付録 2.7.4- 65　免疫関連の下垂体炎（下垂体機能低下症及び続発性副腎機能不全を含む）の AEOSI 解析

001 試験＋002 試験＋006 試験＋010 試験

MK-3475 を投与された悪性黒色腫及び非小細胞肺癌患者（安全性解析対象集団）

Adverse Event Summary
AEOSI - Hypophysitis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1,232		1,567		2,799	
with one or more adverse events	2	(0.3)	3	(0.2)	14	(0.9)	17	(0.6)
with no adverse event	680	(99.7)	1,229	(99.8)	1,553	(99.1)	2,782	(99.4)
with drug-related† adverse events	2	(0.3)	3	(0.2)	11	(0.7)	14	(0.5)
with Grade 3- 5 adverse events	2	(0.3)	3	(0.2)	6	(0.4)	9	(0.3)
with Grade 3- 5 drug-related adverse events	2	(0.3)	3	(0.2)	6	(0.4)	9	(0.3)
with serious adverse events	2	(0.3)	3	(0.2)	7	(0.4)	10	(0.4)
with serious drug-related adverse events	2	(0.3)	3	(0.2)	7	(0.4)	10	(0.4)
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)	4	(0.3)	4	(0.1)
discontinued due to a drug-related adverse event	0	(0.0)	0	(0.0)	4	(0.3)	4	(0.1)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	4	(0.3)	4	(0.1)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	4	(0.3)	4	(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‡ Study medication withdrawn.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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of AEOSI - Hypophysitis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1232		1567		2799	
Subjects with Hypophysitis	2	(0.3)	3	(0.2)	14	(0.9)	17	(0.6)
Time to Onset of First Hypophysitis (days)†								
Mean (Std)	192.0 (121.6)		165.7 (97.3)		118.8 (103.4)		127.1 (101.1)	
Median	192.0		113.0		115.5		113.0	
Range	106 to 278		106 to 278		1 to 363		1 to 363	
Total episodes of Hypophysitis	2		3		15		18	
Average Episodes per subject	1.00		1.00		1.07		1.06	
Episode duration (days)‡								

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Summary of AEOSI - Hypophysitis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Median	Not reached		Not reached		142.0		142.0	
Range	94+ to 97+		49 to 97+		8+ to 385+		8+ to 385+	

(%) = Number of subjects with Hypophysitis / Number of subjects in population.
† Time to onset statistics are based on number of subjects with Hypophysitis.
‡ From product-limit (Kaplan-Meier) method for censored data. 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.
+ indicates the AE episode is not recovered/resolved by the time of the cutoff date or date of death.
Std = Standard Deviation.
Grades are based on NCI CTCAE version 4.0.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Subjects With Adverse Events by Maximum Toxicity Grade
(Incidence >0% in One or More Treatment Groups)
AEOSI- Hypophysitis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1,232		1,567		2,799	
with one or more adverse events	2	(0.3)	3	(0.2)	14	(0.9)	17	(0.6)
Grade 1	0	(0.0)	0	(0.0)	2	(0.1)	2	(0.1)
Grade 2	0	(0.0)	0	(0.0)	6	(0.4)	6	(0.2)
Grade 3	2	(0.3)	3	(0.2)	5	(0.3)	8	(0.3)
Grade 4	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
with no adverse events	680	(99.7)	1,229	(99.8)	1,553	(99.1)	2,782	(99.4)
Endocrine disorders	**2**	**(0.3)**	**3**	**(0.2)**	**14**	**(0.9)**	**17**	**(0.6)**
Grade 1	0	(0.0)	0	(0.0)	2	(0.1)	2	(0.1)
Grade 2	0	(0.0)	0	(0.0)	6	(0.4)	6	(0.2)
Grade 3	2	(0.3)	3	(0.2)	5	(0.3)	8	(0.3)
Grade 4	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Hypophysitis	0	(0.0)	1	(0.1)	8	(0.5)	9	(0.3)
Grade 2	0	(0.0)	0	(0.0)	5	(0.3)	5	(0.2)
Grade 3	0	(0.0)	1	(0.1)	2	(0.1)	3	(0.1)
Grade 4	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Hypopituitarism	2	(0.3)	2	(0.2)	6	(0.4)	8	(0.3)
Grade 1	0	(0.0)	0	(0.0)	2	(0.1)	2	(0.1)
Grade 2	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)

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Subjects With Adverse Events by Maximum Toxicity Grade
(Incidence >0% in One or More Treatment Groups)
AEOSI- Hypophysitis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Hypopituitarism	2	(0.3)	2	(0.2)	6	(0.4)	8	(0.3)
Grade 3	2	(0.3)	2	(0.2)	3	(0.2)	5	(0.2)

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 for MEL: [redacted]).

