**2**	**(0.4)**
Anaphylactoid reaction	0	(0.0)	1	(0.2)
Drug hypersensitivity	0	(0.0)	1	(0.2)
Infections and infestations	**15**	**(5.9)**	**23**	**(4.1)**
Bacterial sepsis	0	(0.0)	1	(0.2)
Bronchitis	0	(0.0)	2	(0.4)
Cellulitis	1	(0.4)	1	(0.2)
Clostridium difficile colitis	1	(0.4)	0	(0.0)
Colonic abscess	1	(0.4)	0	(0.0)
Cystitis	1	(0.4)	0	(0.0)
Encephalitis	0	(0.0)	1	(0.2)
Endocarditis	1	(0.4)	0	(0.0)
Endocarditis staphylococcal	1	(0.4)	0	(0.0)
Erysipelas	1	(0.4)	1	(0.2)
Escherichia bacteraemia	0	(0.0)	1	(0.2)
Gastroenteritis	0	(0.0)	1	(0.2)
Liver abscess	0	(0.0)	1	(0.2)
Lung infection	0	(0.0)	1	(0.2)
Meningitis	0	(0.0)	1	(0.2)
Myelitis	1	(0.4)	0	(0.0)
Pelvic infection	1	(0.4)	0	(0.0)
Pneumonia	3	(1.2)	3	(0.5)
Pyelonephritis	0	(0.0)	1	(0.2)
Respiratory tract infection	1	(0.4)	1	(0.2)
Sepsis	2	(0.8)	4	(0.7)

Confidential

付録 2.7.4-30 最終投与後 90 日までに発現した重篤な有害事象
（いずれかの投与群で発現割合 0%超）
006 試験（MK-3475 併合）（APaT 集団）（続き）

	Control		MK-3475 combined	
	n	(%)	n	(%)
Infections and infestations	**15**	**(5.9)**	**23**	**(4.1)**
Sinusitis	0	(0.0)	1	(0.2)
Soft tissue infection	0	(0.0)	1	(0.2)
Urinary tract infection	1	(0.4)	2	(0.4)
Injury, poisoning and procedural complications	**1**	**(0.4)**	**7**	**(1.3)**
Facial bones fracture	0	(0.0)	1	(0.2)
Femur fracture	0	(0.0)	1	(0.2)
Hip fracture	0	(0.0)	1	(0.2)
Joint injury	0	(0.0)	1	(0.2)
Radiation necrosis	0	(0.0)	2	(0.4)
Rib fracture	0	(0.0)	1	(0.2)
Wound decomposition	1	(0.4)	0	(0.0)
Investigations	**2**	**(0.8)**	**4**	**(0.7)**
Alanine aminotransferase increased	2	(0.8)	1	(0.2)
Aspartate aminotransferase increased	1	(0.4)	2	(0.4)
Blood corticotrophin decreased	0	(0.0)	1	(0.2)
Liver function test abnormal	0	(0.0)	1	(0.2)
Metabolism and nutrition disorders	**4**	**(1.6)**	**14**	**(2.5)**
Dehydration	1	(0.4)	1	(0.2)
Diabetic ketoacidosis	0	(0.0)	1	(0.2)
Failure to thrive	0	(0.0)	1	(0.2)
Gout	0	(0.0)	1	(0.2)
Hypercalcaemia	1	(0.4)	0	(0.0)
Hypoalbuminaemia	0	(0.0)	1	(0.2)
Hypokalaemia	0	(0.0)	3	(0.5)
Hyponatraemia	1	(0.4)	4	(0.7)
Metabolic disorder	0	(0.0)	1	(0.2)
Tumour lysis syndrome	1	(0.4)	0	(0.0)
Type 1 diabetes mellitus	0	(0.0)	1	(0.2)
Musculoskeletal and connective tissue disorders	**1**	**(0.4)**	**8**	**(1.4)**

Confidential

付録 2.7.4-30 最終投与後 90 日までに発現した重篤な有害事象
（いずれかの投与群で発現割合 0%超）
006 試験（MK-3475 併合）（APaT 集団）（続き）

