付録 2.7.4-76 AEOSI-肝炎に対する副腎皮質ホルモン剤使用の一覧

001 試験+002 試験+006 試験（APaT 集団）

Subject ID	Med. Start Day	Med. Duration (Days)	Med. Name	Total Daily Dose	Frequency	Route	Prednisone Equiv.[†] (mg)	Adverse Event for Use	AE Start Day	AE End Day	AE Toxicity Grade
MK-3475 2 mg/kg Q3W											
Trial Number=3475-001, Site Number=0015, Subject ID=000336, Gender=M, Race=White, Age=58 Years, Rel Day of Study Medication Discontinuance[‡]=1											
000336	22	1	Methylprednisolone Sodium Succinate	80	ONCE	Intravenous Administration	100.00	Autoimmune hepatitis	22	54	4
	22	6	Methylprednisolone Sodium Succinate	1	QD	Intravenous Bolus	1.25	Autoimmune hepatitis	22	54	4
	27	6	Prednisone	80	QD	Oral Administration	80.00	Autoimmune hepatitis	22	54	4
	33	5	Prednisone	60	QD	Oral Administration	60.00	Autoimmune hepatitis	22	54	4
	38	4	Prednisone	40	QD	Oral Administration	40.00	Autoimmune hepatitis	22	54	4
	42	19	Prednisone	20	QD	Oral Administration	20.00	Autoimmune hepatitis	22	54	4
	61	16	Prednisone	10	QD	Oral Administration	10.00	Autoimmune hepatitis	22	54	4
	77	6	Prednisone	3	QD	Oral Administration	2.50	Autoimmune hepatitis	22	54	4
Trial Number=3475-002, Site Number=0001, Subject ID=100094, Gender=M, Race=White, Age=64 Years, Rel Day of Study Medication Discontinuance[‡]=											
100094	139	6	Prednisone	100	QD	Oral	100.00	Autoimmune hepatitis	127	165	2
	145	3	Prednisone	50	QD	Oral	50.00	Autoimmune hepatitis	127	165	2
	148	5	Prednisone	40	QD	Oral	40.00	Autoimmune hepatitis	127	165	2
	153	7	Prednisone	30	QD	Oral	30.00	Autoimmune hepatitis	127	165	2
	160	4	Prednisone	20	QD	Oral	20.00	Autoimmune hepatitis	127	165	2
	164	11	Prednisone	10	QD	Oral	10.00	Autoimmune hepatitis	127	165	2

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付録 2.7.4-76 AEOSI-肝炎に対する副腎皮質ホルモン剤使用の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Med. Start Day	Med. Duration (Days)	Med. Name	Total Daily Dose	Frequency	Route	Prednisone Equiv.† (mg)	Adverse Event for Use	AE Start Day	AE End Day	AE Toxicity Grade
	175	14	Prednisone	5	QD	Oral	5.00	Autoimmune hepatitis	127	165	2
	189	49	Prednisone	10	QD	Oral	10.00	Autoimmune hepatitis	127	165	2
	238	44	Prednisone	8	QD	Oral	7.50	Autoimmune hepatitis	127	165	2
Trial Number=3475-002, Site Number=0082, Subject ID=100679, Gender=F, Race=White, Age=73 Years, Rel Day of Study Medication Discontinuance‡=77											
100679	24	7	Prednisolone	50	QD	Oral	50.00	Autoimmune hepatitis	22	66	3
	31	3	Prednisolone	30	QD	Oral	30.00	Autoimmune hepatitis	22	66	3
	34	3	Prednisolone	15	QD	Oral	15.00	Autoimmune hepatitis	22	66	3
	37	3	Prednisolone	5	QD	Oral	5.00	Autoimmune hepatitis	22	66	3
MK-3475 10 mg/kg Q3W											
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	22	8	Prednisone	25	QD	Oral Administration	25.00	Autoimmune hepatitis	22	88	2
	47	1	Prednisone	5	QD	Oral Administration	5.00	Autoimmune hepatitis	22	88	2
	48	8	Prednisone	60	QD	Oral Administration	60.00	Autoimmune hepatitis	22	88	2
	56	7	Prednisone	40	QD	Oral Administration	40.00	Autoimmune hepatitis	22	88	2
	63	21	Prednisone	30	QD	Oral Administration	30.00	Autoimmune hepatitis	22	88	2
Trial Number=3475-002, Site Number=0080, Subject ID=100913, Gender=F, Race=White, Age=53 Years, Rel Day of Study Medication Discontinuance‡=1											
100913	21	14	Prednisolone	170	QD	Intravenous	170.00	Autoimmune hepatitis	8	.	3

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付録 2.7.4-76 AEOSI-肝炎に対する副腎皮質ホルモン剤使用の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Med. Start Day	Med. Duration (Days)	Med. Name	Total Daily Dose	Frequency	Route	Prednisone Equiv.[†] (mg)	Adverse Event for Use	AE Start Day	AE End Day	AE Toxicity Grade
	35	4	Prednisolone	80	QD	Intravenous	80.00	Autoimmune hepatitis	8	.	3
	39	3	Prednisolone	60	QD	Intravenous	60.00	Autoimmune hepatitis	8	.	3
	42	5	Prednisolone	40	QD	Intravenous	40.00	Autoimmune hepatitis	8	.	3
	52	4	Prednisolone	32	QD	Oral	32.00	Autoimmune hepatitis	8	.	3
	56	4	Prednisolone	28	QD	Oral	28.00	Autoimmune hepatitis	8	.	3
	60	4	Prednisolone	24	QD	Oral	24.00	Autoimmune hepatitis	8	.	3
	64	32	Prednisolone	20	QD	Oral	20.00	Autoimmune hepatitis	8	.	3
	96	12	Prednisolone	18	QD	Oral	18.00	Autoimmune hepatitis	8	.	3
	108	14	Prednisolone	12	QD	Oral	12.00	Autoimmune hepatitis	8	.	3
	122	19	Prednisolone	8	QD	Oral	8.00	Autoimmune hepatitis	8	.	3
	141	14	Prednisolone	4	QD	Oral	4.00	Autoimmune hepatitis	8	.	3
Trial Number=3475-006, Site Number=0611, Subject ID=364561, Gender=M, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance[‡]=20											
364561	38	4	Methylprednisolone Sodium Succinate	240	QD	Intravenous	300.00	Autoimmune hepatitis	17	111	3
	42	38	Prednisolone Sodium Metazoate	150	QD	Oral	150.00	Autoimmune hepatitis	17	111	3
	80	12	Prednisolone Sodium Metazoate	100	QD	Oral	100.00	Autoimmune hepatitis	17	111	3
	92	8	Prednisolone Sodium Metazoate	75	QD	Oral	75.00	Autoimmune hepatitis	17	111	3
	100	11	Prednisolone Sodium Metazoate	50	QD	Oral	50.00	Autoimmune hepatitis	17	111	3

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付録 2.7.4-76 AEOSI-肝炎に対する副腎皮質ホルモン剤使用の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Med. Start Day	Med. Duration (Days)	Med. Name	Total Daily Dose	Frequency	Route	Prednisone Equiv.[†] (mg)	Adverse Event for Use	AE Start Day	AE End Day	AE Toxicity Grade
Trial Number=3475-006, Site Number=0611, Subject ID=365059, Gender=M, Race=White, Age=80 Years, Rel Day of Study Medication Discontinuance[‡]=99											
365059	24	5	Methylprednisolone Sodium Succinate	120	QD	Intravenous	150.00	Hepatitis	22	57	3
	29	2	Prednisone	100	QD	Oral	100.00	Hepatitis	22	57	3
	31	26	Prednisone	80	QD	Oral	80.00	Hepatitis	22	57	3
	56	3	Prednisone	15	QD	Oral	15.00	Hepatitis	22	57	3
Trial Number=3475-006, Site Number=1707, Subject ID=364658, Gender=M, Race=White, Age=58 Years, Rel Day of Study Medication Discontinuance[‡]=1											
364658	25	5	Hydrocortisone	800	QID	Intravenous	200.00	Drug-induced liver injury	22	47	4
MK-3475 10 mg/kg Q2W											
Trial Number=3475-006, Site Number=0001, Subject ID=368185, Gender=F, Race=White, Age=42 Years, Rel Day of Study Medication Discontinuance[‡]=279											
368185	56	1	Dexamethasone	8	ONCE	Oral	53.36	Autoimmune hepatitis	54	83	3
	57	10	Dexamethasone	12	BID	Oral	80.04	Autoimmune hepatitis	54	83	3
	67	10	Dexamethasone	12	QD	Oral	80.04	Autoimmune hepatitis	54	83	3
	77	7	Dexamethasone	4	QD	Oral	26.68	Autoimmune hepatitis	54	83	3
	84	7	Dexamethasone	2	QD	Oral	13.34	Autoimmune hepatitis	54	83	3
	91	17	Dexamethasone	2	QOD	Oral	13.34	Autoimmune hepatitis	54	83	3
	60	1	Methylprednisolone Sodium Succinate	1000	ONCE	Intravenous	1250.00	Autoimmune hepatitis	54	83	3
	90	1	Methylprednisolone Sodium Succinate	500	ONCE	Intravenous	625.00	Autoimmune hepatitis	54	83	3

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付録 2.7.4-76 AEOSI-肝炎に対する副腎皮質ホルモン剤使用の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Med. Start Day	Med. Duration (Days)	Med. Name	Total Daily Dose	Frequency	Route	Prednisone Equiv.† (mg)	Adverse Event for Use	AE Start Day	AE End Day	AE Toxicity Grade
Trial Number=3475-006, Site Number=0005, Subject ID=366940, Gender=M, Race=White, Age=65 Years, Rel Day of Study Medication Discontinuance‡=											
366940	54	6	Prednisolone	100	QD	Oral	100.00	Hepatitis	40	182	3
	60	5	Prednisolone	75	QD	Oral	75.00	Hepatitis	40	182	3
	65	7	Prednisolone	50	QD	Oral	50.00	Hepatitis	40	182	3
	72	7	Prednisolone	38	QD	Oral	37.50	Hepatitis	40	182	3
	79	6	Prednisolone	25	QD	Oral	25.00	Hepatitis	40	182	3
	85	7	Prednisolone	13	QD	Oral	12.50	Hepatitis	40	182	3

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付録 2.7.4-76 AEOSI-肝炎に対する副腎皮質ホルモン剤使用の一覧
001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Med. Start Day	Med. Duration (Days)	Med. Name	Total Daily Dose	Frequency	Route	Prednisone Equiv.† (mg)	Adverse Event for Use	AE Start Day	AE End Day	AE Toxicity Grade
Trial Number=3475-006, Site Number=1824, Subject ID=360306, Gender=M, Race=White, Age=71 Years, Rel Day of Study Medication Discontinuance‡=183											
360306	196	4	Methylprednisolone	90	BID	Intravenous	112.50	Autoimmune hepatitis	191	.	3
	199	5	Prednisone	100	BID	Oral	100.00	Autoimmune hepatitis	191	.	3
	204	1	Prednisone	180	OTHER	Oral	180.00	Autoimmune hepatitis	191	.	3
	205	6	Prednisone	80	BID	Oral	80.00	Autoimmune hepatitis	191	.	3
	211	1	Prednisone	140	OTHER	Oral	140.00	Autoimmune hepatitis	191	.	3
	212	6	Prednisone	60	BID	Oral	60.00	Autoimmune hepatitis	191	.	3

付録 2.7.4-76 AEOSI-肝炎に対する副腎皮質ホルモン剤使用の一覧
001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Med. Start Day	Med. Duration (Days)	Med. Name	Total Daily Dose	Frequency	Route	Prednisone Equiv.† (mg)	Adverse Event for Use	AE Start Day	AE End Day	AE Toxicity Grade
	218	1	Prednisone	100	OTHER	Oral	100.00	Autoimmune hepatitis	191	.	3
	219	6	Prednisone	40	BID	Oral	40.00	Autoimmune hepatitis	191	.	3
	232	5	Prednisone	20	BID	Oral	20.00	Autoimmune hepatitis	191	.	3

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

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付録 2.7.4-77 AEOSI-下垂体炎を発現した患者の一覧

001 試験+002 試験+006 試験（APaT 集団）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 2 mg/kg Q3W										
Trial Number=3475-001, Site Number=0011, Subject ID=000291, Gender=M, Race=White, Age=73 Years, Rel Day of Study Medication Discontinuance†=44										
000291	Safety Follow-up	52 58	Hypophysitis Hypophysitis	6 Days Continuing	Severe Moderate	4 2	Y	Y Y	Interrupted N/A	Resolved 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	Hypophysitis	3.32 Months	Moderate	2	Y	Y	Discontinued	Resolved
Trial Number=3475-001, Site Number=0018, Subject ID=000466, Gender=M, Race=White, Age=71 Years, Rel Day of Study Medication Discontinuance†=										
000466	Treatment Cycle 9	186	Hypopituitarism	Continuing	Mild	1		Y		Not Resolved
Trial Number=3475-001, Site Number=0018, Subject ID=000469, Gender=F, Race=White, Age=63 Years, Rel Day of Study Medication Discontinuance†=239										
000469	Treatment Cycle 8	169	Hypopituitarism	Continuing	Moderate	2		N		Not Resolved
Trial Number=3475-002, Site Number=0170, Subject ID=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
MK-3475 10 mg/kg Q3W										
Trial Number=3475-002, Site Number=0080, Subject ID=100674, Gender=M, Race=White, Age=65 Years, Rel Day of Study Medication Discontinuance†=23										
100674	Safety Follow-up	28	Hypopituitarism	Continuing		3	Y	Y	Discontinued	Not Resolved
Trial Number=3475-002, Site Number=0161, Subject ID=101265, Gender=M, Race=White, Age=67 Years, Rel Day of Study Medication Discontinuance†=71										

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付録 2.7.4-77 AEOSI-下垂体炎を発現した患者の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q3W										
Trial Number=3475-002, Site Number=0161, Subject ID=101265, Gender=M, Race=White, Age=67 Years, Rel Day of Study Medication Discontinuance†=71										
101265	Safety Follow-up	100	Hypophysitis	Continuing		2	N	Y	N/A	Not Resolved
Trial Number=3475-002, Site Number=0170, Subject ID=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
Trial Number=3475-006, Site Number=0706, Subject ID=369387, Gender=M, Race=White, Age=74 Years, Rel Day of Study Medication Discontinuance†=128										
369387	Safety Follow-up	148	Hypophysitis	2.57 Weeks		2	N	N	Interrupted	Resolved
Trial Number=3475-006, Site Number=1703, Subject ID=362670, Gender=M, Race=White, Age=63 Years, Rel Day of Study Medication Discontinuance†=										
362670	Treatment Cycle 10	219	Hypophysitis	2.04 Months		3	Y	Y	Interrupted	Sequelae
MK-3475 10 mg/kg Q2W										
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	Treatment Cycle 2	15	Hypophysitis	Continuing	Moderate	2		N		Not Resolved
Trial Number=3475-001, Site Number=0021, Subject ID=000078, Gender=F, Race=White, Age=38 Years, Rel Day of Study Medication Discontinuance†=										
000078	Treatment Cycle 15	198	Hypopituitarism	4.67 Months	Mild	1		Y		Resolved
Trial Number=3475-006, Site Number=0003, Subject ID=362318, Gender=M, Race=White, Age=76 Years, Rel Day of Study Medication Discontinuance†=										
362318	Treatment Cycle 10	131	Hypopituitarism	1.71 Weeks		3	Y	Y	Interrupted	Sequelae

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付録 2.7.4-77 AEOSI-下垂体炎を発現した患者の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q2W										
Trial Number=3475-006, Site Number=0003, Subject ID=362318, Gender=M, Race=White, Age=76 Years, Rel Day of Study Medication Discontinuance[†]=										
362318	Treatment Cycle 10	143	Hypopituitarism	Continuing		2	N	Y	None	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.
(MK-3475 PN001 Database Cutoff Date: [redacted].
(MK-3475 PN002 Database Cutoff Date: 12MAY2014).
(MK-3475 PN006 Database Cutoff Date: 03SEP2014).