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

(MK-3475 PN002 Database Cutoff Date: [redacted]).

(MK-3475 PN006 Database Cutoff Date: 03MAR2015).

(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of Concomitant Corticosteroid Use for AEOSI - Hypophysitis PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475 (APaT Population)

	P010 (N=682)		PN001 Lung, PN010 (N=1232)		PN001 Mel, PN002, PN006 (N=1567)		PN001,PN002, PN006, PN010 (N=2799)	
	n	%	n	%	n	%	n	%
Subjects with one or more Hypophysitis	2		3		14		17	
Treated with systemic corticosteroid	2	100.0	3	100.0	13	92.9	16	94.1
High starting dose†	0	0	1	33.3	5	35.7	6	35.3
Low starting dose‡	2	100.0	2	66.7	8	57.1	10	58.8
Not treated with systemic corticosteroid	0	0	0	0	1	7.1	1	5.9

The number of Subjects with one or more Hypophysitis is used as the denominator for the percentage calculation.
† 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.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of Concomitant Corticosteroid Use for AEOSI - Hypophysitis Episodes
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010	PN001 Lung, PN010	PN001 Mel, PN002, PN006	PN001,PN002, PN006, PN010
Total Episodes	2	3	15	18
High Starting Dose (%) †	**0 (0.0)**	**1 (33.3)**	**5 (33.3)**	**6 (33.3)**
Starting dose (mg/day)				
Mean (Std)	0 (0)	75 (.)	85 (43)	83 (39)
Median (Range)	0 (0-0)	75 (75-75)	75 (50-160)	75 (50-160)
Duration (days)§				
Mean (Std)	0 (0)	29 (.)	3 (3)	8 (11)
Median (Range)	0 (0-0)	29 (29-29)	2 (1-7)	4 (1-29)
Low Starting Dose (%) ‡	**2 (100.0)**	**2 (66.7)**	**9 (60.0)**	**11 (61.1)**
Starting dose (mg/day)				
Mean (Std)	14 (15)	14 (15)	13 (8)	13 (9)
Median (Range)	14 (4-25)	14 (4-25)	10 (5-25)	10 (4-25)
Duration (days)§				
Mean (Std)	44 (60)	44 (60)	88 (117)	80 (108)
Median (Range)	44 (1-86)	44 (1-86)	9 (1-300)	9 (1-300)
Not Treated with Systemic Corticosteroid (%)	**0 (0.0)**	**0 (0.0)**	**1 (6.7)**	**1 (5.6)**

† 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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Listing of Subjects With Adverse Events
AEOSI- Hypophysitis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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	Hypophysitis	6 Days	Severe	4	Y	Y	Interrupted	Resolved
		58	Hypophysitis	Continuing	Moderate	2		Y	N/A	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
Trial Number=3475-010, Site Number=1403, Subject ID=301594, Gender=M, Race=Asian, Age=78 Years, Rel Day of Study Medication Discontinuance†=										
301594	Treatment Cycle 5	106	Hypopituitarism	Continuing		3	Y	Y	Reduced	Not Resolved
MK-3475 10 mg/kg Q3W										
Trial Number=3475-001, Site Number=0023, Subject ID=001589, Gender=M, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance†=169										