	Control		MK-3475 combined	
	n	(%)	n	(%)
Musculoskeletal and connective tissue disorders	**1**	**(0.4)**	**8**	**(1.4)**
Back pain	0	(0.0)	1	(0.2)
Myalgia	0	(0.0)	1	(0.2)
Pain in extremity	1	(0.4)	2	(0.4)
Pathological fracture	0	(0.0)	5	(0.9)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)	**9**	**(3.5)**	**20**	**(3.6)**
Adenocarcinoma gastric	0	(0.0)	1	(0.2)
Basal cell carcinoma	0	(0.0)	2	(0.4)
Basosquamous carcinoma	0	(0.0)	1	(0.2)
Chronic lymphocytic leukaemia	1	(0.4)	0	(0.0)
Desmoplastic melanoma	0	(0.0)	1	(0.2)
Gastrointestinal carcinoma	0	(0.0)	1	(0.2)
Intracranial tumour haemorrhage	0	(0.0)	2	(0.4)
Lymphangiosis carcinomatosa	0	(0.0)	1	(0.2)
Malignant melanoma	0	(0.0)	1	(0.2)
Metastases to central nervous system	2	(0.8)	3	(0.5)
Metastatic malignant melanoma	0	(0.0)	2	(0.4)
Papillary thyroid cancer	0	(0.0)	2	(0.4)
Papilloma	0	(0.0)	1	(0.2)
Squamous cell carcinoma	2	(0.8)	3	(0.5)
Tumour haemorrhage	3	(1.2)	0	(0.0)
Tumour pain	1	(0.4)	0	(0.0)
Nervous system disorders	**6**	**(2.3)**	**15**	**(2.7)**
Brain oedema	2	(0.8)	1	(0.2)
Cerebral haemorrhage	0	(0.0)	2	(0.4)
Cerebrovascular accident	0	(0.0)	1	(0.2)
Convulsion	0	(0.0)	3	(0.5)
Dizziness	1	(0.4)	0	(0.0)
Encephalopathy	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)

C Confidential

付録 2.7.4-30 最終投与後 90 日までに発現した重篤な有害事象
（いずれかの投与群で発現割合 0%超）
006 試験（MK-3475 併合）（APaT 集団）（続き）

	Control		MK-3475 combined	
	n	(%)	n	(%)
Nervous system disorders	**6**	**(2.3)**	**15**	**(2.7)**
Haemorrhagic stroke	0	(0.0)	1	(0.2)
Horner's syndrome	1	(0.4)	0	(0.0)
Hydrocephalus	0	(0.0)	1	(0.2)
Partial seizures	0	(0.0)	1	(0.2)
Peripheral motor neuropathy	0	(0.0)	1	(0.2)
Sciatica	0	(0.0)	1	(0.2)
Spinal cord compression	0	(0.0)	1	(0.2)
Transient ischaemic attack	1	(0.4)	0	(0.0)
Psychiatric disorders	**3**	**(1.2)**	**3**	**(0.5)**
Completed suicide	0	(0.0)	1	(0.2)
Confusional state	2	(0.8)	1	(0.2)
Depression	0	(0.0)	1	(0.2)
Mental status changes	1	(0.4)	0	(0.0)
Renal and urinary disorders	**5**	**(2.0)**	**10**	**(1.8)**
Hydronephrosis	1	(0.4)	0	(0.0)
Renal failure	2	(0.8)	3	(0.5)
Renal failure acute	1	(0.4)	4	(0.7)
Renal failure chronic	0	(0.0)	1	(0.2)
Tubulointerstitial nephritis	1	(0.4)	1	(0.2)
Urinary retention	0	(0.0)	1	(0.2)
Respiratory, thoracic and mediastinal disorders	**7**	**(2.7)**	**22**	**(4.0)**
Bronchospasm	0	(0.0)	1	(0.2)
Chronic obstructive pulmonary disease	0	(0.0)	1	(0.2)
Cough	0	(0.0)	2	(0.4)
Dyspnoea	1	(0.4)	2	(0.4)
Haemoptysis	0	(0.0)	3	(0.5)
Hypoxia	1	(0.4)	1	(0.2)
Pleural effusion	1	(0.4)	2	(0.4)
Pneumonia aspiration	1	(0.4)	0	(0.0)
Pneumonitis	2	(0.8)	4	(0.7)
Pulmonary embolism	1	(0.4)	5	(0.9)

C Confidential

付録 2.7.4-30 最終投与後 90 日までに発現した重篤な有害事象
（いずれかの投与群で発現割合 0%超）
006 試験（MK-3475 併合）（APaT 集団）（続き）