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付録 2.7.4-78 AEOSI-下垂体炎に対する副腎皮質ホルモン剤使用の一覧

001 試験+002 試験+006 試験（APaT 集団）

Subject ID	Med. Start Day	Med. Duration (Days)	Med. Name	Total Daily Dose	Frequency	Route	Prednisone Equiv.† (mg)	Adverse Event for Use	AE Start Day	AE End Day	AE Toxicity Grade
MK-3475 2 mg/kg Q3W											
Trial Number=3475-001, Site Number=0011, Subject ID=000291, Gender=M, Race=White, Age=73 Years, Rel Day of Study Medication Discontinuance‡=44											
000291	52	1	Hydrocortisone	300	Q8H	Intravenous Administration	75.00	Hypophysitis	52	57	4
	53	12	Prednisone	60	QD	Oral Administration	60.00	Hypophysitis	52	57	4
	64	2	Prednisone	60	QD	Oral Administration	60.00	Hypophysitis	52	57	4
	65	6	Prednisone	50	QD	Oral Administration	50.00	Hypophysitis	52	57	4
	70	1	Prednisone	40	QD	Oral Administration	40.00	Hypophysitis	52	57	4
	71	1	Prednisone	30	QD	Oral Administration	30.00	Hypophysitis	52	57	4
	72	1	Prednisone	20	QD	Oral Administration	20.00	Hypophysitis	52	57	4
	73	1	Prednisone	10	QD	Oral Administration	10.00	Hypophysitis	52	57	4
	74	1	Prednisone	8	QD	Oral Administration	7.50	Hypophysitis	52	57	4
	75	.	Prednisone	5	QD	Oral Administration	5.00	Hypophysitis	52	57	4
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	44	2	Hydrocortisone	300	Q8H	Intravenous Administration	75.00	Hypophysitis	40	140	2
	45	1	Hydrocortisone	200	Q6H	Intravenous Administration	50.00	Hypophysitis	40	140	2
	56	3	Hydrocortisone	25	QD	Oral Administration	6.25	Hypophysitis	40	140	2
	56	3	Hydrocortisone	100	BID	Oral Administration	25.00	Hypophysitis	40	140	2

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付録 2.7.4-78 AEOSI-下垂体炎に対する副腎皮質ホルモン剤使用の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Med. Start Day	Med. Duration (Days)	Med. Name	Total Daily Dose	Frequency	Route	Prednisone Equiv.† (mg)	Adverse Event for Use	AE Start Day	AE End Day	AE Toxicity Grade
	59	3	Hydrocortisone	100	BID	Oral Administration	25.00	Hypophysitis	40	140	2
	62	3	Hydrocortisone	25	QD	Oral Administration	6.25	Hypophysitis	40	140	2
	62	3	Hydrocortisone	50	QD	Oral Administration	12.50	Hypophysitis	40	140	2
	65	3	Hydrocortisone	20	QD	Oral Administration	5.00	Hypophysitis	40	140	2
	65	3	Hydrocortisone	30	QD	Oral Administration	7.50	Hypophysitis	40	140	2
	68	157	Hydrocortisone	10	QD	Oral Administration	2.50	Hypophysitis	40	140	2
	68	157	Hydrocortisone	15	QD	Oral Administration	3.75	Hypophysitis	40	140	2
	225	.	Hydrocortisone	5	QD	Oral Administration	1.25	Hypophysitis	40	140	2
	225	.	Hydrocortisone	20	QD	Oral Administration	5.00	Hypophysitis	40	140	2
Trial Number=3475-001, Site Number=0018, Subject ID=000466, Gender=M, Race=White, Age=71 Years, Rel Day of Study Medication Discontinuance‡=											
000466	186	.	Hydrocortisone	10	QD	Oral Administration	2.50	Hypopituitarism	186	.	1
	186	90	Hydrocortisone	20	QD	Oral Administration	5.00	Hypopituitarism	186	.	1
	276	.	Hydrocortisone	15	QD	Oral Administration	3.75	Hypopituitarism	186	.	1
Trial Number=3475-001, Site Number=0018, Subject ID=000469, Gender=F, Race=White, Age=63 Years, Rel Day of Study Medication Discontinuance‡=239											
000469	169	.	Hydrocortisone	40	BID	Oral Administration	10.00	Hypopituitarism	169	.	2
Trial Number=3475-002, Site Number=0170, Subject ID=101510, Gender=F, Race=White, Age=69 Years, Rel Day of Study Medication Discontinuance‡=1											
101510	16	5	Methylprednisolone	50	QD	Intravenous	62.50	Hypophysitis	1	29	3

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付録 2.7.4-78 AEOSI-下垂体炎に対する副腎皮質ホルモン剤使用の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Med. Start Day	Med. Duration (Days)	Med. Name	Total Daily Dose	Frequency	Route	Prednisone Equiv.† (mg)	Adverse Event for Use	AE Start Day	AE End Day	AE Toxicity Grade
	20	5	Prednisolone	25	OTHER	Oral	25.00	Hypophysitis	1	29	3
	25	5	Prednisolone	15	BID	Oral	15.00	Hypophysitis	1	29	3
	30	5	Prednisolone	10	QD	Oral	10.00	Hypophysitis	1	29	3
	35	.	Prednisolone	5	QD	Oral	5.00	Hypophysitis	1	29	3
MK-3475 10 mg/kg Q3W											
Trial Number=3475-002, Site Number=0080, Subject ID=100674, Gender=M, Race=White, Age=65 Years, Rel Day of Study Medication Discontinuance‡=23											
100674	30	.	Hydrocortisone	30	QD	Oral	7.50	Hypopituitarism	28	.	3
	30	1	Hydrocortisone	60	QD	Oral	15.00	Hypopituitarism	28	.	3
	30	1	Hydrocortisone	10	QD	Oral	2.50	Hypopituitarism	28	.	3
	31	1	Hydrocortisone	50	QD	Oral	12.50	Hypopituitarism	28	.	3
Trial Number=3475-002, Site Number=0170, Subject ID=100622, Gender=M, Race=White, Age=76 Years, Rel Day of Study Medication Discontinuance‡=1											
100622	27	1	Hydrocortisone	100	ONCE	Intravenous	25.00	Hypopituitarism	13	43	3
	28	3	Hydrocortisone	100	BID	Oral	25.00	Hypopituitarism	13	43	3
	31	1	Hydrocortisone	60	ONCE	Oral	15.00	Hypopituitarism	13	43	3
	32	11	Hydrocortisone	30	BID	Oral	7.50	Hypopituitarism	13	43	3
	43	.	Hydrocortisone	20	BID	Oral	5.00	Hypopituitarism	13	43	3
Trial Number=3475-006, Site Number=0706, Subject ID=369387, Gender=M, Race=White, Age=74 Years, Rel Day of Study Medication Discontinuance‡=128											

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付録 2.7.4-78 AEOSI-下垂体炎に対する副腎皮質ホルモン剤使用の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Med. Start Day	Med. Duration (Days)	Med. Name	Total Daily Dose	Frequency	Route	Prednisone Equiv.† (mg)	Adverse Event for Use	AE Start Day	AE End Day	AE Toxicity Grade
369387	158	8	Prednisolone	20	QD	Oral	20.00	Hypophysitis	148	165	2
Trial Number=3475-006, Site Number=1703, Subject ID=362670, Gender=M, Race=White, Age=63 Years, Rel Day of Study Medication Discontinuance‡=											
362670	220	.	Hydrocortisone	40	TID	Oral	10.00	Hypophysitis	219	280	3
MK-3475 10 mg/kg Q2W											
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	88	7	Prednisone	10	QD	Oral Administration	10.00	Hypophysitis	15	.	2
Trial Number=3475-001, Site Number=0021, Subject ID=000078, Gender=F, Race=White, Age=38 Years, Rel Day of Study Medication Discontinuance‡=											

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付録 2.7.4-78 AEOSI-下垂体炎に対する副腎皮質ホルモン剤使用の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Med. Start Day	Med. Duration (Days)	Med. Name	Total Daily Dose	Frequency	Route	Prednisone Equiv.† (mg)	Adverse Event for Use	AE Start Day	AE End Day	AE Toxicity Grade
000078	212	118	Hydrocortisone	20	QD	Oral Administration	5.00	Hypopituitarism	198	339	1
Trial Number=3475-006, Site Number=0003, Subject ID=362318, Gender=M, Race=White, Age=76 Years, Rel Day of Study Medication Discontinuance‡=											
362318	139	1	Hydrocortisone	200	BID	Intravenous	50.00	Hypopituitarism	131	142	3
	140	1	Hydrocortisone	50	ONCE	Intravenous	12.50	Hypopituitarism	131	142	3
	140	1	Hydrocortisone	20	ONCE	Oral	5.00	Hypopituitarism	131	142	3
	141	1	Hydrocortisone	60	ONCE	Oral	15.00	Hypopituitarism	131	142	3
	142	1	Hydrocortisone	50	ONCE	Oral	12.50	Hypopituitarism	131	142	3

付録 2.7.4-78 AEOSI-下垂体炎に対する副腎皮質ホルモン剤使用の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Med. Start Day	Med. Duration (Days)	Med. Name	Total Daily Dose	Frequency	Route	Prednisone Equiv.† (mg)	Adverse Event for Use	AE Start Day	AE End Day	AE Toxicity Grade
	143	9	Hydrocortisone	30	QD	Oral	7.50	Hypopituitarism	143	.	2
	152	19	Hydrocortisone	20	BID	Oral	5.00	Hypopituitarism	143	.	2
	171	.	Hydrocortisone	30	QD	Oral	7.50	Hypopituitarism	143	.	2

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

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付録 2.7.4-79 AEOSI-下垂体炎に対する副腎皮質ホルモン剤使用の一覧

041 試験（APaT 集団）

Subject ID	Med. Start Day	Med. Duration (Days)	Med. Name	Total Daily Dose	Frequency	Route	Prednisone Equiv.† (mg)	Adverse Event for Use	AE Start Day	AE End Day	AE Toxicity Grade
MK-3475 2 mg/kg Q3W											
Trial Number=3475-041, Site Number=0012, Subject ID=041011, Gender=Female, Race=Asian, Age=43 Years, Rel Day of Study Medication Discontinuance‡=211											
041011	267	35	Hydrocortisone	10	QD	Oral	2.50	Hypophysitis	220	.	2
	302	.	Hydrocortisone	15	BID	Oral	3.75	Hypophysitis	220	.	2
Trial Number=3475-041, Site Number=0012, Subject ID=041017, Gender=Male, Race=Asian, Age=56 Years, Rel Day of Study Medication Discontinuance‡=											
041017	249	.	Hydrocortisone	10	QD	Oral	2.50	Hypophysitis	242	.	3
	249	8	Prednisolone	40	QD	Oral	40.00	Hypophysitis	242	.	3
	257	7	Prednisolone	30	QD	Oral	30.00	Hypophysitis	242	.	3
	264	6	Prednisolone	20	QD	Oral	20.00	Hypophysitis	242	.	3
	270	19	Prednisolone	10	QD	Oral	10.00	Hypophysitis	242	.	3

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付録 2.7.4-79 AEOSI-下垂体炎に対する副腎皮質ホルモン剤使用の一覧

041 試験（APaT 集団）（続き）

Subject ID	Med. Start Day	Med. Duration (Days)	Med. Name	Total Daily Dose	Frequency	Route	Prednisone Equiv.[†] (mg)	Adverse Event for Use	AE Start Day	AE End Day	AE Toxicity Grade
	289	10	Prednisolone	5	QD	Oral	5.00	Hypophysitis	242	.	3

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

Data Source: [資料5.3.5.2.3: P041V01]

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付録 2.7.4-80 AEOSI-副腎機能不全を発現した患者の一覧

001 試験+002 試験+006 試験（APaT 集団）

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 2 mg/kg Q3W										
Trial Number=3475-001, Site Number=0012, Subject ID=000389, Gender=F, Race=White, Age=68 Years, Rel Day of Last Recorded Dose of Study Medication=22										
000389	Safety Follow-up	44	Adrenal insufficiency	6 Days	Severe	3		N	N/A	Resolved
		49	Adrenal insufficiency	Continuing	Moderate	2		N	N/A	Not Resolved
Trial Number=3475-002, Site Number=0034, Subject ID=101258, Gender=F, Race=White, Age=70 Years, Rel Day of Last Recorded Dose of Study Medication=237										
101258	Treatment Cycle 6	132	Adrenocortical insufficiency acute	4 Days		3	Y	N	None	Resolved
MK-3475 10 mg/kg Q3W										
Trial Number=3475-001, Site Number=0010, Subject ID=000332, Gender=M, Race=White, Age=83 Years, Rel Day of Last Recorded Dose of Study Medication=1										
000332	Safety Follow-up	26	Adrenal insufficiency	Continuing	Mild	1		N	N/A	Not Resolved
Trial Number=3475-001, Site Number=0010, Subject ID=001220, Gender=M, Race=White, Age=73 Years, Rel Day of Last Recorded Dose of Study Medication=337										
001220	Treatment Cycle 10	189	Adrenal insufficiency	5 Days	Mild	1		Y	N/A	Resolved
		194	Adrenal insufficiency	3 Days	Severe	3	Y	Y		Resolved
		197	Adrenal insufficiency	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0011, Subject ID=000413, Gender=M, Race=White, Age=87 Years, Rel Day of Last Recorded Dose of Study Medication=374										
000413	Treatment Cycle 13	360	Adrenal insufficiency	4 Days	Severe	3	Y	Y	Interrupted	Resolved
		363	Adrenal insufficiency	Continuing	Moderate	2		Y		Not Resolved

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付録 2.7.4-80 AEOSI-副腎機能不全を発現した患者の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Onset 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=000148, Gender=F, Race=White, Age=66 Years, Rel Day of Last Recorded Dose of Study Medication=673										
000148	Treatment Cycle 24	505	Adrenal insufficiency	4.14 Weeks	Moderate	2		Y	Interrupted	Resolved
Trial Number=3475-002, Site Number=0130, Subject ID=100919, Gender=F, Race=White, Age=51 Years, Rel Day of Last Recorded Dose of Study Medication=96										
100919	Safety Follow-up	108	Adrenocortical insufficiency acute	Continuing		3	Y	N	None	Not Resolved
Trial Number=3475-006, Site Number=0612, Subject ID=361134, Gender=F, Race=White, Age=53 Years, Rel Day of Last Recorded Dose of Study Medication=204										
361134	Treatment Cycle 6	128	Adrenal insufficiency	Continuing		2	N	Y	None	Not Resolved
MK-3475 10 mg/kg Q2W										
Trial Number=3475-001, Site Number=0013, Subject ID=000084, Gender=F, Race=White, Age=52 Years, Rel Day of Last Recorded Dose of Study Medication=43										
000084	Safety Follow-up	58	Adrenal insufficiency	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-006, Site Number=0704, Subject ID=360742, Gender=F, Race=White, Age=83 Years, Rel Day of Last Recorded Dose of Study Medication=154										
360742	Treatment Cycle 6	83	Adrenal insufficiency	Continuing		3	Y	Y	Interrupted	Not Resolved
Trial Number=3475-006, Site Number=0704, Subject ID=366882, Gender=M, Race=White, Age=77 Years, Rel Day of Last Recorded Dose of Study Medication=144										

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付録 2.7.4-80 AEOSI-副腎機能不全を発現した患者の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Onset Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q2W										
Trial Number=3475-006, Site Number=0704, Subject ID=366882, Gender=M, Race=White, Age=77 Years, Rel Day of Last Recorded Dose of Study Medication=144										
366882	Safety Follow-up	158	Adrenal insufficiency	Continuing		4	Y	Y	Discontinued	Not Resolved

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

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

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

Grades are based on NCI CTCAE version 4.0..