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Listing of Subjects With Adverse Events
AEOSI- Hypophysitis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q3W										
Trial Number=3475-001, Site Number=0023, Subject ID=001589, Gender=M, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance†=169										
001589	Treatment Cycle 4	113	Hypophysitis	4.14 Weeks	Severe	3	Y	Y	Interrupted	Resolved
		142	Hypophysitis	6 Days	Moderate	2		Y		Resolved
		148	Hypophysitis	2 Weeks	Mild	1		Y		Resolved
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										
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	Resolved
Trial Number=3475-010, Site Number=1421, Subject ID=311479, Gender=M, Race=Asian, Age=49 Years, Rel Day of Study Medication Discontinuance†=										
311479	Treatment Cycle 11	278	Hypopituitarism	Continuing		3	Y	Y	Interrupted	Not Resolved

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Listing of Subjects With Adverse Events
AEOSI- Hypophysitis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=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
		143	Hypopituitarism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=1819, Subject ID=365965, Gender=M, Race=White, Age=40 Years, Rel Day of Study Medication Discontinuance†=										

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Listing of Subjects With Adverse Events
AEOSI- Hypophysitis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=365965, Gender=M, Race=White, Age=40 Years, Rel Day of Study Medication Discontinuance[†]=										
365965	Treatment Cycle 26	363	Hypophysitis	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 for MEL: [redacted]).

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

(MK-3475 PN002 Database Cutoff Date: [redacted]).

(MK-3475 PN006 Database Cutoff Date: 03MAR2015).

(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Listing of Concomitant Systemic Corticosteroid Use for AEOSI - Hypophysitis Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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	IIypophysitis	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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Listing of Concomitant Systemic Corticosteroid Use for AEOSI - Hypophysitis Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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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Listing of Concomitant Systemic Corticosteroid Use for AEOSI - Hypophysitis Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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
Trial Number=3475-010, Site Number=1403, Subject ID=301594, Gender=M, Race=Asian, Age=78 Years, Rel Day of Study Medication Discontinuance‡=											
301594	106	1	Hydrocortisone Sodium Succinate	100	QD	Intravenous	25.00	Hypopituitarism	106	.	3
MK-3475 10 mg/kg Q3W											
Trial Number=3475-001, Site Number=0023, Subject ID=001589, Gender=M, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance‡=169											
001589	113	29	Prednisolone	75	QD	Oral Administration	75.00	Hypophysitis	113	141	3
	142	6	Prednisolone	50	QD	Oral Administration	50.00	Hypophysitis	142	147	2
	148	14	Prednisolone	25	QD	Oral Administration	25.00	Hypophysitis	148	161	1
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	-82	60	Hydrocortisone	10	BID	Oral	2.50	Hypopituitarism	28	.	3
	30	.	Hydrocortisone	100	QD	Oral	25.00	Hypopituitarism	28	.	3
	30	1	Hydrocortisone	100	QD	Oral	25.00	Hypopituitarism	28	.	3
	30	1	Hydrocortisone	100	QD	Oral	25.00	Hypopituitarism	28	.	3
	31	1	Hydrocortisone	80	QD	Oral	20.00	Hypopituitarism	28	.	3

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Listing of Concomitant Systemic Corticosteroid Use for AEOSI - Hypophysitis Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=3475-002, 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											
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
Trial Number=3475-010, Site Number=1421, Subject ID=311479, Gender=M, Race=Asian, Age=49 Years, Rel Day of Study Medication Discontinuance‡=											
311479	286	.	Hydrocortisone	15	BID	Oral	3.75	Hypopituitarism	278	.	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‡=											
000078	212	118	Hydrocortisone	20	QD	Oral Administration	5.00	Hypopituitarism	198	339	1

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Listing of Concomitant Systemic Corticosteroid Use for AEOSI - Hypophysitis Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=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

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Listing of Concomitant Systemic Corticosteroid Use for AEOSI - Hypophysitis Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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
	142	1	Hydrocortisone	50	ONCE	Oral	12.50	Hypopituitarism	131	142	3
	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
Trial Number=3475-006, Site Number=1819, Subject ID=365965, Gender=M, Race=White, Age=40 Years, Rel Day of Study Medication Discontinuance‡=											

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Listing of Concomitant Systemic Corticosteroid Use for AEOSI - Hypophysitis Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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
365965	365	7	Dexamethasone	24	BID	Oral	160.08	Hypophysitis	363	.	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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Subjects With Adverse Events by Outcome
(Incidence > 0% in One or More Treatment Groups)
AEOSI- Hypophysitis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