	Control		MK-3475 combined	
	n	(%)	n	(%)
Respiratory, thoracic and mediastinal disorders	**7**	**(2.7)**	**22**	**(4.0)**
Pulmonary thrombosis	0	(0.0)	1	(0.2)
Skin and subcutaneous tissue disorders	**2**	**(0.8)**	**3**	**(0.5)**
Drug eruption	1	(0.4)	0	(0.0)
Lichen planus	0	(0.0)	1	(0.2)
Rash	1	(0.4)	2	(0.4)
Vascular disorders	**1**	**(0.4)**	**8**	**(1.4)**
Aortic stenosis	0	(0.0)	1	(0.2)
Deep vein thrombosis	0	(0.0)	1	(0.2)
Haematoma	0	(0.0)	1	(0.2)
Hypotension	0	(0.0)	1	(0.2)
Orthostatic hypotension	0	(0.0)	1	(0.2)
Superior vena cava occlusion	0	(0.0)	1	(0.2)
Thrombosis	1	(0.4)	0	(0.0)
Vein disorder	0	(0.0)	1	(0.2)
Venous thrombosis	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.
SAEs were followed 90 days after last dose of study treatment.
(Database Cutoff Date: 03SEP2014).

Data Source: [資料5.3.5.1.2: P006V01]

Confidential

付録 2.7.4-31 最終投与後 90 日までに発現した重篤な有害事象の一覧

006 試験（APaT 集団）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Action Taken	Outcome
Control									
Trial Number=3475-006, Site Number=0001, Subject ID=363489, Gender=M, Race=White, Age=69 Years, Rel Day of Study Medication Discontinuance†=64									
363489	Treatment Cycle 1	15	Cellulitis	1.14 Weeks		Y	N	None	Resolved
Trial Number=3475-006, Site Number=0002, Subject ID=368229, Gender=M, Race=White, Age=86 Years, Rel Day of Study Medication Discontinuance†=64									
368229	Treatment Cycle 2	29	Squamous cell carcinoma	2.33 Months		Y	N	None	Resolved
	Extended Safety Follow-up	123	Endocarditis staphylococcal	1.54 Months		Y	N	N/A	Resolved
Trial Number=3475-006, Site Number=0003, Subject ID=361456, Gender=M, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=1									
361456	Safety Follow-up	13	Lower gastrointestinal haemorrhage	1.14 Weeks		Y	N	None	Resolved
Trial Number=3475-006, Site Number=0003, Subject ID=367445, Gender=M, Race=White, Age=67 Years, Rel Day of Study Medication Discontinuance†=48									
367445	Safety Follow-up	67	Metastases to central nervous system	Continuing		Y	N	N/A	Not Resolved

C Confidential

付録 2.7.4-31 最終投与後 90 日までに発現した重篤な有害事象の一覧
006 試験（APaT 集団）（続き）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Action Taken	Outcome
Control									
Trial Number=3475-006, Site Number=0004, Subject ID=360136, Gender=F, Race=White, Age=25 Years, Rel Day of Study Medication Discontinuance†=40									
360136	Safety Follow-up	62	Pyrexia	1.29 Weeks		Y	N	N/A	Resolved
		62	Vomiting	1.29 Weeks		Y	N	N/A	Resolved
Trial Number=3475-006, Site Number=0004, Subject ID=366132, Gender=F, Race=White, Age=56 Years, Rel Day of Study Medication Discontinuance†=62									
366132	Safety Follow-up	83	Hypophysitis	2.29 Weeks		Y	Y	None	Resolved
		84	Horner's syndrome	2.14 Weeks		Y	Y	None	Resolved
		84	Hyponatraemia	2.14 Weeks		Y	Y	None	Resolved
		90	Diplopia	1.29 Weeks		Y	Y	None	Resolved
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		Y	Y	Discontinued	Resolved
Trial Number=3475-006, Site Number=0004, Subject ID=369055, Gender=M, Race=White, Age=45 Years, Rel Day of Study Medication Discontinuance†=65									
369055	Treatment Cycle 2	35	Wound decomposition	3.35 Months		Y	N	None	Resolved

C Confidential

付録 2.7.4-31 最終投与後 90 日までに発現した重篤な有害事象の一覧
006 試験（APaT 集団）（続き）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Action Taken	Outcome
Control									
Trial Number=3475-006, Site Number=0004, Subject ID=369055, Gender=M, Race=White, Age=45 Years, Rel Day of Study Medication Discontinuance†=65									
369055	Safety Follow-up	93	Adrenal insufficiency	2.73 Months		Y	Y	N/A	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		Y	Y	Discontinued	Resolved
Trial Number=3475-006, Site Number=0102, Subject ID=361021, Gender=F, Race=White, Age=39 Years, Rel Day of Study Medication Discontinuance†=24									
361021	Treatment Cycle 1	11	Pain	4 Days		Y	N	None	Resolved
		15	Thrombosis	2 Days		Y	N	None	Sequelae
		21	Vomiting	1.57 Weeks		Y	N	None	Resolved
	Safety Follow-up	45	Tumour pain	1.57 Weeks		Y	N	N/A	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	Treatment Cycle 1	18	Enteritis	4 Days		Y	N	None	Resolved
	Safety Follow-up	30	Gastrooesophageal reflux disease	1.57 Weeks		Y	N	None	Resolved