(MK-3475 PN-001 Database Cutoff Date: [redacted].

(MK-3475 PN-002 Database Cutoff Date: 12MAY2014).

(MK-3475 PN-006 Database Cutoff Date: 03SEP2014).

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付録 2.7.4-81 AEOSI-副腎機能不全に対する副腎皮質ホルモン剤使用の一覧

001 試験+002 試験+006 試験（APaT 集団）

Subject ID	Med. Start Day	Med. Duration (Days)	Med. Name	Total Daily Dose	Frequency	Route	Prednisone Equiv.† (mg)	Adverse Event for Use	AE Start Day	AE End Day	AE Toxicity Grade
MK-3475 2 mg/kg Q3W											
Trial Number=3475-002, Site Number=0034, Subject ID=101258, Gender=F, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance†=											
101258	133	.	Dexamethasone	1	BID	Oral	5.00	Adrenocortical insufficiency acute	132	135	3
	133	.	Dexamethasone	4	PRN	Intravenous	26.68	Adrenocortical insufficiency acute	132	135	3
	133	.	Dexamethasone	8	PRN	Intramuscular	53.36	Adrenocortical insufficiency acute	132	135	3
	133	1	Dexamethasone	10	QD	Intravenous	66.70	Adrenocortical insufficiency acute	132	135	3
	133	1	Dexamethasone Sodium Phosphate	4	ONCE	Intramuscular	26.68	Adrenocortical insufficiency acute	132	135	3
	133	2	Fludrocortisone	0	QD	Oral	0.02	Adrenocortical insufficiency acute	132	135	3
MK-3475 10 mg/kg Q3W											
Trial Number=3475-001, Site Number=0010, Subject ID=001220, Gender=M, Race=White, Age=73 Years, Rel Day of Study Medication Discontinuance†=											
001220	196	8	Hydrocortisone	80	BID	Oral Administration	20.00	Adrenal insufficiency	197	.	2
Trial Number=3475-001, Site Number=0011, Subject ID=000413, Gender=M, Race=White, Age=87 Years, Rel Day of Study Medication Discontinuance†=											
000413	362	13	Dexamethasone	4	QD	Oral Administration	26.68	Adrenal insufficiency	360	363	3
	374	23	Dexamethasone	1	QD	Oral Administration	6.67	Adrenal insufficiency	363	.	2
Trial Number=3475-001, Site Number=0019, Subject ID=000148, Gender=F, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=											
000148	512	46	Prednisone	10	QD	Oral Administration	10.00	Adrenal insufficiency	505	533	2
	512	47	Prednisone	15	QD	Oral Administration	15.00	Adrenal insufficiency	505	533	2

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付録 2.7.4-81 AEOSI-副腎機能不全に対する副腎皮質ホルモン剤使用の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Med. Start Day	Med. Duration (Days)	Med. Name	Total Daily Dose	Frequency	Route	Prednisone Equiv.† (mg)	Adverse Event for Use	AE Start Day	AE End Day	AE Toxicity Grade
	558	60	Prednisone	3	QD	Oral Administration	2.50	Adrenal insufficiency	505	533	2
	558	115	Prednisone	5	QD	Oral Administration	5.00	Adrenal insufficiency	505	533	2
	618	55	Prednisone	2	QD	Oral Administration	2.00	Adrenal insufficiency	505	533	2
Trial Number=3475-006, Site Number=0612, Subject ID=361134, Gender=F, Race=White, Age=53 Years, Rel Day of Study Medication Discontinuance‡=											
361134	128	.	Hydrocortisone	20	TID	Oral	5.00	Adrenal insufficiency	128	.	2
MK-3475 10 mg/kg Q2W											
Trial Number=3475-001, Site Number=0013, Subject ID=000084, Gender=F, Race=White, Age=52 Years, Rel Day of Study Medication Discontinuance‡=43											
000084	58	2	Hydrocortisone	20	QD	Oral Administration	5.00	Adrenal insufficiency	58	.	2
	58	2	Hydrocortisone	10	QD	Oral Administration	2.50	Adrenal insufficiency	58	.	2
	102	.	Hydrocortisone	10	QD	Oral Administration	2.50	Adrenal insufficiency	58	.	2
	102	.	Hydrocortisone	5	QD	Oral Administration	1.25	Adrenal insufficiency	58	.	2
Trial Number=3475-006, Site Number=0704, Subject ID=360742, Gender=F, Race=White, Age=83 Years, Rel Day of Study Medication Discontinuance‡=154											
360742	105	17	Hydrocortisone	35	BID	Oral	8.75	Adrenal insufficiency	83	.	3
	105	17	Hydrocortisone	35	BID	Oral	8.75	Adrenal insufficiency	83	.	3
	108	1	Hydrocortisone	100	QD	Intravenous	25.00	Adrenal insufficiency	83	.	3
	109	2	Hydrocortisone	50	QD	Intravenous	12.50	Adrenal insufficiency	83	.	3
	122	123	Hydrocortisone	30	TID	Oral	7.50	Adrenal insufficiency	83	.	3

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付録 2.7.4-81 AEOSI-副腎機能不全に対する副腎皮質ホルモン剤使用の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Med. Start Day	Med. Duration (Days)	Med. Name	Total Daily Dose	Frequency	Route	Prednisone Equiv.[†] (mg)	Adverse Event for Use	AE Start Day	AE End Day	AE Toxicity Grade
Trial Number=3475-006, Site Number=0704, Subject ID=366882, Gender=M, Race=White, Age=77 Years, Rel Day of Study Medication Discontinuance[‡]=144											
366882	166	8	Dexamethasone Sodium Phosphate	16	QID	Oral	106.72	Adrenal insufficiency	158	.	4
	166	8	Dexamethasone Sodium Phosphate	16	QID	Oral	106.72	Adrenal insufficiency	158	.	4
	174	1	Dexamethasone Sodium Phosphate	14	QID	Oral	93.38	Adrenal insufficiency	158	.	4
	175	1	Dexamethasone Sodium Phosphate	12	QID	Oral	80.04	Adrenal insufficiency	158	.	4
	175	1	Dexamethasone Sodium Phosphate	12	QID	Oral	80.04	Adrenal insufficiency	158	.	4
	176	1	Dexamethasone Sodium Phosphate	10	QID	Oral	66.70	Adrenal insufficiency	158	.	4
	177	1	Dexamethasone Sodium Phosphate	8	QID	Oral	53.36	Adrenal insufficiency	158	.	4
	178	1	Dexamethasone Sodium Phosphate	7	QID	Oral	46.69	Adrenal insufficiency	158	.	4
	178	1	Dexamethasone Sodium Phosphate	7	QID	Oral	46.69	Adrenal insufficiency	158	.	4
	179	1	Dexamethasone Sodium Phosphate	6	QID	Oral	40.02	Adrenal insufficiency	158	.	4
	180	1	Dexamethasone Sodium Phosphate	5	QID	Oral	33.35	Adrenal insufficiency	158	.	4
	180	1	Dexamethasone Sodium Phosphate	5	QID	Oral	33.35	Adrenal insufficiency	158	.	4
	181	1	Dexamethasone Sodium Phosphate	4	QID	Oral	26.68	Adrenal insufficiency	158	.	4
	181	1	Dexamethasone Sodium Phosphate	4	QID	Oral	26.68	Adrenal insufficiency	158	.	4
	182	1	Dexamethasone Sodium Phosphate	3	TID	Oral	20.01	Adrenal insufficiency	158	.	4
	183	1	Dexamethasone Sodium Phosphate	2	BID	Oral	13.34	Adrenal insufficiency	158	.	4

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付録 2.7.4-81 AEOSI-副腎機能不全に対する副腎皮質ホルモン剤使用の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Med. Start Day	Med. Duration (Days)	Med. Name	Total Daily Dose	Frequency	Route	Prednisone Equiv.† (mg)	Adverse Event for Use	AE Start Day	AE End Day	AE Toxicity Grade
	183	1	Dexamethasone Sodium Phosphate	2	BID	Oral	13.34	Adrenal insufficiency	158	.	4
	184	1	Dexamethasone Sodium Phosphate	1	QD	Oral	6.67	Adrenal insufficiency	158	.	4
	184	1	Dexamethasone Sodium Phosphate	1	QD	Oral	6.67	Adrenal insufficiency	158	.	4
	162	.	Hydrocortisone	15	QD	Oral	3.75	Adrenal insufficiency	158	.	4
	162	.	Hydrocortisone	15	QD	Oral	3.75	Adrenal insufficiency	158	.	4
	166	1	Hydrocortisone	100	ONCE	Intravenous	25.00	Adrenal insufficiency	158	.	4

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

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付録 2.7.4-82 AEOSI-1 型糖尿病を発現した患者の一覧

001 試験+002 試験+006 試験（APaT 集団）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q3W										
Trial Number=3475-001, Site Number=0020, Subject ID=000400, Gender=F, Race=White, Age=57 Years, Rel Day of Study Medication Discontinuance†=										
000400	Treatment Cycle 18	386	Type 1 diabetes mellitus	Continuing	Moderate	2	Y	Y		Not Resolved
Trial Number=3475-006, Site Number=1823, Subject ID=362113, Gender=F, Race=White, Age=64 Years, Rel Day of Study Medication Discontinuance†=85										
362113	Safety Follow-up	106	Type 1 diabetes mellitus	Continuing		4	Y	Y	Discontinued	Not Resolved
MK-3475 10 mg/kg Q2W										
Trial Number=3475-006, Site Number=0901, Subject ID=362011, Gender=F, Race=White, Age=89 Years, Rel Day of Study Medication Discontinuance†=29										
362011	Safety Follow-up	37	Diabetic ketoacidosis	2 Months		3	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.

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

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

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

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

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付録 2.7.4-83 AEOSI-ぶどう膜炎を発現した患者の一覧

001 試験+002 試験+006 試験（APaT 集団）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 2 mg/kg Q3W										
Trial Number=3475-001, Site Number=0019, Subject ID=000279, Gender=M, Race=White, Age=64 Years, Rel Day of Study Medication Discontinuance†=147										
000279	Treatment Cycle 6	107	Uveitis	1.57 Weeks	Moderate	2		Y		Resolved
MK-3475 10 mg/kg Q3W										
Trial Number=3475-001, Site Number=0010, Subject ID=001271, Gender=M, Race=White, Age=60 Years, Rel Day of Study Medication Discontinuance†=										
001271	Treatment Cycle 3	53	Uveitis	3.57 Weeks	Moderate	2		Y		Resolved
Trial Number=3475-001, Site Number=0011, Subject ID=000144, Gender=F, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance†=										
000144	Treatment Cycle 2	30	Uveitis	1.86 Weeks	Moderate	2		Y	Interrupted	Resolved
	Treatment Cycle 3	42	Uveitis	8.31 Months	Mild	1		Y		Resolved
Trial Number=3475-001, Site Number=0011, Subject ID=001361, Gender=F, Race=White, Age=47 Years, Rel Day of Study Medication Discontinuance†=										
001361	Treatment Cycle 12	233	Iridocyclitis	1.25 Months	Moderate	2		Y		Resolved
Trial Number=3475-001, Site Number=0020, Subject ID=000205, Gender=F, Race=White, Age=37 Years, Rel Day of Study Medication Discontinuance†=293										
000205	Treatment Cycle 3	47	Uveitis	2.14 Weeks	Moderate	2		Y		Resolved
		62	Uveitis	4 Weeks	Mild	1		Y		Resolved
Trial Number=3475-002, Site Number=0053, Subject ID=101867, Gender=M, Race=White, Age=69 Years, Rel Day of Study Medication Discontinuance†=										
101867	Treatment Cycle 4	64	Uveitis	2.86 Weeks		2	N	Y	None	Resolved
	Treatment Cycle 6	106	Uveitis	1.41 Months		1	N	Y	None	Resolved

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付録 2.7.4-83 AEOSI-ぶどう膜炎を発現した患者の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q3W										
Trial Number=3475-002, Site Number=0080, Subject ID=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
Trial Number=3475-006, Site Number=1300, Subject ID=360851, Gender=M, Race=White, Age=71 Years, Rel Day of Study Medication Discontinuance†=93										
360851	Treatment Cycle 3	63	Uveitis	4.29 Weeks		2	N	Y	Interrupted	Resolved
Trial Number=3475-006, Site Number=1711, Subject ID=363852, Gender=M, Race=White, Age=65 Years, Rel Day of Study Medication Discontinuance†=										
363852	Treatment Cycle 3	63	Iridocyclitis	1.18 Months		2	N	Y	None	Resolved
Trial Number=3475-006, Site Number=1816, Subject ID=364466, Gender=M, Race=White, Age=71 Years, Rel Day of Study Medication Discontinuance†=250										
364466	Treatment Cycle 2	33	Uveitis	2.4 Months		2	N	Y	None	Resolved
MK-3475 10 mg/kg Q2W										
Trial Number=3475-001, Site Number=0010, Subject ID=001204, Gender=M, Race=White, Age=61 Years, Rel Day of Study Medication Discontinuance†=										
001204	Treatment Cycle 16	225	Iritis	Continuing	Mild	1		Y		Not Resolved
Trial Number=3475-006, Site Number=0300, Subject ID=366627, Gender=F, Race=White, Age=63 Years, Rel Day of Study Medication Discontinuance†=										

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付録 2.7.4-83 AEOSI-ぶどう膜炎を発現した患者の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q2W										
Trial Number=3475-006, Site Number=0300, Subject ID=366627, Gender=F, Race=White, Age=63 Years, Rel Day of Study Medication Discontinuance[†]=										
366627	Treatment Cycle 4	44	Uveitis	Continuing		2	N	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 subject relative to the start of study medication.

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

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

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

Grades are based on NCI CTCAE version 4.0.