		P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	Outcome	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population		682		1,232		1,567		2,799	
With one or more adverse events	Overall	2	(0.3)	3	(0.2)	14	(0.9)	17	(0.6)
	Fatal	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
	Not Resolved	2	(0.3)	2	(0.2)	8	(0.5)	10	(0.4)
	Resolved	0	(0.0)	1	(0.1)	4	(0.3)	5	(0.2)
	Sequelae	0	(0.0)	0	(0.0)	2	(0.1)	2	(0.1)
	Unknown	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

Outcome: Resolved = RECOVERED/RESOLVED, Not resolved = NOT RECOVERED/NOT RESOLVED.
Every subject is counted once for the AE outcome, with the order: Fatal>Not Resolved>Resolving>Unknown>Sequelae>Resolved.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Adverse Event Summary
AEOSI - Adrenal Insufficiency
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1,232		1,567		2,799	
with one or more adverse events	5	(0.7)	9	(0.7)	13	(0.8)	22	(0.8)
with no adverse event	677	(99.3)	1,223	(99.3)	1,554	(99.2)	2,777	(99.2)
with drug-related† adverse events	3	(0.4)	7	(0.6)	9	(0.6)	16	(0.6)
with Grade 3- 5 adverse events	1	(0.1)	2	(0.2)	8	(0.5)	10	(0.4)
with Grade 3- 5 drug-related adverse events	1	(0.1)	2	(0.2)	5	(0.3)	7	(0.3)
with serious adverse events	1	(0.1)	3	(0.2)	7	(0.4)	10	(0.4)
with serious drug-related adverse events	1	(0.1)	3	(0.2)	5	(0.3)	8	(0.3)
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)	1	(0.1)	1	(0.0)
discontinued due to a drug-related adverse event	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	1	(0.1)	1	(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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of AEOSI - Adrenal Insufficiency
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1232		1567		2799	
Subjects with Adrenal Insufficiency	5	(0.7)	9	(0.7)	13	(0.8)	22	(0.8)
Time to Onset of First Adrenal Insufficiency (days)†								
Mean (Std)	217.2 (98.7)		186.4 (80.7)		195.3 (155.1)		191.7 (127.5)	
Median	237.0		169.0		132.0		160.0	
Range	64 to 323		64 to 323		26 to 505		26 to 505	
Total episodes of Adrenal Insufficiency	5		9		13		22	
Average Episodes per subject	1.00		1.00		1.00		1.00	
Episode duration (days)‡								

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Summary of AEOSI - Adrenal Insufficiency
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Median	Not reached		Not reached		Not reached		Not reached	
Range	15 to 311+		15 to 311+		4 to 696+		4 to 696+	

(%) = Number of subjects with Adrenal Insufficiency / Number of subjects in population.
† Time to onset statistics are based on number of subjects with Adrenal Insufficiency.
‡ From product-limit (Kaplan-Meier) method for censored data. 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.
+ indicates the AE episode is not recovered/resolved by the time of the cutoff date or date of death.
Std = Standard Deviation.
Grades are based on NCI CTCAE version 4.0.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Subjects With Adverse Events by Maximum Toxicity Grade
(Incidence >0% in One or More Treatment Groups)
AEOSI- Adrenal Insufficiency
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1,232		1,567		2,799	
with one or more adverse events	5	(0.7)	9	(0.7)	13	(0.8)	22	(0.8)
Grade 1	1	(0.1)	1	(0.1)	2	(0.1)	3	(0.1)
Grade 2	3	(0.4)	6	(0.5)	3	(0.2)	9	(0.3)
Grade 3	1	(0.1)	2	(0.2)	7	(0.4)	9	(0.3)
Grade 4	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
with no adverse events	677	(99.3)	1,223	(99.3)	1,554	(99.2)	2,777	(99.2)
Endocrine disorders	**5**	**(0.7)**	**9**	**(0.7)**	**13**	**(0.8)**	**22**	**(0.8)**
Grade 1	1	(0.1)	1	(0.1)	2	(0.1)	3	(0.1)
Grade 2	3	(0.4)	6	(0.5)	3	(0.2)	9	(0.3)
Grade 3	1	(0.1)	2	(0.2)	7	(0.4)	9	(0.3)
Grade 4	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Adrenal insufficiency	5	(0.7)	9	(0.7)	11	(0.7)	20	(0.7)
Grade 1	1	(0.1)	1	(0.1)	2	(0.1)	3	(0.1)
Grade 2	3	(0.4)	6	(0.5)	3	(0.2)	9	(0.3)
Grade 3	1	(0.1)	2	(0.2)	5	(0.3)	7	(0.3)
Grade 4	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Adrenocortical insufficiency acute	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Grade 3	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Secondary adrenocortical insufficiency	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)