C Confidential

付録 2.7.4-31 最終投与後 90 日までに発現した重篤な有害事象の一覧

006 試験（APaT 集団）（続き）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Action Taken	Outcome
Control									
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	43	Pyrexia	1.57 Weeks		Y	N	Interrupted	Resolved
		50	Chronic lymphocytic leukaemia	Continuing		Y	N	Discontinued	Not Resolved
Trial Number=3475-006, Site Number=0309, Subject ID=363628, Gender=F, Race=White, Age=60 Years, Rel Day of Study Medication Discontinuance†=79									
363628	Treatment Cycle 3	52	Diarrhoea	1.14 Weeks		Y	Y	Interrupted	Resolved
	Extended Safety Follow-up	126	Dehydration	3 Days		Y	N	None	Resolved
Trial Number=3475-006, Site Number=0400, Subject ID=363227, Gender=F, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=71									
363227	Treatment Cycle 1	18	Enterocolitis	4 Days		Y	Y	Interrupted	Resolved
	Extended Safety Follow-up	106	Renal failure acute	1.57 Weeks		Y	Y	None	Resolved
		108	Pneumonitis	1.48 Months		Y	Y	None	Resolved

C Confidential

付録 2.7.4-31 最終投与後 90 日までに発現した重篤な有害事象の一覧

006 試験（APaT 集団）（続き）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Action Taken	Outcome
Control									
Trial Number=3475-006, Site Number=0407, Subject ID=361511, Gender=M, Race=White, Age=69 Years, Rel Day of Study Medication Discontinuance†=65									
361511	Treatment Cycle 2	43	Hypopituitarism	2.14 Months		Y	Y	None	Resolved
	Extended Safety Follow-up	140	Pelvic infection	1.14 Weeks		Y	N	None	Resolved
Trial Number=3475-006, Site Number=0501, Subject ID=360445, Gender=M, Race=White, Age=42 Years, Rel Day of Study Medication Discontinuance†=22									
360445	Treatment Cycle 1	10	Tumour haemorrhage	4 Weeks		Y	N	None	Resolved
	Extended Safety Follow-up	81	Tumour lysis syndrome	2 Days		Y	N	N/A	Fatal
Trial Number=3475-006, Site Number=0601, Subject ID=367283, Gender=M, Race=White, Age=55 Years, Rel Day of Study Medication Discontinuance†=64									
367283	Extended Safety Follow-up	99	Vomiting	Continuing		Y	N	N/A	Not Resolved
		110	Pneumonia aspiration	Continuing		Y	N	N/A	Not Resolved

C Confidential

付録 2.7.4-31 最終投与後 90 日までに発現した重篤な有害事象の一覧
006 試験（APaT 集団）（続き）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Action Taken	Outcome
Control									
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		Y	N	Discontinued	Resolved
Trial Number=3475-006, Site Number=0605, Subject ID=363183, Gender=M, Race=White, Age=56 Years, Rel Day of Study Medication Discontinuance†=64									
363183	Safety Follow-up	80	Encephalopathy	1.57 Weeks		Y	Y	N/A	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	Treatment Cycle 1	7	Intestinal stenosis	3 Weeks		Y	N	Interrupted	Resolved
	Safety Follow-up	65	Colonic abscess	1.28 Months		Y	Y	Discontinued	Resolved
Trial Number=3475-006, Site Number=0605, Subject ID=368705, Gender=M, Race=White, Age=78 Years, Rel Day of Study Medication Discontinuance†=64									
368705	Safety Follow-up	77	Confusional state	4 Days		Y	Y	None	Resolved
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		Y	Y	Discontinued	Resolved

C Confidential

付録 2.7.4-31 最終投与後 90 日までに発現した重篤な有害事象の一覧
006 試験（APaT 集団）（続き）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Action Taken	Outcome
Control									
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		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		Y	Y	Discontinued	Resolved
Trial Number=3475-006, Site Number=0701, Subject ID=367979, Gender=F, Race=White, Age=78 Years, Rel Day of Study Medication Discontinuance†=64									
367979	Safety Follow-up	67	Erysipelas	1.71 Weeks		Y	N	None	Resolved
Trial Number=3475-006, Site Number=0702, Subject ID=360465, Gender=F, Race=White, Age=73 Years, Rel Day of Study Medication Discontinuance†=42									
360465	Treatment Cycle 2	23	Pleural effusion	2.86 Weeks		Y	N	None	Resolved
	Safety Follow-up	59	Pleural effusion	1.29 Weeks		Y	N	None	Resolved
		71	Atrial flutter	2 Days		Y	N	Interrupted	Sequelae
Trial Number=3475-006, Site Number=0702, Subject ID=361483, Gender=F, Race=White, Age=68 Years, Rel Day of Study Medication Discontinuance†=22									