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

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

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

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付録 2.7.4-84 AEOSI-ぶどう膜炎に対する副腎皮質ホルモン剤使用の一覧

001 試験+002 試験+006 試験（APaT 集団）

Subject ID	Med. Start Day	Med. Duration (Days)	Med. Name	Total Daily Dose	Frequency	Route	Prednisone Equiv.[†] (mg)	Adverse Event for Use	AE Start Day	AE End Day	AE Toxicity Grade
MK-3475 10 mg/kg Q2W											
Trial Number=3475-006, Site Number=0300, Subject ID=366627, Gender=F, Race=White, Age=63 Years											
366627	69	1	Prednisone	30	QD	Oral	30.00	Uveitis	44	.	2

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

C Confidential

付録 2.7.4-85 有害事象の要約（AEOSI- ぶどう膜炎）
041 試験（APaT 集団）

	Subjects With Advanced Melanoma	
	n	(%)
Subjects in population	42	
with one or more adverse events	1	(2.4)
with no adverse event	41	(97.6)
with drug-related† adverse events	1	(2.4)
with toxicity grade 3-5 adverse events	0	(0.0)
with toxicity grade 3-5 drug-related adverse events	0	(0.0)
with serious adverse events	0	(0.0)
with serious drug-related adverse events	0	(0.0)
who died	0	(0.0)
who died due to a drug-related adverse event	0	(0.0)
discontinued‡ due to an adverse event	0	(0.0)
discontinued due to a drug-related adverse event	0	(0.0)
discontinued due to a serious adverse event	0	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)

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

‡Study medication withdrawn.

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

(Database Cutoff Date: [redacted].

Data Source: [資料5.3.5.2.3: P041V01]

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付録 2.7.4-86 Grade 別有害事象（AEOSI-ぶどう膜炎）（発現割合 0%超）
041 試験（APaT 集団）

	Subjects With Advanced Melanoma	
	n	(%)
Subjects in population	42	
with one or more adverse events	1	(2.4)
with no adverse events	41	(97.6)
Eye disorders	**1**	**(2.4)**
Grade 2	1	(2.4)
Uveitis	1	(2.4)
Grade 2	1	(2.4)

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

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

Only the highest reported grade of a given adverse event is counted for the individual subject.

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.

Adverse event terms are from MedDRA Version 18.0.

(Data Cutoff Date: [redacted].

Data Source: [資料5.3.5.2.3: P041V01]

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付録 2.7.4-87 AEOSI-ぶどう膜炎が発現するまでの期間及び罹患時間の要約
041 試験（APaT 集団）

	Subjects With Advanced Melanoma n	(%)
Subjects in population	42	
Subjects with Uveitis	1	(2.4)
Time to Onset of First Uveitis† (days)		
Mean (Std)	158.0	
Median (Range)	158.0 (158, 158)	
Total episodes of Uveitis	1	
Average Episodes per Subject	1.00	
Episode duration‡ (days)		
Median (Range)	32.0 (32, 32)	

(%) = Number of patients with Uveitis / Number of patients in population.

† Time to onset statistics are based on number of patients with Uveitis.

‡ Episode duration is based on a time-to-event analysis. If an adverse event is not resolved at the time of analysis or the patient died without adverse event resolved, the duration is censored at either data cutoff date or date of death, whichever occurred first.

Std = Standard Deviation.

Grades are based on NCI CTCAE version 4.0.

(Database Cutoff Date: [redacted].

Data Source: [資料5.3.5.2.3: P041V01]

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付録 2.7.4-88 AEOSI-筋炎を発現した患者の一覧

001 試験+002 試験+006 試験（APaT 集団）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 2 mg/kg Q3W										
Trial Number=3475-001, Site Number=0015, Subject ID=000464, Gender=M, Race=White, Age=68 Years, Rel Day of Study Medication Discontinuance†=										
000464	Treatment Cycle 9	192	Myositis	Continuing	Mild	1		N	N/A	Not Resolved
MK-3475 10 mg/kg Q3W										
Trial Number=3475-001, Site Number=0011, Subject ID=000068, Gender=M, Race=White, Age=46 Years, Rel Day of Study Medication Discontinuance†=83										
000068	Safety Follow-up	101	Rhabdomyolysis	2.66 Months	Severe	3	Y	Y	Discontinued	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										
000482	Treatment Cycle 22	459	Myositis	Continuing	Moderate	2		Y	Discontinued	Not Resolved
Trial Number=3475-006, Site Number=1815, Subject ID=369449, Gender=M, Race=White, Age=69 Years, Rel Day of Study Medication Discontinuance†=148										
369449	Treatment Cycle 2	20	Myositis	4.24 Months		2	N	Y	Interrupted	Resolved
Trial Number=3475-006, Site Number=1818, Subject ID=364877, Gender=M, Race=White, Age=80 Years, Rel Day of Study Medication Discontinuance†=										
364877	Treatment Cycle 5	85	Myositis	Continuing		1	N	N	None	Not Resolved
MK-3475 10 mg/kg Q2W										
Trial Number=3475-001, Site Number=0015, Subject ID=000039, Gender=M, Race=White, Age=58 Years, Rel Day of Study Medication Discontinuance†=337										
000039	Treatment Cycle 19	258	Myopathy	2.63 Months	Mild	1		Y		Resolved

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付録 2.7.4-88 AEOSI-筋炎を発現した患者の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q2W										
Trial Number=3475-001, Site Number=0015, Subject ID=000039, Gender=M, Race=White, Age=58 Years, Rel Day of Study Medication Discontinuance†=337										
000039	Safety Follow-up	365	Myopathy	4.5 Months	Moderate	2	Y	Y	Discontinued	Resolved

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

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

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

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

Grades are based on NCI CTCAE version 4.0.

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

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

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

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付録 2.7.4-89 AEOSI-皮膚反応を発現した患者の一覧

001 試験+002 試験+006 試験（APaT 集団）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 2 mg/kg Q3W										
Trial Number=3475-002, Site Number=0054, Subject ID=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
Trial Number=3475-002, Site Number=0140, Subject ID=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
MK-3475 10 mg/kg Q3W										
Trial Number=3475-001, Site Number=0008, Subject ID=000100, Gender=F, Race=White, Age=62 Years, Rel Day of Study Medication Discontinuance†=701										
000100	Treatment Cycle 14	288	Exfoliative rash	Continuing	Mild	1		Y	N/A	Not Resolved
Trial Number=3475-001, Site Number=0008, Subject ID=001367, Gender=F, Race=White, Age=62 Years, Rel Day of Study Medication Discontinuance†=										
001367	Treatment Cycle 9	172	Rash	1.71 Weeks	Severe	3	Y	N		Resolved
Trial Number=3475-001, Site Number=0010, Subject ID=000452, Gender=F, Race=White, Age=33 Years, Rel Day of Study Medication Discontinuance†=233										
000452	Treatment Cycle 6	117	Rash generalised	4 Days	Severe	3	Y	N	Interrupted	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 6	159	Pruritus	4 Days	Severe	3		Y		Resolved
Trial Number=3475-001, Site Number=0012, Subject ID=000305, Gender=M, Race=White, Age=76 Years, Rel Day of Study Medication Discontinuance†=										
000305	Treatment Cycle 13	271	Rash	3.14 Weeks	Severe	3		Y	Interrupted	Resolved

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付録 2.7.4-89 AEOSI-皮膚反応を発現した患者の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q3W										
Trial Number=3475-001, Site Number=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
Trial Number=3475-001, Site Number=0019, Subject ID=000297, Gender=M, Race=White, Age=76 Years, Rel Day of Study Medication Discontinuance†=211										
000297	Safety Follow-up	232	Rash maculo-papular	3.14 Weeks	Severe	3		Y	Interrupted	Resolved
Trial Number=3475-002, Site Number=0053, Subject ID=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
Trial Number=3475-002, Site Number=0088, Subject ID=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
Trial Number=3475-006, Site Number=1503, Subject ID=360532, Gender=F, Race=White, Age=57 Years, Rel Day of Study Medication Discontinuance†=										
360532	Treatment Cycle 3	57	Dermatitis bullous	5.82 Months		1	N	N	None	Resolved
Trial Number=3475-006, Site Number=1703, Subject ID=363479, Gender=M, Race=White, Age=64 Years, Rel Day of Study Medication Discontinuance†=										
363479	Treatment Cycle 7	148	Pruritus	3.48 Months		3	N	N	Interrupted	Resolved
Trial Number=3475-006, Site Number=1809, Subject ID=362971, Gender=M, Race=White, Age=56 Years, Rel Day of Study Medication Discontinuance†=										
362971	Treatment Cycle 8	169	Rash maculo-papular	3.29 Weeks		3	N	Y	Interrupted	Resolved
Trial Number=3475-006, Site Number=1823, Subject ID=362113, Gender=F, Race=White, Age=64 Years, Rel Day of Study Medication Discontinuance†=85										

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付録 2.7.4-89 AEOSI-皮膚反応を発現した患者の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q3W										
Trial Number=3475-006, Site Number=1823, Subject ID=362113, Gender=F, Race=White, Age=64 Years, Rel Day of Study Medication Discontinuance†=85										
362113	Treatment Cycle 4	64	Exfoliative rash	3.14 Weeks		1	N	Y	None	Resolved
MK-3475 10 mg/kg Q2W										
Trial Number=3475-001, Site Number=0010, Subject ID=000030, Gender=F, Race=White, Age=81 Years, Rel Day of Study Medication Discontinuance†=309										
000030	Treatment Cycle 16	225	Rash	5.52 Months	Severe	3		Y	Interrupted	Resolved
		225	Rash	Continuing	Severe	3		Y	Interrupted	Not Resolved
Trial Number=3475-001, Site Number=0010, Subject ID=000042, Gender=M, Race=White, Age=25 Years, Rel Day of Study Medication Discontinuance†=731										
000042	Treatment Cycle 37	591	Pruritus	1.14 Weeks	Severe	3		Y		Resolved
Trial Number=3475-001, Site Number=0010, Subject ID=000087, Gender=M, Race=White, Age=67 Years, Rel Day of Study Medication Discontinuance†=										
000087	Treatment Cycle 8	128	Dermatitis exfoliative	1.22 Months	Moderate	2		Y	N/A	Resolved
Trial Number=3475-001, Site Number=0019, Subject ID=001352, Gender=M, Race=White, Age=79 Years, Rel Day of Study Medication Discontinuance†=57										

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付録 2.7.4-89 AEOSI-皮膚反応を発現した患者の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q2W										
Trial Number=3475-001, Site Number=0019, Subject ID=001352, Gender=M, Race=White, Age=79 Years, Rel Day of Study Medication Discontinuance[†]=57										
001352	Safety Follow-up	71	Pruritus	Continuing	Severe	3		N	N/A	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.

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

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

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

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付録 2.7.4-90 AEOSI-皮膚反応に対する副腎皮質ホルモン剤使用の一覧

001 試験+002 試験+006 試験（APaT 集団）

Subject ID	Med. Start Day	Med. Duration (Days)	Med. Name	Total Daily Dose	Frequency	Route	Prednisone Equiv.† (mg)	Adverse Event for Use	AE Start Day	AE End Day	AE Toxicity Grade
MK-3475 2 mg/kg Q3W											
Trial Number=3475-002, Site Number=0140, Subject ID=100006, Gender=M, Race=White, Age=76 Years, Rel Day of Study Medication Discontinuance‡=1											
100006	22	8	Prednisone	80	QD	Oral	80.00	Stevens-Johnson syndrome	4	129	3
	30	6	Prednisone	50	QD	Oral	50.00	Stevens-Johnson syndrome	4	129	3
	36	3	Prednisone	30	QD	Oral	30.00	Stevens-Johnson syndrome	4	129	3
	39	2	Prednisone	10	QD	Oral	10.00	Stevens-Johnson syndrome	4	129	3
	41	2	Prednisone	5	QD	Oral	5.00	Stevens-Johnson syndrome	4	129	3
MK-3475 10 mg/kg Q3W											
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	33	4	Prednisone	60	QD	Oral Administration	60.00	Rash generalised	33	40	3
	37	5	Prednisone	50	QD	Oral Administration	50.00	Rash generalised	33	40	3
Trial Number=3475-001, Site Number=0019, Subject ID=000297, Gender=M, Race=White, Age=76 Years, Rel Day of Study Medication Discontinuance‡=211											
000297	232	6	Methylprednisolone	128	QID	Oral Administration	160.00	Rash maculo-papular	232	253	3
Trial Number=3475-002, Site Number=0053, Subject ID=101851, Gender=M, Race=White, Age=89 Years, Rel Day of Study Medication Discontinuance‡=235											
101851	85	7	Prednisone	60	QD	Oral	60.00	Rash maculo-papular	43	109	3
	92	3	Prednisone	40	QD	Oral	40.00	Rash maculo-papular	43	109	3
	101	3	Prednisone	5	QD	Oral	5.00	Rash maculo-papular	43	109	3

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付録 2.7.4-90 AEOSI-皮膚反応に対する副腎皮質ホルモン剤使用の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Med. Start Day	Med. Duration (Days)	Med. Name	Total Daily Dose	Frequency	Route	Prednisone Equiv.† (mg)	Adverse Event for Use	AE Start Day	AE End Day	AE Toxicity Grade
Trial Number=3475-006, Site Number=1809, Subject ID=362971, Gender=M, Race=White, Age=56 Years, Rel Day of Study Medication Discontinuance‡=											
362971	169	24	Prednisone	10	QD	Oral	10.00	Rash maculo-papular	169	191	3
MK-3475 10 mg/kg Q2W											
Trial Number=3475-001, Site Number=0010, Subject ID=000042, Gender=M, Race=White, Age=25 Years, Rel Day of Study Medication Discontinuance‡=731											
000042	591	7	Methylprednisolone	1	OTHER	Oral Administration	1.25	Pruritus	591	598	3

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

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付録 2.7.4-91 有害事象の要約（AEOSI-皮膚反応）
041 試験（APaT 集団）

	Subjects With Advanced Melanoma	
	n	(%)
Subjects in population	42	
with one or more adverse events	1	(2.4)
with no adverse event	41	(97.6)
with drug-related† adverse events	1	(2.4)
with toxicity grade 3-5 adverse events	0	(0.0)
with toxicity grade 3-5 drug-related adverse events	0	(0.0)
with serious adverse events	0	(0.0)
with serious drug-related adverse events	0	(0.0)
who died	0	(0.0)
who died due to a drug-related adverse event	0	(0.0)
discontinued‡ due to an adverse event	0	(0.0)
discontinued due to a drug-related adverse event	0	(0.0)
discontinued due to a serious adverse event	0	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)

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

‡Study medication withdrawn.

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

(Database Cutoff Date: [redacted]).

Data Source: [資料5.3.5.2.3: P041V01]

付録 2.7.4-92 Grade 別有害事象（AEOSI-皮膚反応）（発現割合 0%超）
041 試験（APaT 集団）

	Subjects With Advanced Melanoma	
	n	(%)
Subjects in population	42	
with one or more adverse events	1	(2.4)
with no adverse events	41	(97.6)
Skin and subcutaneous tissue disorders	**1**	**(2.4)**
Grade 1	1	(2.4)
Toxic skin eruption	1	(2.4)
Grade 1	1	(2.4)

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

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

Only the highest reported grade of a given adverse event is counted for the individual subject.

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.

Adverse event terms are from MedDRA Version 18.0.

(Data Cutoff Date: [redacted].

Data Source: [資料5.3.5.2.3: P041V01]

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付録 2.7.4-93 AEOSI-皮膚反応が発現するまでの期間及び罹患期間の要約
041 試験（APaT 集団）

	Subjects With Advanced Melanoma n	(%)
Subjects in population	42	
Subjects with Skin-B	1	(2.4)
Time to Onset of First Skin-B† (days)		
Mean (Std)	13.0	
Median (Range)	13.0 (13, 13)	
Total episodes of Skin-B	1	
Average Episodes per Subject	1.00	
Episode duration‡ (days)		
Median (Range)	31.0 (31, 31)	

(%) = Number of patients with Skin-B / Number of patients in population.