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Subjects With Adverse Events by Maximum Toxicity Grade
(Incidence >0% in One or More Treatment Groups)
AEOSI- Adrenal Insufficiency
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Secondary adrenocortical insufficiency	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Grade 3	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)

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 for MEL: [redacted]).

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

(MK-3475 PN002 Database Cutoff Date: [redacted].

(MK-3475 PN006 Database Cutoff Date: 03MAR2015).

(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of Concomitant Corticosteroid Use for AEOSI - Adrenal Insufficiency PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475 (APaT Population)

	P010 (N=682)		PN001 Lung, PN010 (N=1232)		PN001 Mel, PN002, PN006 (N=1567)		PN001,PN002, PN006, PN010 (N=2799)	
	n	%	n	%	n	%	n	%
Subjects with one or more Adrenal Insufficiency	5		9		13		22	
Treated with systemic corticosteroid	4	80.0	8	88.9	8	61.5	16	72.7
High starting dose†	1	20.0	1	11.1	1	7.7	2	9.1
Low starting dose‡	3	60.0	7	77.8	7	53.8	14	63.6
Not treated with systemic corticosteroid	1	20.0	1	11.1	5	38.5	6	27.3

The number of Subjects with one or more Adrenal Insufficiency is used as the denominator for the percentage calculation.
† 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.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of Concomitant Corticosteroid Use for AEOSI - Adrenal Insufficiency Episodes PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475 (APaT Population)

	P010	PN001 Lung, PN010	PN001 Mel, PN002, PN006	PN001,PN002, PN006, PN010
Total Episodes	5	9	13	22
High Starting Dose (%) †	**1 (20.0)**	**1 (11.1)**	**1 (7.7)**	**2 (9.1)**
Starting dose (mg/day)				
Mean (Std)	40 (.)	40 (.)	67 (.)	53 (19)
Median (Range)	40 (40-40)	40 (40-40)	67 (67-67)	53 (40-67)
Duration (days)§				
Mean (Std)	6 (.)	6 (.)	1 (.)	4 (4)
Median (Range)	6 (6-6)	6 (6-6)	1 (1-1)	4 (1-6)
Low Starting Dose (%) ‡	**3 (60.0)**	**7 (77.8)**	**7 (53.8)**	**14 (63.6)**
Starting dose (mg/day)				
Mean (Std)	5 (4)	5 (4)	13 (10)	9 (8)
Median (Range)	5 (1-10)	5 (1-10)	9 (4-27)	5 (1-27)
Duration (days)§				
Mean (Std)	111 (167)	129 (136)	84 (117)	106 (124)
Median (Range)	28 (1-303)	65 (1-303)	17 (1-260)	38 (1-303)
Not Treated with Systemic Corticosteroid (%)	**1 (20.0)**	**1 (11.1)**	**5 (38.5)**	**6 (27.3)**