Confidential

付録 2.7.4-31 最終投与後 90 日までに発現した重篤な有害事象の一覧

006 試験（APaT 集団）（続き）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Action Taken	Outcome
Control									
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		Y	Y	Discontinued	Not Resolved
	Extended Safety Follow-up	92	Endocarditis	1.57 Weeks		Y	N	N/A	Fatal
Trial Number=3475-006, Site Number=0900, Subject ID=364698, Gender=F, Race=White, Age=76 Years, Rel Day of Study Medication Discontinuance†=22									
364698	Extended Safety Follow-up	53	Cardio-respiratory arrest	2 Days		Y	N	N/A	Fatal
Trial Number=3475-006, Site Number=0900, Subject ID=368009, Gender=F, Race=White, Age=79 Years, Rel Day of Study Medication Discontinuance†=43									
368009	Treatment Cycle 1	5	Abdominal pain	1.14 Weeks		Y	N	None	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		Y	N	Discontinued	Fatal

C Confidential

付録 2.7.4-31 最終投与後 90 日までに発現した重篤な有害事象の一覧

006 試験（APaT 集団）（続き）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Action Taken	Outcome
Control									
Trial Number=3475-006, Site Number=0901, Subject ID=368436, Gender=M, Race=White, Age=84 Years, Rel Day of Study Medication Discontinuance†=65									
368436	Treatment Cycle 3	62	Diarrhoea	2.46 Months		Y	Y	N/A	Resolved
Trial Number=3475-006, Site Number=0902, Subject ID=365519, Gender=F, Race=White, Age=50 Years, Rel Day of Study Medication Discontinuance†=63									
365519	Treatment Cycle 3	62	Pyrexia	1.71 Weeks		Y	N	N/A	Resolved
Trial Number=3475-006, Site Number=1201, Subject ID=360611, Gender=F, Race=White, Age=51 Years, Rel Day of Study Medication Discontinuance†=64									
360611	Safety Follow-up	76	Colitis	1.74 Months		Y	Y	None	Resolved
Trial Number=3475-006, Site Number=1201, Subject ID=367796, Gender=F, Race=White, Age=57 Years, Rel Day of Study Medication Discontinuance†=22									
367796	Treatment Cycle 1	17	Hypophysitis	Continuing		Y	Y	None	Not Resolved
Trial Number=3475-006, Site Number=1301, Subject ID=367604, Gender=F, Race=White, Age=44 Years, Rel Day of Study Medication Discontinuance†=64									
367604	Treatment Cycle 3	51	Dyspnoea	1.57 Weeks		Y	N	None	Sequelae

Confidential

付録 2.7.4-31 最終投与後 90 日までに発現した重篤な有害事象の一覧
006 試験（APaT 集団）（続き）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Ser-ious	Related	Action Taken	Outcome
Control									
Trial Number=3475-006, Site Number=1400, Subject ID=365535, Gender=M, Race=White, Age=52 Years, Rel Day of Study Medication Discontinuance†=64									
365535	Safety Follow-up	87	Alanine aminotransferase increased	1.38 Months		Y	Y	N/A	Resolved
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		Y	Y	Discontinued	Resolved
Trial Number=3475-006, Site Number=1401, Subject ID=363163, Gender=M, Race=White, Age=51 Years, Rel Day of Study Medication Discontinuance†=22									
363163	Treatment Cycle 1	5	Constipation	Continuing		Y	N	None	Not Resolved
Trial Number=3475-006, Site Number=1401, Subject ID=363308, Gender=M, Race=White, Age=50 Years, Rel Day of Study Medication Discontinuance†=									
363308	Treatment Cycle 1	12	Nausea	6 Days		Y	N	None	Resolved
		14	Dizziness	4 Days		Y	N	None	Resolved
	Safety Follow-up	72	Diarrhoea	3.71 Weeks		Y	Y	None	Resolved
Trial Number=3475-006, Site Number=1401, Subject ID=365078, Gender=M, Race=White, Age=63 Years, Rel Day of Study Medication Discontinuance†=22									

C Confidential