† Time to onset statistics are based on number of patients with Skin-B.

‡ Episode duration is based on a time-to-event analysis. If an adverse event is not resolved at the time of analysis or the patient died without adverse event resolved, the duration is censored at either data cutoff date or date of death, whichever occurred first.

Std = Standard Deviation.

Grades are based on NCI CTCAE version 4.0.

(Database Cutoff Date: [redacted].

Data Source: [資料5.3.5.2.3: P041V01]

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付録 2.7.4-94 AEOSI-膵炎を発現した患者の一覧

001 試験+002 試験+006 試験（APaT 集団）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 2 mg/kg Q3W										
Trial Number=3475-002, Site Number=0088, Subject ID=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
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	Severe	3	Y	Y	Discontinued	Not Resolved
Trial Number=3475-006, Site Number=0002, Subject ID=361272, Gender=M, Race=White, Age=68 Years, Rel Day of Study Medication Discontinuance†=										
361272	Treatment Cycle 9	183	Pancreatitis	4 Days		3	Y	N	Interrupted	Resolved
Trial Number=3475-006, Site Number=0100, Subject ID=364614, Gender=M, Race=White, Age=68 Years, Rel Day of Study Medication Discontinuance†=63										
364614	Safety Follow-up	84	Pancreatitis	3.86 Weeks		2	N	Y	Interrupted	Resolved
MK-3475 10 mg/kg Q2W										
Trial Number=3475-006, Site Number=1710, Subject ID=364567, Gender=M, Race=White, Age=73 Years, Rel Day of Study Medication Discontinuance†=113										

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付録 2.7.4-94 AEOSI-膵炎を発現した患者の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q2W										
Trial Number=3475-006, Site Number=1710, Subject ID=364567, Gender=M, Race=White, Age=73 Years, Rel Day of Study Medication Discontinuance†=113										
364567	Safety Follow-up	116	Autoimmune pancreatitis	3.86 Weeks		3	Y	Y	Discontinued	Sequelae

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

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

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

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

Grades are based on NCI CTCAE version 4.0.

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

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

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

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付録 2.7.4-95 AEOSI-膵炎に対する副腎皮質ホルモン剤使用の一覧

001 試験+002 試験+006 試験（APaT 集団）

Subject ID	Med. Start Day	Med. Duration (Days)	Med. Name	Total Daily Dose	Frequency	Route	Prednisone Equiv.† (mg)	Adverse Event for Use	AE Start Day	AE End Day	AE Toxicity Grade
MK-3475 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	84	.	Prednisone	10	QD	Oral Administration	10.00	Pancreatitis	76	.	3
Trial Number=3475-006, Site Number=0100, Subject ID=364614, Gender=M, Race=White, Age=68 Years, Rel Day of Study Medication Discontinuance†=63											
364614	92	3	Methylprednisolone	80	QD	Oral	100.00	Pancreatitis	84	110	2
	95	11	Methylprednisolone	60	QD	Oral	75.00	Pancreatitis	84	110	2
	106	2	Methylprednisolone	40	QD	Oral	50.00	Pancreatitis	84	110	2
	108	1	Methylprednisolone	20	QD	Oral	25.00	Pancreatitis	84	110	2
	109	2	Methylprednisolone	10	QD	Oral	12.50	Pancreatitis	84	110	2
MK-3475 10 mg/kg Q2W											
Trial Number=3475-006, Site Number=1710, Subject ID=364567, Gender=M, Race=White, Age=73 Years, Rel Day of Study Medication Discontinuance†=113											
364567	132	5	Hydrocortisone	800	QID	Intravenous	200.00	Autoimmune pancreatitis	116	142	3
	132	5	Hydrocortisone	800	QID	Intravenous	200.00	Autoimmune pancreatitis	116	142	3
	137	19	Prednisolone	50	QD	Oral	50.00	Autoimmune pancreatitis	116	142	3
	137	19	Prednisolone	50	QD	Oral	50.00	Autoimmune pancreatitis	116	142	3
	155	7	Prednisolone	40	QD	Oral	40.00	Autoimmune pancreatitis	116	142	3
	155	7	Prednisolone	40	QD	Oral	40.00	Autoimmune pancreatitis	116	142	3

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付録 2.7.4-95 AEOSI-膵炎に対する副腎皮質ホルモン剤使用の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Med. Start Day	Med. Duration (Days)	Med. Name	Total Daily Dose	Frequency	Route	Prednisone Equiv.† (mg)	Adverse Event for Use	AE Start Day	AE End Day	AE Toxicity Grade
	162	7	Prednisolone	30	QD	Oral	30.00	Autoimmune pancreatitis	116	142	3

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

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付録 2.7.4-96 AEOSI-腎炎を発現した患者の一覧

001 試験+002 試験+006 試験（APaT 集団）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 2 mg/kg Q3W										
Trial Number=3475-002, Site Number=0112, Subject ID=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
MK-3475 10 mg/kg Q3W										
Trial Number=3475-006, Site Number=0605, Subject ID=363218, Gender=M, Race=White, Age=75 Years, Rel Day of Study Medication Discontinuance†=190										
363218	Safety Follow-up	215	Renal failure	Continuing		3	Y	Y	Discontinued	Not Resolved
Trial Number=3475-006, Site Number=0902, Subject ID=361025, Gender=M, Race=White, Age=76 Years, Rel Day of Study Medication Discontinuance†=										
361025	Treatment Cycle 7	156	Tubulointerstitial nephritis	1.08 Months		2	Y	Y	Interrupted	Resolved
MK-3475 10 mg/kg Q2W										
Trial Number=3475-001, Site Number=0010, Subject ID=000054, Gender=M, Race=White, Age=68 Years, Rel Day of Study Medication Discontinuance†=199										
000054	Post-study	353	Nephritis autoimmune	3.25 Months	Moderate	2	Y	Y		Resolved
Trial Number=3475-001, Site Number=0015, Subject ID=000048, Gender=M, Race=White, Age=57 Years, Rel Day of Study Medication Discontinuance†=365										
000048	Safety Follow-up	388	Renal failure acute	1.12 Months	Severe	4	Y	Y	Discontinued	Resolved
Trial Number=3475-001, Site Number=0021, Subject ID=000058, Gender=F, Race=White, Age=58 Years, Rel Day of Study Medication Discontinuance†=1										
000058	Safety Follow-up	12	Renal failure	2.14 Weeks	Severe	3	Y	Y		Resolved

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付録 2.7.4-96 AEOSI-腎炎を発現した患者の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q2W										
Trial Number=3475-006, Site Number=1711, Subject ID=368852, Gender=F, Race=White, Age=48 Years, Rel Day of Study Medication Discontinuance[†]=29										
368852	Safety Follow-up	41	Renal failure acute	Continuing		3	Y	Y	N/A	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.

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

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

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

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付録 2.7.4-97 AEOSI-腎炎に対する副腎皮質ホルモン剤使用の一覧

001 試験+002 試験+006 試験（APaT 集団）

Subject ID	Med. Start Day	Med. Duration (Days)	Med. Name	Total Daily Dose	Frequency	Route	Prednisone Equiv.† (mg)	Adverse Event for Use	AE Start Day	AE End Day	AE Toxicity Grade
MK-3475 2 mg/kg Q3W											
Trial Number=3475-002, Site Number=0112, Subject ID=101216, Gender=M, Race=White, Age=67 Years, Rel Day of Study Medication Discontinuance‡=41											
101216	75	15	Prednisone	100	QD	Oral	100.00	Tubulointerstitial nephritis	62	.	2
	90	13	Prednisone	60	QD	Oral	60.00	Tubulointerstitial nephritis	62	.	2
	103	14	Prednisone	30	QD	Oral	30.00	Tubulointerstitial nephritis	62	.	2
	117	15	Prednisone	20	QD	Oral	20.00	Tubulointerstitial nephritis	62	.	2
	132	.	Prednisone	10	QD	Oral	10.00	Tubulointerstitial nephritis	62	.	2
MK-3475 10 mg/kg Q3W											
Trial Number=3475-006, Site Number=0902, Subject ID=361025, Gender=M, Race=White, Age=76 Years, Rel Day of Study Medication Discontinuance‡=											
361025	174	3	Prednisone	70	QD	Oral	70.00	Tubulointerstitial nephritis	156	188	2
	177	3	Prednisone	60	QD	Oral	60.00	Tubulointerstitial nephritis	156	188	2
	180	3	Prednisone	50	QD	Oral	50.00	Tubulointerstitial nephritis	156	188	2
	183	3	Prednisone	40	QD	Oral	40.00	Tubulointerstitial nephritis	156	188	2
	186	3	Prednisone	30	QD	Oral	30.00	Tubulointerstitial nephritis	156	188	2
	189	21	Prednisone	10	QD	Oral	10.00	Tubulointerstitial nephritis	156	188	2
MK-3475 10 mg/kg Q2W											
Trial Number=3475-001, Site Number=0010, Subject ID=000054, Gender=M, Race=White, Age=68 Years, Rel Day of Study Medication Discontinuance‡=199											

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付録 2.7.4-97 AEOSI-腎炎に対する副腎皮質ホルモン剤使用の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Med. Start Day	Med. Duration (Days)	Med. Name	Total Daily Dose	Frequency	Route	Prednisone Equiv.† (mg)	Adverse Event for Use	AE Start Day	AE End Day	AE Toxicity Grade
000054	353	15	Prednisone	80	QD	Oral Administration	80.00	Nephritis autoimmune	353	451	2
	368	5	Prednisone	60	QD	Oral Administration	60.00	Nephritis autoimmune	353	451	2
	373	9	Prednisone	40	QD	Oral Administration	40.00	Nephritis autoimmune	353	451	2
	381	15	Prednisone	30	QD	Oral Administration	30.00	Nephritis autoimmune	353	451	2
	396	14	Prednisone	20	QD	Oral Administration	20.00	Nephritis autoimmune	353	451	2
	410	14	Prednisone	10	QD	Oral Administration	10.00	Nephritis autoimmune	353	451	2
	424	28	Prednisone	5	QD	Oral Administration	5.00	Nephritis autoimmune	353	451	2
Trial Number=3475-001, Site Number=0015, Subject ID=000048, Gender=M, Race=White, Age=57 Years, Rel Day of Study Medication Discontinuance‡=365											
000048	388	19	Prednisone	80	QD	Oral Administration	80.00	Renal failure acute	388	421	4
	406	8	Prednisone	60	QD	Oral Administration	60.00	Renal failure acute	388	421	4
	413	8	Prednisone	50	QD	Oral Administration	50.00	Renal failure acute	388	421	4
	420	7	Prednisone	40	QD	Oral Administration	40.00	Renal failure acute	388	421	4
	426	8	Prednisone	30	QD	Oral Administration	30.00	Renal failure acute	388	421	4
	433	8	Prednisone	20	QD	Oral Administration	20.00	Renal failure acute	388	421	4
	440	15	Prednisone	10	QD	Oral Administration	10.00	Renal failure acute	388	421	4
	454	15	Prednisone	5	QD	Oral Administration	5.00	Renal failure acute	388	421	4
	468	15	Prednisone	3	QD	Oral Administration	2.50	Renal failure acute	388	421	4

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付録 2.7.4-97 AEOSI-腎炎に対する副腎皮質ホルモン剤使用の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Med. Start Day	Med. Duration (Days)	Med. Name	Total Daily Dose	Frequency	Route	Prednisone Equiv.† (mg)	Adverse Event for Use	AE Start Day	AE End Day	AE Toxicity Grade
Trial Number=3475-001, Site Number=0021, Subject ID=000058, Gender=F, Race=White, Age=58 Years, Rel Day of Study Medication Discontinuance‡=1											
000058	22	48	Prednisone	60	TID	Oral Administration	60.00	Renal failure	12	26	3
	70	34	Prednisone	45	QD	Oral Administration	45.00	Renal failure	12	26	3
	104	27	Prednisone	25	QD	Oral Administration	25.00	Renal failure	12	26	3
	131	18	Prednisone	18	QD	Oral Administration	18.00	Renal failure	12	26	3
	149	28	Prednisone	16	QD	Oral Administration	16.00	Renal failure	12	26	3
	177	21	Prednisone	12	QD	Oral Administration	12.00	Renal failure	12	26	3

付録 2.7.4-97 AEOSI-腎炎に対する副腎皮質ホルモン剤使用の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Med. Start Day	Med. Duration (Days)	Med. Name	Total Daily Dose	Frequency	Route	Prednisone Equiv.† (mg)	Adverse Event for Use	AE Start Day	AE End Day	AE Toxicity Grade
	198	46	Prednisone	10	QD	Oral Administration	10.00	Renal failure	12	26	3
	244	92	Prednisone	5	QD	Oral Administration	5.00	Renal failure	12	26	3
Trial Number=3475-006, Site Number=1711, Subject ID=368852, Gender=F, Race=White, Age=48 Years, Rel Day of Study Medication Discontinuance‡=29											
368852	54	.	Prednisone	20	QD	Oral	20.00	Renal failure acute	41	.	3

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

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付録 2.7.4-98 有害事象の要約（AEOSI-ニューロパチー）
001 試験+002 試験+006 試験（APaT 集団）

	MK-3475 2 mg/kg Q3W		MK-3475 10 mg/kg Q3W		MK-3475 10 mg/kg Q2W		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	340		769		458		1,567	
with one or more adverse events	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
with no adverse event	340	(100.0)	768	(99.9)	458	(100.0)	1,566	(99.9)
with drug-related† adverse events	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
with Grade 3- 5 adverse events	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
with Grade 3- 5 drug-related adverse events	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
with serious adverse events	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
with serious drug-related adverse events	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
who died	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
with drug-related death	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued‡ due to an adverse event	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
discontinued due to a drug-related adverse event	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
discontinued due to a serious adverse event	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
discontinued due to a serious drug-related adverse event	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)

Grades are based on NCI CTCAE version 4.0.
† Determined by the investigator to be related to the drug.
‡ Study medication withdrawn.
(MK-3475 PN001 Database Cutoff Date: [redacted].
(MK-3475 PN002 Database Cutoff Date: 12MAY2014).
(MK-3475 PN006 Database Cutoff Date: 03SEP2014).

付録 2.7.4-99 Grade 別有害事象（AEOSI-ニューロパチー）
（いずれかの投与群で発現割合 0%超）
001 試験+002 試験+006 試験（APaT 集団）

	MK-3475 2 mg/kg Q3W		MK-3475 10 mg/kg Q3W		MK-3475 10 mg/kg Q2W		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	340		769		458		1,567	
with one or more adverse events	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
with no adverse events	340	(100.0)	768	(99.9)	458	(100.0)	1,566	(99.9)
Nervous system disorders	**0**	**(0.0)**	**1**	**(0.1)**	**0**	**(0.0)**	**1**	**(0.1)**
Guillain-Barre syndrome	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Grade 4	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)

Every subject is counted a single time for each applicable specific adverse event. A subject with multiple adverse events within a system organ class is counted a single time for that system organ class.
A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns is greater than or equal to the incidence specified in the report title, after rounding.
Only the highest reported grade of a given adverse event is counted for the individual subject.
Grades are based on NCI CTCAE version 4.0.
(MK-3475 PN001 Database Cutoff Date: [redacted].
(MK-3475 PN002 Database Cutoff Date: 12MAY2014).
(MK-3475 PN006 Database Cutoff Date: 03SEP2014).