† 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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Listing of Subjects With Adverse Events
AEOSI- Adrenal Insufficiency
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=0012, Subject ID=000389, Gender=F, Race=White, Age=68 Years, Rel Day of Study Medication Discontinuance†=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 Study Medication Discontinuance†=384										
101258	Treatment Cycle 6	132	Adrenal insufficiency	4 Days		3	Y	N	None	Resolved
Trial Number=3475-010, Site Number=0130, Subject ID=308513, Gender=F, Race=White, Age=67 Years, Rel Day of Study Medication Discontinuance†=246										
308513	Treatment Cycle 9	189	Adrenal insufficiency	2.14 Weeks		2	N	Y	Interrupted	Resolved
Trial Number=3475-010, Site Number=1438, Subject ID=312992, Gender=F, Race=Asian, Age=65 Years, Rel Day of Study Medication Discontinuance†=259										
312992	Safety Follow-up	273	Adrenal insufficiency	Continuing		1	N	Y	Interrupted	Not Resolved
MK-3475 10 mg/kg Q3W										
Trial Number=3475-001, Site Number=0001, Subject ID=001027, Gender=F, Race=White, Age=71 Years, Rel Day of Study Medication Discontinuance†=										
001027	Treatment Cycle 9	169	Adrenal insufficiency	4.6 Months	Mild	1		Y		Resolved
	Treatment Cycle 12	309	Adrenal insufficiency	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0010, Subject ID=000332, Gender=M, Race=White, Age=83 Years, Rel Day of Study Medication Discontinuance†=1										
000332	Safety Follow-up	26	Adrenal insufficiency	Continuing	Mild	1		N	N/A	Not Resolved

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Listing of Subjects With Adverse Events
AEOSI- Adrenal Insufficiency
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=0010, Subject ID=001220, Gender=M, Race=White, Age=73 Years, Rel Day of Study Medication Discontinuance†=										
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 Study Medication Discontinuance†=										
000413	Treatment Cycle 13	360	Adrenal insufficiency	4 Days	Severe	3	Y	Y	Interrupted	Resolved
		363	Adrenal insufficiency	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0019, Subject ID=000148, Gender=F, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=										
000148	Treatment Cycle 24	505	Adrenal insufficiency	4.14 Weeks	Moderate	2		Y	Interrupted	Resolved
Trial Number=3475-001, Site Number=0028, Subject ID=001178, Gender=F, Race=White, Age=68 Years, Rel Day of Study Medication Discontinuance†=288										
001178	Treatment Cycle 7	155	Adrenal insufficiency	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0073, Subject ID=001578, Gender=F, Race=Asian, Age=76 Years, Rel Day of Study Medication Discontinuance†=										
001578	Treatment Cycle 5	106	Adrenal insufficiency	Continuing	Moderate	2	Y	Y	Interrupted	Not Resolved
Trial Number=3475-001, Site Number=0134, Subject ID=001160, Gender=F, Race=White, Age=74 Years, Rel Day of Study Medication Discontinuance†=										
001160	Treatment Cycle 8	162	Adrenal insufficiency	1.29 Weeks	Severe	3	Y	Y	Interrupted	Resolved
		171	Adrenal insufficiency	Continuing	Moderate	2		Y		Not Resolved

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Listing of Subjects With Adverse Events
AEOSI- Adrenal Insufficiency
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=0111, Subject ID=100335, Gender=M, Race=White, Age=56 Years, Rel Day of Study Medication Discontinuance†=378										
100335	Safety Follow-up	398	Secondary adrenocortical insufficiency	Continuing		3	Y	Y	None	Not Resolved
Trial Number=3475-002, Site Number=0130, Subject ID=100919, Gender=F, Race=White, Age=51 Years, Rel Day of Study Medication Discontinuance†=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 Study Medication Discontinuance†=										
361134	Treatment Cycle 6	128	Adrenal insufficiency	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-010, Site Number=0085, Subject ID=312745, Gender=M, Race=White, Age=53 Years, Rel Day of Study Medication Discontinuance†=113										
312745	Treatment Cycle 4	64	Adrenal insufficiency	3.52 Months		2	N	N	None	Resolved
Trial Number=3475-010, Site Number=0183, Subject ID=301027, Gender=M, Race=White, Age=64 Years, Rel Day of Study Medication Discontinuance†=										
301027	Treatment Cycle 11	237	Adrenal insufficiency	Continuing		2	N	N	None	Not Resolved
Trial Number=3475-010, Site Number=1424, Subject ID=301369, Gender=F, Race=Asian, Age=74 Years, Rel Day of Study Medication Discontinuance†=										
301369	Treatment Cycle 16	323	Adrenal insufficiency	Continuing		3	Y	Y	Interrupted	Not Resolved
MK-3475 10 mg/kg Q2W										

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Listing of Subjects With Adverse Events
AEOSI- Adrenal Insufficiency
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=0013, Subject ID=000084, Gender=F, Race=White, Age=52 Years, Rel Day of Study Medication Discontinuance†=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 Study Medication Discontinuance†=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 Study Medication Discontinuance†=144										
366882	Safety Follow-up	158	Adrenal insufficiency	Continuing		4	Y	Y	Discontinued	Not Resolved
Trial Number=3475-006, Site Number=1819, Subject ID=365965, Gender=M, Race=White, Age=40 Years, Rel Day of Study Medication Discontinuance†=										
365965	Treatment Cycle 26	350	Adrenal insufficiency	2 Weeks		1	N	Y	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 for MEL: [redacted]).