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付録 2.7.4-100 AEOSI-ニューロパチーが発現するまでの期間及び罹患期間の要約

001 試験+002 試験+006 試験（APaT 集団）

	MK-3475 2 mg/kg Q3W n (%)	MK-3475 10 mg/kg Q3W n (%)	MK-3475 10 mg/kg Q2W n (%)	Total n (%)
Subjects in population	340	769	458	1567
Subjects with Neuropathy	0	1 (0.1)	0	1 (0.1)
Time to Onset of First Neuropathy (days)†				
Mean (Std)	0	28.0	0	28.0
Median	0.0	28.0	0.0	28.0
Range	0 to 0	28 to 28	0 to 0	28 to 28
Total episodes of Neuropathy	0	1	0	1
Average Episodes per subject	0	1.00	0	1.00
Episode duration (days)‡				
Median	0	96.0	0	96.0
Range	0 to 0	96 to 96	0 to 0	96 to 96

(%) = Number of subjects with Neuropathy / Number of subjects in population.

† Time to onset statistics are based on number of subjects with Neuropathy.

‡ Episode duration is based on a time-to-event analysis. If an adverse event is not resolved at the time of analysis or the patient died without adverse event resolved, the duration is censored at either data cutoff date or date of death, whichever occurred first.

Std = Standard Deviation.

Grades are based on NCI CTCAE version 4.0.

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

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

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

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付録 2.7.4-101 AEOSI-ニューロパチーを発現した患者の一覧

001 試験+002 試験+006 試験（APaT 集団）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q3W										
Trial Number=3475-006, Site Number=1707, Subject ID=364658, Gender=M, Race=White, Age=58 Years, Rel Day of Study Medication Discontinuance[†]=1										
364658	Safety Follow-up	28	Guillain-Barre syndrome	3.15 Months		4	Y	Y	Discontinued	Sequelae

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

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

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

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

Grades are based on NCI CTCAE version 4.0.

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

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

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

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付録 2.7.4-102 AEOSI-ニューロパチーに対する副腎皮質ホルモン剤の使用の要約 001 試験+002 試験+006 試験（APaT 集団）

	MK-3475 2 mg/kg Q3W (N=340)		MK-3475 10 mg/kg Q3W (N=769)		MK-3475 10 mg/kg Q2W (N=458)		Total (N=1567)	
	n	%	n	%	n	%	n	%
Subjects with one or more Neuropathy	0		1		0		1	
Treated with systemic corticosteroid	0	0	1	100.0	0	0	1	100.0
Not treated with systemic corticosteroid	0	0	0	0	0	0	0	0

The number of Subjects with one or more Neuropathy is used as the denominator for the percentage calculation.
(MK-3475 PN001 Database Cutoff Date: [redacted].
(MK-3475 PN002 Database Cutoff Date: 12MAY2014).
(MK-3475 PN006 Database Cutoff Date: 03SEP2014).

付録 2.7.4-103 AEOSI-ニューロパチーに対する副腎皮質ホルモン剤の用量の要約 001 試験+002 試験+006 試験（APaT 集団）

	MK-3475 2 mg/kg Q3W	MK-3475 10 mg/kg Q3W	MK-3475 10 mg/kg Q2W	Total
Total Episodes	0	1	0	1
High Starting Dose (%) †	**0 (0.0)**	**1 (100.0)**	**0 (0.0)**	**1 (100.0)**
Starting dose (mg/day)				
Mean (Std)	0 (0)	107 (.)	0 (0)	107 (.)
Median (Range)	0 (0-0)	107 (107-107)	0 (0-0)	107 (107-107)
Duration (days)§				
Mean (Std)	0 (0)	240 (.)	0 (0)	240 (.)
Median (Range)	0 (0-0)	240 (240-240)	0 (0-0)	240 (240-240)
Low Starting Dose (%) ‡	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**
Not Treated with Systemic Corticosteroid (%)	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**

† High starting dose corticosteroid treatment is defined as ≥ 40 mg/day prednisone or equivalent.
‡ Low starting dose corticosteroid treatment is defined as < 40 mg/day prednisone or equivalent.
§ Ongoing corticosteroid treatment is censored at the cutoff date or date of death, whichever occurs first.
(MK-3475 PN001 Database Cutoff Date: [redacted]
(MK-3475 PN002 Database Cutoff Date: 12MAY2014).
(MK-3475 PN006 Database Cutoff Date: 03SEP2014).

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付録 2.7.4-104 AEOSI-ニューロパチーに対する副腎皮質ホルモン剤使用の一覧

001 試験+002 試験+006 試験（APaT 集団）

Subject ID	Med. Start Day	Med. Duration (Days)	Med. Name	Total Daily Dose	Frequency	Route	Prednisone Equiv.† (mg)	Adverse Event for Use	AE Start Day	AE End Day	AE Toxicity Grade
MK-3475 10 mg/kg Q3W											
Trial Number=3475-006, Site Number=1707, Subject ID=364658, Gender=M, Race=White, Age=58 Years, Rel Day of Study Medication Discontinuance‡=1											
364658	29	.	Dexamethasone	16	BID	Intravenous	106.72	Guillain-Barre syndrome	28	123	4

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

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付録 2.7.4-105 AEOSI-Infusion reaction を発現した患者の一覧

001 試験+002 試験+006 試験（APaT 集団）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 2 mg/kg Q3W										
Trial Number=3475-001, Site Number=0010, Subject ID=000254, Gender=F, Race=White, Age=41 Years, Rel Day of Study Medication Discontinuance†=										
000254	Treatment Cycle 18	361	Drug hypersensitivity	Continuing	Mild	1		N	N/A	Not Resolved
Trial Number=3475-001, Site Number=0020, Subject ID=000322, Gender=M, Race=White, Age=34 Years, Rel Day of Study Medication Discontinuance†=										
000322	Treatment Cycle 20	421	Hypersensitivity	2.14 Weeks	Mild	1		N		Resolved
Trial Number=3475-001, Site Number=0023, Subject ID=000316, Gender=M, Race=White, Age=68 Years, Rel Day of Study Medication Discontinuance†=358										
000316	Treatment Cycle 8	163	Drug hypersensitivity	1 Days	Mild	1		Y	N/A	Resolved
Trial Number=3475-002, Site Number=0029, Subject ID=100019, Gender=F, Race=White, Age=72 Years, Rel Day of Study Medication Discontinuance†=182										
100019	Treatment Cycle 6	108	Cytokine release syndrome	3.5 Hours		1	N	Y	None	Resolved
		111	Cytokine release syndrome	3.75 Hours		1	N	Y	None	Resolved
		113	Cytokine release syndrome	2 Days		1	N	Y	None	Resolved
	Treatment Cycle 7	129	Cytokine release syndrome	2 Days		1	N	Y	None	Resolved
Trial Number=3475-002, Site Number=0061, Subject ID=100049, Gender=M, Race=White, Age=57 Years, Rel Day of Study Medication Discontinuance†=										
100049	Treatment Cycle 11	216	Hypersensitivity	1.25 Months		1	N	Y	None	Resolved
MK-3475 10 mg/kg Q3W										
Trial Number=3475-001, Site Number=0011, Subject ID=000167, Gender=F, Race=White, Age=32 Years, Rel Day of Study Medication Discontinuance†=140										
000167	Treatment Cycle 3	43	Infusion related reaction	1 Days	Mild	1		Y		Resolved

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付録 2.7.4-105 AEOSI-Infusion reaction を発現した患者の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q3W										
Trial Number=3475-001, Site Number=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=0015, Subject ID=000070, Gender=M, Race=White, Age=60 Years, Rel Day of Study Medication Discontinuance†=										
000070	Treatment Cycle 25	521	Hypersensitivity	Continuing	Mild	1		N	N/A	Not Resolved
Trial Number=3475-001, Site Number=0016, Subject ID=000330, Gender=M, Race=White, Age=73 Years, Rel Day of Study Medication Discontinuance†=85										
000330	Treatment Cycle 5	85	Cytokine release syndrome	Continuing	Mild	1		Y	N/A	Not Resolved
Trial Number=3475-001, Site Number=0019, Subject ID=000278, Gender=F, Race=White, Age=29 Years, Rel Day of Study Medication Discontinuance†=										
000278	Treatment Cycle 10	191	Infusion related reaction	1 Days	Moderate	2		Y	Interrupted	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	Treatment Cycle 2	42	Drug hypersensitivity	1 Days	Mild	1		N	N/A	Resolved
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
Trial Number=3475-002, Site Number=0012, Subject ID=100046, Gender=F, Race=White, Age=54 Years, Rel Day of Study Medication Discontinuance†=										
100046	Treatment Cycle 9	176	Hypersensitivity	Continuing		1	N	N	None	Not Resolved
Trial Number=3475-002, Site Number=0012, Subject ID=101279, Gender=M, Race=White, Age=68 Years, Rel Day of Study Medication Discontinuance†=87										

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付録 2.7.4-105 AEOSI-Infusion reaction を発現した患者の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q3W										
Trial Number=3475-002, Site Number=0012, Subject ID=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
Trial Number=3475-002, Site Number=0016, Subject ID=100647, Gender=F, Race=White, Age=74 Years, Rel Day of Study Medication Discontinuance†=274										
100647	Treatment Cycle 1	1	Drug hypersensitivity	1.41 Months		2	N	Y	Reduced	Resolved
Trial Number=3475-002, Site Number=0025, Subject ID=100676, Gender=M, Race=White, Age=44 Years, Rel Day of Study Medication Discontinuance†=84										
100676	Treatment Cycle 2	21	Infusion related reaction	1.37 Hours		2	N	Y	None	Resolved
Trial Number=3475-002, Site Number=0102, Subject ID=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
Trial Number=3475-006, Site Number=0007, Subject ID=367327, Gender=M, Race=White, Age=56 Years, Rel Day of Study Medication Discontinuance†=29										
367327	Treatment Cycle 2	29	Hypersensitivity	31 Minutes		1	N	Y	Interrupted	Resolved
Trial Number=3475-006, Site Number=0300, Subject ID=362752, Gender=F, Race=White, Age=52 Years, Rel Day of Study Medication Discontinuance†=211										
362752	Treatment Cycle 4	64	Infusion related reaction	1 Hours		2	N	Y	Interrupted	Resolved
Trial Number=3475-006, Site Number=0312, Subject ID=363354, Gender=F, Race=White, Age=46 Years, Rel Day of Study Medication Discontinuance†=22										
363354	Treatment Cycle 2	22	Infusion related reaction	15 Minutes		2	N	Y	Interrupted	Resolved
Trial Number=3475-006, Site Number=0312, Subject ID=363673, Gender=M, Race=White, Age=88 Years, Rel Day of Study Medication Discontinuance†=42										

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付録 2.7.4-105 AEOSI-Infusion reaction を発現した患者の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q3W										
Trial Number=3475-006, Site Number=0312, Subject ID=363673, Gender=M, Race=White, Age=88 Years, Rel Day of Study Medication Discontinuance†=42										
363673	Treatment Cycle 2	21	Infusion related reaction	25 Minutes		2	N	Y	Interrupted	Resolved
Trial Number=3475-006, Site Number=1201, Subject ID=364788, Gender=F, Race=White, Age=53 Years, Rel Day of Study Medication Discontinuance†=41										
364788	Treatment Cycle 2	22	Hypersensitivity	7 Minutes		1	N	Y	Interrupted	Resolved
Trial Number=3475-006, Site Number=1402, Subject ID=368856, Gender=M, Race=White, Age=61 Years, Rel Day of Study Medication Discontinuance†=85										
368856	Treatment Cycle 2	22	Hypersensitivity	1 Hours		2	N	Y	Interrupted	Resolved
Trial Number=3475-006, Site Number=1601, Subject ID=363494, Gender=M, Race=White, Age=51 Years, Rel Day of Study Medication Discontinuance†=										
363494	Treatment Cycle 14	293	Hypersensitivity	Continuing		1	N	N	None	Not Resolved
Trial Number=3475-006, Site Number=1807, Subject ID=365454, Gender=F, Race=White, Age=59 Years, Rel Day of Study Medication Discontinuance†=141										
365454	Treatment Cycle 2	22	Infusion related reaction	55 Minutes		2	N	Y	Interrupted	Resolved
MK-3475 10 mg/kg Q2W										
Trial Number=3475-001, Site Number=0010, Subject ID=000045, Gender=M, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance†=441										
000045	Treatment Cycle 7	98	Drug hypersensitivity	1 Days	Mild	1		N	N/A	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 23	347	Drug hypersensitivity	2.43 Months	Moderate	2		N		Resolved

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付録 2.7.4-105 AEOSI-Infusion reaction を発現した患者の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q2W										
Trial Number=3475-001, Site Number=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=3475-006, Site Number=0004, Subject ID=361200, Gender=F, Race=White, Age=52 Years, Rel Day of Study Medication Discontinuance†=										
361200	Treatment Cycle 13	167	Infusion related reaction	4.14 Weeks		2	N	Y	None	Resolved
Trial Number=3475-006, Site Number=0007, Subject ID=360582, Gender=M, Race=White, Age=32 Years, Rel Day of Study Medication Discontinuance†=										
360582	Treatment Cycle 4	42	Hypersensitivity	15 Minutes		2	N	Y	None	Resolved
	Treatment Cycle 18	238	Hypersensitivity	30 Minutes		1	N	Y	None	Resolved
Trial Number=3475-006, Site Number=1201, Subject ID=368842, Gender=F, Race=White, Age=60 Years, Rel Day of Study Medication Discontinuance†=44										
368842	Treatment Cycle 2	16	Hypersensitivity	23.98 Hours		1	N	Y	None	Resolved
Trial Number=3475-006, Site Number=1502, Subject ID=367365, Gender=M, Race=White, Age=43 Years, Rel Day of Study Medication Discontinuance†=										
367365	Treatment Cycle 11	157	Infusion related reaction	1.29 Weeks		1	N	Y	None	Resolved
Trial Number=3475-006, Site Number=1600, Subject ID=368466, Gender=M, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=14										
368466	Treatment Cycle 2	14	Drug hypersensitivity	2.33 Hours		3	Y	Y	Discontinued	Resolved
Trial Number=3475-006, Site Number=1804, Subject ID=364306, Gender=M, Race=White, Age=68 Years, Rel Day of Study Medication Discontinuance†=										
364306	Treatment Cycle 5	58	Hypersensitivity	Continuing		1	N	N	None	Resolving

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付録 2.7.4-105 AEOSI-Infusion reaction を発現した患者の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q2W										
Trial Number=3475-006, Site Number=1819, Subject ID=368835, Gender=M, Race=White, Age=36 Years, Rel Day of Study Medication Discontinuance[†]=30										
368835	Safety Follow-up	51	Infusion related reaction	23 Hours		2	N	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.

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

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

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

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付録 2.7.4-106 AEOSI-Infusion reaction に対する副腎皮質ホルモン剤使用の一覧

001 試験+002 試験+006 試験（APaT 集団）

Subject ID	Med. Start Day	Med. Duration (Days)	Med. Name	Total Daily Dose	Frequency	Route	Prednisone Equiv.† (mg)	Adverse Event for Use	AE Start Day	AE End Day	AE Toxicity Grade
MK-3475 10 mg/kg Q3W											
Trial Number=3475-002, Site Number=0102, Subject ID=100305, Gender=M, Race=White, Age=54 Years, Rel Day of Study Medication Discontinuance‡=85											
100305	85	1	Methylprednisolone	80	PRN	Intravenous	100.00	Anaphylactic reaction	85	.	4
	86	3	Prednisone	30	QD	Oral	30.00	Anaphylactic reaction	85	.	4
	89	3	Prednisone	20	QD	Oral	20.00	Anaphylactic reaction	85	.	4
	92	3	Prednisone	10	QD	Oral	10.00	Anaphylactic reaction	85	.	4
Trial Number=3475-006, Site Number=0007, Subject ID=367327, Gender=M, Race=White, Age=56 Years, Rel Day of Study Medication Discontinuance‡=29											
367327	29	1	Hydrocortisone	100	ONCE	Intravenous	25.00	Hypersensitivity	29	.	1
Trial Number=3475-006, Site Number=0300, Subject ID=362752, Gender=F, Race=White, Age=52 Years, Rel Day of Study Medication Discontinuance‡=211											
362752	64	1	Hydrocortisone	100	ONCE	Intravenous	25.00	Infusion related reaction	64	.	2
Trial Number=3475-006, Site Number=0312, Subject ID=363354, Gender=F, Race=White, Age=46 Years, Rel Day of Study Medication Discontinuance‡=22											
363354	22	1	Dexamethasone	20	ONCE	Intravenous	133.40	Infusion related reaction	22	.	2
Trial Number=3475-006, Site Number=1201, Subject ID=364788, Gender=F, Race=White, Age=53 Years, Rel Day of Study Medication Discontinuance‡=41											
364788	22	1	Hydrocortisone	100	ONCE	Intravenous	25.00	Hypersensitivity	22	.	1
Trial Number=3475-006, Site Number=1807, Subject ID=365454, Gender=F, Race=White, Age=59 Years, Rel Day of Study Medication Discontinuance‡=141											
365454	22	1	Hydrocortisone	50	ONCE	Intravenous	12.50	Infusion related reaction	22	.	2
MK-3475 10 mg/kg Q2W											

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付録 2.7.4-106 AEOSI-Infusion reaction に対する副腎皮質ホルモン剤使用の一覧

001 試験+002 試験+006 試験（APaT 集団）（続き）

Subject ID	Med. Start Day	Med. Duration (Days)	Med. Name	Total Daily Dose	Frequency	Route	Prednisone Equiv.[†] (mg)	Adverse Event for Use	AE Start Day	AE End Day	AE Toxicity Grade
Trial Number=3475-006, Site Number=0007, Subject ID=360582, Gender=M, Race=White, Age=32 Years, Rel Day of Study Medication Discontinuance[‡]=											
360582	42	1	Hydrocortisone	100	ONCE	Intravenous	25.00	Hypersensitivity	42	.	2
	238	1	Hydrocortisone	100	ONCE	Intravenous	25.00	Hypersensitivity	238	.	1
Trial Number=3475-006, Site Number=1600, Subject ID=368466, Gender=M, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance[‡]=14											
368466	14	1	Betamethasone Sodium Phosphate	16	BID	Intravenous	133.28	Drug hypersensitivity	14	.	3
Trial Number=3475-006, Site Number=1804, Subject ID=364306, Gender=M, Race=White, Age=68 Years, Rel Day of Study Medication Discontinuance[‡]=											
364306	65	9	Dexamethasone	4	PRN	Oral	26.68	Hypersensitivity	58	.	1

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

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付録 2.7.4-107 有害事象の要約（AEOSI-筋無力症候群）
001 試験+002 試験+006 試験（APaT 集団）

	MK-3475 2 mg/kg Q3W		MK-3475 10 mg/kg Q3W		MK-3475 10 mg/kg Q2W		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	340		769		458		1,567	
with one or more adverse events	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
with no adverse event	340	(100.0)	768	(99.9)	458	(100.0)	1,566	(99.9)
with drug-related† adverse events	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
with Grade 3- 5 adverse events	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
with Grade 3- 5 drug-related adverse events	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
with serious adverse events	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
with serious drug-related adverse events	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
who died	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
with drug-related death	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued‡ due to an adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

Grades are based on NCI CTCAE version 4.0.
† Determined by the investigator to be related to the drug.
‡ Study medication withdrawn.
(MK-3475 PN001 Database Cutoff Date: [redacted])
(MK-3475 PN002 Database Cutoff Date: 12MAY2014).
(MK-3475 PN006 Database Cutoff Date: 03SEP2014).

付録 2.7.4-108 Grade 別有害事象（AEOSI-筋無力症候群）
（いずれかの投与群で発現割合 0%超）
001 試験+002 試験+006 試験（APaT 集団）

	MK-3475 2 mg/kg Q3W		MK-3475 10 mg/kg Q3W		MK-3475 10 mg/kg Q2W		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	340		769		458		1,567	
with one or more adverse events	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
with no adverse events	340	(100.0)	768	(99.9)	458	(100.0)	1,566	(99.9)
Nervous system disorders	**0**	**(0.0)**	**1**	**(0.1)**	**0**	**(0.0)**	**1**	**(0.1)**
Myasthenic syndrome	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Grade 3	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)

Every subject is counted a single time for each applicable specific adverse event. A subject with multiple adverse events within a system organ class is counted a single time for that system organ class.
A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns is greater than or equal to the incidence specified in the report title, after rounding.
Only the highest reported grade of a given adverse event is counted for the individual subject.
Grades are based on NCI CTCAE version 4.0.
(MK-3475 PN001 Database Cutoff Date: [redacted]).
(MK-3475 PN002 Database Cutoff Date: 12MAY2014).
(MK-3475 PN006 Database Cutoff Date: 03SEP2014).

C Confidential

付録 2.7.4-109 AEOSI-筋無力症候群が発現するまでの期間及び罹患期間の要約

001 試験+002 試験+006 試験（APaT 集団）

	MK-3475 2 mg/kg Q3W n (%)	MK-3475 10 mg/kg Q3W n (%)	MK-3475 10 mg/kg Q2W n (%)	Total n (%)
Subjects in population	340	769	458	1567
Subjects with Myasthenic Syndrome	0	1 (0.1)	0	1 (0.1)
Time to Onset of First Myasthenic Syndrome (days)†				
Mean (Std)	0	74.0	0	74.0
Median	0.0	74.0	0.0	74.0
Range	0 to 0	74 to 74	0 to 0	74 to 74
Total episodes of Myasthenic Syndrome	0	1	0	1
Average Episodes per subject	0	1.00	0	1.00
Episode duration (days)‡				
Median	0	255.0	0	255.0
Range	0 to 0	255 to 255	0 to 0	255 to 255

(%) = Number of subjects with Myasthenic Syndrome / Number of subjects in population.
† Time to onset statistics are based on number of subjects with Myasthenic Syndrome.
‡ Episode duration is based on a time-to-event analysis. If an adverse event is not resolved at the time of analysis or the patient died without adverse event resolved, the duration is censored at either data cutoff date or date of death, whichever occurred first.
Std = Standard Deviation.
Grades are based on NCI CTCAE version 4.0.
(MK-3475 PN001 Database Cutoff Date: [redacted]
(MK-3475 PN002 Database Cutoff Date: 12MAY2014).
(MK-3475 PN006 Database Cutoff Date: 03SEP2014).

C Confidential

付録 2.7.4-110 AEOSI-筋無力症候群を発現した患者の一覧

001 試験+002 試験+006 試験（APaT 集団）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q3W										
Trial Number=3475-002, Site Number=0083, Subject ID=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

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

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

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

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

Grades are based on NCI CTCAE version 4.0.

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

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

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

C Confidential

付録 2.7.4-111 AEOSI-筋無力症候群に対する副腎皮質ホルモン剤の使用の要約 001 試験+002 試験+006 試験（APaT 集団）

	MK-3475 2 mg/kg Q3W (N=340)		MK-3475 10 mg/kg Q3W (N=769)		MK-3475 10 mg/kg Q2W (N=458)		Total (N=1567)	
	n	%	n	%	n	%	n	%
Subjects with one or more Myasthenic Syndrome	0		1		0		1	
Treated with systemic corticosteroid	0	0	1	100.0	0	0	1	100.0
Not treated with systemic corticosteroid	0	0	0	0	0	0	0	0

The number of Subjects with one or more Myasthenic Syndrome is used as the denominator for the percentage calculation.
(MK-3475 PN001 Database Cutoff Date: [redacted].
(MK-3475 PN002 Database Cutoff Date: 12MAY2014).
(MK-3475 PN006 Database Cutoff Date: 03SEP2014).

付録 2.7.4-112 AEOSI-筋無力症候群に対する副腎皮質ホルモン剤の用量の要約 001 試験+002 試験+006 試験（APaT 集団）

	MK-3475 2 mg/kg Q3W	MK-3475 10 mg/kg Q3W	MK-3475 10 mg/kg Q2W	Total
Total Episodes	0	1	0	1
High Starting Dose (%) †	**0 (0.0)**	**1 (100.0)**	**0 (0.0)**	**1 (100.0)**
Starting dose (mg/day)				
Mean (Std)	0 (0)	1250 (.)	0 (0)	1250 (.)
Median (Range)	0 (0-0)	1250 (1250-1250)	0 (0-0)	1250 (1250-1250)
Duration (days)§				
Mean (Std)	0 (0)	3 (.)	0 (0)	3 (.)
Median (Range)	0 (0-0)	3 (3-3)	0 (0-0)	3 (3-3)
Low Starting Dose (%) ‡	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**
Not Treated with Systemic Corticosteroid (%)	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**

† High starting dose corticosteroid treatment is defined as ≥ 40 mg/day prednisone or equivalent.
‡ Low starting dose corticosteroid treatment is defined as < 40 mg/day prednisone or equivalent.
§ Ongoing corticosteroid treatment is censored at the cutoff date or date of death, whichever occurs first.
(MK-3475 PN001 Database Cutoff Date: [redacted].
(MK-3475 PN002 Database Cutoff Date: 12MAY2014).
(MK-3475 PN006 Database Cutoff Date: 03SEP2014).

C Confidential

付録 2.7.4-113 AEOSI-筋無力症候群に対する副腎皮質ホルモン剤使用の一覧

001 試験+002 試験+006 試験（APaT 集団）

Subject ID	Med. Start Day	Med. Duration (Days)	Med. Name	Total Daily Dose	Frequency	Route	Prednisone Equiv.† (mg)	Adverse Event for Use	AE Start Day	AE End Day	AE Toxicity Grade
MK-3475 10 mg/kg Q3W											
Trial Number=3475-002, Site Number=0083, Subject ID=100042, Gender=F, Race=White, Age=69 Years, Rel Day of Study Medication Discontinuance‡=64											
100042	109	12	Cortisone	40	QD	Oral	8.00	Myasthenic syndrome	74	328	3
	120	16	Cortisone	30	QD	Oral	6.00	Myasthenic syndrome	74	328	3
	87	3	Methylprednisolone	1000	QD	Intravenous	1250.00	Myasthenic syndrome	74	328	3
	104	6	Prednisolone	60	QD	Oral	60.00	Myasthenic syndrome	74	328	3
	135	31	Prednisolone	5	QD	Oral	5.00	Myasthenic syndrome	74	328	3

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

C Confidential

付録 2.7.4-114 有害事象の要約（AEOSI-心膜炎）
001 試験+002 試験+006 試験（APaT 集団）

	MK-3475 2 mg/kg Q3W		MK-3475 10 mg/kg Q3W		MK-3475 10 mg/kg Q2W		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	340		769		458		1,567	
with one or more adverse events	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)
with no adverse event	339	(99.7)	769	(100.0)	458	(100.0)	1,566	(99.9)
with drug-related† adverse events	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)
with Grade 3- 5 adverse events	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)
with Grade 3- 5 drug-related adverse events	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)
with serious adverse events	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)
with serious drug-related adverse events	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)
who died	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
with drug-related death	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued‡ due to an adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

Grades are based on NCI CTCAE version 4.0.
† Determined by the investigator to be related to the drug.
‡ Study medication withdrawn.
(MK-3475 PN001 Database Cutoff Date: [redacted].
(MK-3475 PN002 Database Cutoff Date: 12MAY2014).
(MK-3475 PN006 Database Cutoff Date: 03SEP2014).

付録 2.7.4-115 Grade 別有害事象（AEOSI-心膜炎）
（いずれかの投与群で発現割合 0%超）
001 試験+002 試験+006 試験（APaT 集団）

	MK-3475 2 mg/kg Q3W		MK-3475 10 mg/kg Q3W		MK-3475 10 mg/kg Q2W		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	340		769		458		1,567	
with one or more adverse events	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)
with no adverse events	339	(99.7)	769	(100.0)	458	(100.0)	1,566	(99.9)
Cardiac disorders	**1**	**(0.3)**	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.1)**
Pericarditis	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)
Grade 3	1	(0.3)	0	(0.0)	0	(0.0)	1	(0.1)

Every subject is counted a single time for each applicable specific adverse event. A subject with multiple adverse events within a system organ class is counted a single time for that system organ class.
A system organ class or specific adverse event appears on this report only if its incidence in one or more of the columns is greater than or equal to the incidence specified in the report title, after rounding.
Only the highest reported grade of a given adverse event is counted for the individual subject.
Grades are based on NCI CTCAE version 4.0.
(MK-3475 PN001 Database Cutoff Date: [redacted]
(MK-3475 PN002 Database Cutoff Date: 12MAY2014).
(MK-3475 PN006 Database Cutoff Date: 03SEP2014).

Confidential

付録 2.7.4-116 AEOSI-心膜炎が発現するまでの期間及び罹患期間の要約

001 試験+002 試験+006 試験（APaT 集団）

	MK-3475 2 mg/kg Q3W n (%)	MK-3475 10 mg/kg Q3W n (%)	MK-3475 10 mg/kg Q2W n (%)	Total n (%)
Subjects in population	340	769	458	1567
Subjects with Pericarditis	1 (0.3)	0	0	1 (0.1)
Time to Onset of First Pericarditis (days)†				
Mean (Std)	3.0	0	0	3.0
Median	3.0	0.0	0.0	3.0
Range	3 to 3	0 to 0	0 to 0	3 to 3
Total episodes of Pericarditis	1	0	0	1
Average Episodes per subject	1.00	0	0	1.00
Episode duration (days)‡				
Median	11.0	0	0	11.0
Range	11 to 11	0 to 0	0 to 0	11 to 11

(%) = Number of subjects with Pericarditis / Number of subjects in population.
† Time to onset statistics are based on number of subjects with Pericarditis.
‡ Episode duration is based on a time-to-event analysis. If an adverse event is not resolved at the time of analysis or the patient died without adverse event resolved, the duration is censored at either data cutoff date or date of death, whichever occurred first.
Std = Standard Deviation.
Grades are based on NCI CTCAE version 4.0.
(MK-3475 PN001 Database Cutoff Date: [redacted].
(MK-3475 PN002 Database Cutoff Date: 12MAY2014).
(MK-3475 PN006 Database Cutoff Date: 03SEP2014).

C Confidential

付録 2.7.4-117 AEOSI-心膜炎を発現した患者の一覧

001 試験+002 試験+006 試験（APaT 集団）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 2 mg/kg Q3W										
Trial Number=3475-001, Site Number=0021, Subject ID=000496, Gender=M, Race=White, Age=43 Years, Rel Day of Study Medication Discontinuance†=526										
000496	Treatment Cycle 1	3	Pericarditis	1.57 Weeks	Severe	3	Y	Y		Resolved

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

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

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

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

Grades are based on NCI CTCAE version 4.0.

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

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

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

C Confidential

付録 2.7.4-118 有害事象の要約（AEOSI-血管炎）

001 試験+002 試験+006 試験（APaT 集団）

	MK-3475 2 mg/kg Q3W		MK-3475 10 mg/kg Q3W		MK-3475 10 mg/kg Q2W		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	340		769		458		1,567	
with one or more adverse events	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
with no adverse event	340	(100.0)	768	(99.9)	458	(100.0)	1,566	(99.9)
with drug-related[†] adverse events	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
with Grade 3- 5 adverse events	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
with Grade 3- 5 drug-related adverse events	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
with serious adverse events	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
who died	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
with drug-related death	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued[‡] due to an adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

Grades are based on NCI CTCAE version 4.0.
[†] Determined by the investigator to be related to the drug.
[‡] Study medication withdrawn.
(MK-3475 PN001 Database Cutoff Date: [redacted].
(MK-3475 PN002 Database Cutoff Date: 12MAY2014).
(MK-3475 PN006 Database Cutoff Date: 03SEP2014).

Confidential

付録 2.7.4-119 Grade 別有害事象（AEOSI-血管炎）
（いずれかの投与群で発現割合 0%超）
001 試験+002 試験+006 試験（APaT 集団）

	MK-3475 2 mg/kg Q3W		MK-3475 10 mg/kg Q3W		MK-3475 10 mg/kg Q2W		Total	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	340		769		458		1,567	
with one or more adverse events	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
with no adverse events	340	(100.0)	768	(99.9)	458	(100.0)	1,566	(99.9)
Vascular disorders	**0**	**(0.0)**	**1**	**(0.1)**	**0**	**(0.0)**	**1**	**(0.1)**
Vasculitis	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)
Grade 1	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.1)

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

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

Only the highest reported grade of a given adverse event is counted for the individual subject.

Grades are based on NCI CTCAE version 4.0.

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

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

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

Confidential

付録 2.7.4-120 AEOSI-血管炎が発現するまでの期間及び罹患期間の要約

001 試験+002 試験+006 試験（APaT 集団）

	MK-3475 2 mg/kg Q3W n (%)	MK-3475 10 mg/kg Q3W n (%)	MK-3475 10 mg/kg Q2W n (%)	Total n (%)
Subjects in population	340	769	458	1567
Subjects with Vasculitis	0	1 (0.1)	0	1 (0.1)
Time to Onset of First Vasculitis (days)†				
Mean (Std)	0	45.0	0	45.0
Median	0.0	45.0	0.0	45.0
Range	0 to 0	45 to 45	0 to 0	45 to 45
Total episodes of Vasculitis	0	1	0	1
Average Episodes per subject	0	1.00	0	1.00
Episode duration (days)‡				
Median	0	145.0	0	145.0
Range	0 to 0	145 to 145	0 to 0	145 to 145

(%) = Number of subjects with Vasculitis / Number of subjects in population.

† Time to onset statistics are based on number of subjects with Vasculitis.

‡ Episode duration is based on a time-to-event analysis. If an adverse event is not resolved at the time of analysis or the patient died without adverse event resolved, the duration is censored at either data cutoff date or date of death, whichever occurred first.

Std = Standard Deviation.

Grades are based on NCI CTCAE version 4.0.

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

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

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

C Confidential

付録 2.7.4-121 AEOSI-血管炎を発現した患者の一覧

001 試験+002 試験+006 試験（APaT 集団）

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q3W										
Trial Number=3475-002, Site Number=0070, Subject ID=100691, Gender=M, Race=White, Age=44 Years										
100691	Treatment Cycle 3	45	Vasculitis	4.76 Months		1	N	Y	None	Resolved

Action Taken: None = DOSE NOT CHANGED, Reduced = DOSE REDUCED, Interrupted = DRUG INTERRUPTED, Discontinued = DRUG WITHDRAWN, Increased = DOSE INCREASED, N/A = NOT APPLICABLE.
Outcome: Resolved = RECOVERED/RESOLVED, Resolving = RECOVERING/RESOLVING, Sequelae = RECOVERED/RESOLVED WITH SEQUELAE, Not resolved = NOT RECOVERED/NOT RESOLVED.
Related: Investigator-assessed relationship of the adverse event to study medication.
Grades are based on NCI CTCAE version 4.0.
(MK-3475 PN001 Database Cutoff Date: [redacted].
(MK-3475 PN002 Database Cutoff Date: 12MAY2014).
(MK-3475 PN006 Database Cutoff Date: 03SEP2014).

Confidential

付録 2.7.4-122 臨床検査値の Grade がベースラインより悪化した患者の要約
001 試験パート B2+D（APaT 集団）

Laboratory Test	Ipi-naïve 2 mg/kg Q3W (N=51)	Ipi-naïve 10 mg/kg Q3W (N=52)	Ipi-exposed 2 mg/kg Q3W (N=89)	Ipi-exposed 10 mg/kg Q3W (N=84)	Total (N=276)
APTT Increased					
Improved from baseline	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Worsened from baseline	5 (9.8)	2 (3.8)	2 (2.2)	2 (2.4)	11 (4.0)
Clinically meaningful† worsened from baseline	0 (0.0)	0 (0.0)	1 (1.1)	1 (1.2)	2 (0.7)
Alanine Aminotransferase Increased					
Improved from baseline	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	1 (0.4)
Worsened from baseline	19 (37.3)	16 (30.8)	20 (22.5)	17 (20.2)	72 (26.1)
Clinically meaningful† worsened from baseline	5 (9.8)	1 (1.9)	3 (3.4)	1 (1.2)	10 (3.6)
Albumin Decreased					
Improved from baseline	0 (0.0)	0 (0.0)	0 (0.0)	1 (1.2)	1 (0.4)
Worsened from baseline	18 (35.3)	24 (46.2)	31 (34.8)	37 (44.0)	110 (39.9)
Clinically meaningful† worsened from baseline	9 (17.6)	9 (17.3)	6 (6.7)	7 (8.3)	31 (11.2)
Alkaline Phosphatase Increased					
Improved from baseline	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Worsened from baseline	16 (31.4)	16 (30.8)	17 (19.1)	18 (21.4)	67 (24.3)
Clinically meaningful† worsened from baseline	5 (9.8)	3 (5.8)	3 (3.4)	3 (3.6)	14 (5.1)
Aspartate Aminotransferase Increased					

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付録 2.7.4-122 臨床検査値の Grade がベースラインより悪化した患者の要約

001 試験パート B2+D（APaT 集団）（続き）

Laboratory Test	Ipi-naïve 2 mg/kg Q3W (N=51)	Ipi-naïve 10 mg/kg Q3W (N=52)	Ipi-exposed 2 mg/kg Q3W (N=89)	Ipi-exposed 10 mg/kg Q3W (N=84)	Total (N=276)
Aspartate Aminotransferase Increased					
Improved from baseline	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Worsened from baseline	19 (37.3)	13 (25.0)	27 (30.3)	18 (21.4)	77 (27.9)
Clinically meaningful† worsened from baseline	1 (2.0)	1 (1.9)	6 (6.7)	4 (4.8)	12 (4.3)
Bilirubinn Increased					
Improved from baseline	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Worsened from baseline	6 (11.8)	4 (7.7)	13 (14.6)	13 (15.5)	36 (13.0)
Clinically meaningful† worsened from baseline	3 (5.9)	1 (1.9)	4 (4.5)	6 (7.1)	14 (5.1)
Calcium Decreased					
Improved from baseline	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Worsened from baseline	16 (31.4)	22 (42.3)	22 (24.7)	21 (25.0)	81 (29.3)
Clinically meaningful† worsened from baseline	0 (0.0)	2 (3.8)	1 (1.1)	2 (2.4)	5 (1.8)
Calcium Increased					
Improved from baseline	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Worsened from baseline	4 (7.8)	3 (5.8)	6 (6.7)	4 (4.8)	17 (6.2)
Clinically meaningful† worsened from baseline	1 (2.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Cholesterol					

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001 試験パート B2+D（APaT 集団）（続き）

Laboratory Test	Ipi-naïve 2 mg/kg Q3W (N=51)	Ipi-naïve 10 mg/kg Q3W (N=52)	Ipi-exposed 2 mg/kg Q3W (N=89)	Ipi-exposed 10 mg/kg Q3W (N=84)	Total (N=276)
Cholesterol					
Improved from baseline	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Worsened from baseline	15 (29.4)	14 (26.9)	20 (22.5)	12 (14.3)	61 (22.1)
Clinically meaningful[†] worsened from baseline	0 (0.0)	0 (0.0)	3 (3.4)	1 (1.2)	4 (1.4)
Creatinine Increased					
Improved from baseline	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Worsened from baseline	7 (13.7)	6 (11.5)	12 (13.5)	14 (16.7)	39 (14.1)
Clinically meaningful[†] worsened from baseline	0 (0.0)	1 (1.9)	1 (1.1)	1 (1.2)	3 (1.1)
Glucose Decreased					
Improved from baseline	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Worsened from baseline	4 (7.8)	9 (17.3)	10 (11.2)	7 (8.3)	30 (10.9)
Clinically meaningful[†] worsened from baseline	0 (0.0)	3 (5.8)	2 (2.2)	0 (0.0)	5 (1.8)
Glucose Increased					
Improved from baseline	1 (2.0)	2 (3.8)	1 (1.1)	0 (0.0)	4 (1.4)
Worsened from baseline	26 (51.0)	25 (48.1)	38 (42.7)	46 (54.8)	135 (48.9)
Clinically meaningful[†] worsened from baseline	5 (9.8)	6 (11.5)	5 (5.6)	11 (13.1)	27 (9.8)
Hemoglobin Decreased					

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001 試験パート B2+D（APaT 集団）（続き）

Laboratory Test	Ipi-naïve 2 mg/kg Q3W (N=51)	Ipi-naïve 10 mg/kg Q3W (N=52)	Ipi-exposed 2 mg/kg Q3W (N=89)	Ipi-exposed 10 mg/kg Q3W (N=84)	Total (N=276)
Hemoglobin Decreased					
Improved from baseline	0 (0.0)	0 (0.0)	1 (1.1)	1 (1.2)	2 (0.7)
Worsened from baseline	23 (45.1)	29 (55.8)	53 (59.6)	45 (53.6)	150 (54.3)
Clinically meaningful† worsened from baseline	4 (7.8)	9 (17.3)	13 (14.6)	11 (13.1)	37 (13.4)
Leukocytes Decreased					
Improved from baseline	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Worsened from baseline	7 (13.7)	10 (19.2)	15 (16.9)	13 (15.5)	45 (16.3)
Clinically meaningful† worsened from baseline	1 (2.0)	4 (7.7)	0 (0.0)	5 (6.0)	10 (3.6)
Lymphocytes Decreased					
Improved from baseline	1 (2.0)	1 (1.9)	0 (0.0)	0 (0.0)	2 (0.7)
Worsened from baseline	16 (31.4)	21 (40.4)	23 (25.8)	25 (29.8)	85 (30.8)
Clinically meaningful† worsened from baseline	6 (11.8)	11 (21.2)	15 (16.9)	10 (11.9)	42 (15.2)
Magnesium Decreased					
Improved from baseline	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Worsened from baseline	7 (13.7)	7 (13.5)	8 (9.0)	9 (10.7)	31 (11.2)
Clinically meaningful† worsened from baseline	1 (2.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.4)
Magnesium Increased					

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001 試験パート B2+D（APaT 集団）（続き）

Laboratory Test	Ipi-naïve 2 mg/kg Q3W (N=51)	Ipi-naïve 10 mg/kg Q3W (N=52)	Ipi-exposed 2 mg/kg Q3W (N=89)	Ipi-exposed 10 mg/kg Q3W (N=84)	Total (N=276)
Magnesium Increased					
Improved from baseline	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Worsened from baseline	9 (17.6)	4 (7.7)	5 (5.6)	7 (8.3)	25 (9.1)
Clinically meaningful† worsened from baseline	1 (2.0)	0 (0.0)	0 (0.0)	2 (2.4)	3 (1.1)
Neutrophils Decreased					
Improved from baseline	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Worsened from baseline	2 (3.9)	6 (11.5)	5 (5.6)	4 (4.8)	17 (6.2)
Clinically meaningful† worsened from baseline	1 (2.0)	3 (5.8)	0 (0.0)	3 (3.6)	7 (2.5)
Phosphate Decreased					
Improved from baseline	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	1 (0.4)
Worsened from baseline	11 (21.6)	11 (21.2)	12 (13.5)	10 (11.9)	44 (15.9)
Clinically meaningful† worsened from baseline	11 (21.6)	11 (21.2)	12 (13.5)	10 (11.9)	44 (15.9)
Potassium Decreased					
Improved from baseline	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Worsened from baseline	3 (5.9)	5 (9.6)	11 (12.4)	7 (8.3)	26 (9.4)
Clinically meaningful† worsened from baseline	0 (0.0)	1 (1.9)	1 (1.1)	1 (1.2)	3 (1.1)
Potassium Increased					

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付録 2.7.4-122 臨床検査値の Grade がベースラインより悪化した患者の要約

001 試験パート B2+D（APaT 集団）（続き）

Laboratory Test	Ipi-naïve 2 mg/kg Q3W (N=51)	Ipi-naïve 10 mg/kg Q3W (N=52)	Ipi-exposed 2 mg/kg Q3W (N=89)	Ipi-exposed 10 mg/kg Q3W (N=84)	Total (N=276)
Potassium Increased					
Improved from baseline	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Worsened from baseline	11 (21.6)	9 (17.3)	11 (12.4)	9 (10.7)	40 (14.5)
Clinically meaningful† worsened from baseline	1 (2.0)	2 (3.8)	3 (3.4)	1 (1.2)	7 (2.5)
Prothrombin Intl. Normalized Ratio In					
Improved from baseline	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Worsened from baseline	2 (3.9)	2 (3.8)	7 (7.9)	6 (7.1)	17 (6.2)
Clinically meaningful† worsened from baseline	0 (0.0)	0 (0.0)	4 (4.5)	1 (1.2)	5 (1.8)
Sodium Decreased					
Improved from baseline	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Worsened from baseline	22 (43.1)	17 (32.7)	36 (40.4)	26 (31.0)	101 (36.6)
Clinically meaningful† worsened from baseline	4 (7.8)	5 (9.6)	8 (9.0)	0 (0.0)	17 (6.2)
Triglycerides					
Improved from baseline	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Worsened from baseline	22 (43.1)	17 (32.7)	28 (31.5)	21 (25.0)	88 (31.9)

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001 試験パート B2+D（APaT 集団）（続き）

Laboratory Test	Ipi-naïve 2 mg/kg Q3W (N=51)	Ipi-naïve 10 mg/kg Q3W (N=52)	Ipi-exposed 2 mg/kg Q3W (N=89)	Ipi-exposed 10 mg/kg Q3W (N=84)	Total (N=276)
Triglycerides					
Clinically meaningful† worsened from baseline	0 (0.0)	0 (0.0)	1 (1.1)	0 (0.0)	1 (0.4)

A missing baseline value was set to Grade 0.
† A clinically meaningful worsening in CTCAE grade was defined as a shift from less than Grade 3 to Grade 3 , 4 or 5 or a shift from Grade 0 to Grade 2.
(Database Cutoff Date: [redacted]

Data Source: [資料5.3.5.2.1.2: P001V02]

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