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

(MK-3475 PN002 Database Cutoff Date: [redacted]).

(MK-3475 PN006 Database Cutoff Date: 03MAR2015).

(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Listing of Concomitant Systemic Corticosteroid Use for AEOSI - Adrenal Insufficiency Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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[‡]=384											
101258	133	.	Dexamethasone	2	BID	Oral	10.01	Adrenal insufficiency	132	135	3
	133	1	Dexamethasone	10	OTHER	Intravenous	66.70	Adrenal insufficiency	132	135	3
	133	3	Dexamethasone	4	OTHER	Intravenous	26.68	Adrenal insufficiency	132	135	3
	133	3	Dexamethasone	8	OTHER	Intramuscular	53.36	Adrenal insufficiency	132	135	3
	133	2	Fludrocortisone	0	QD	Oral	0.02	Adrenal insufficiency	132	135	3
Trial Number=3475-010, Site Number=0130, Subject ID=308513, Gender=F, Race=White, Age=67 Years, Rel Day of Study Medication Discontinuance[‡]=246											
308513	189	6	Prednisolone	40	QD	Oral	40.00	Adrenal insufficiency	189	203	2
	195	3	Prednisolone	20	QD	Oral	20.00	Adrenal insufficiency	189	203	2
	198	8	Prednisolone	10	QD	Oral	10.00	Adrenal insufficiency	189	203	2
	206	6	Prednisolone	8	QD	Oral	7.50	Adrenal insufficiency	189	203	2
	212	7	Prednisolone	5	QD	Oral	5.00	Adrenal insufficiency	189	203	2
	219	34	Prednisolone	3	QD	Oral	2.50	Adrenal insufficiency	189	203	2
MK-3475 10 mg/kg Q3W											
Trial Number=3475-001, Site Number=0001, Subject ID=001027, Gender=F, Race=White, Age=71 Years, Rel Day of Study Medication Discontinuance[‡]=											
001027	169	.	Hydrocortisone	10	QD	Oral Administration	2.50	Adrenal insufficiency	169	308	1

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Listing of Concomitant Systemic Corticosteroid Use for AEOSI - Adrenal Insufficiency Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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
	169	.	Hydrocortisone	10	QD	Oral Administration	2.50	Adrenal insufficiency	309	.	2
	309	5	Prednisone	40	QD	Oral Administration	40.00	Adrenal insufficiency	309	.	2
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
	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=3475-001, Site Number=0028, Subject ID=001178, Gender=F, Race=White, Age=68 Years, Rel Day of Study Medication Discontinuance‡=288											
001178	155	.	Prednisone	10	BID	Oral Administration	10.00	Adrenal insufficiency	155	.	2
Trial Number=3475-001, Site Number=0073, Subject ID=001578, Gender=F, Race=Asian, Age=76 Years, Rel Day of Study Medication Discontinuance‡=											
001578	106	1	Hydrocortisone	10	QD	Oral Administration	2.50	Adrenal insufficiency	106	.	2

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Listing of Concomitant Systemic Corticosteroid Use for AEOSI - Adrenal Insufficiency Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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
	107	.	Hydrocortisone	30	QD	Oral Administration	7.50	Adrenal insufficiency	106	.	2
Trial Number=3475-001, Site Number=0134, Subject ID=001160, Gender=F, Race=White, Age=74 Years, Rel Day of Study Medication Discontinuance‡=											
001160	170	.	Hydrocortisone	25	QD	Oral Administration	6.25	Adrenal insufficiency	171	.	2
	312	.	Hydrocortisone	20	BID	Oral Administration	5.00	Adrenal insufficiency	171	.	2
Trial Number=3475-002, Site Number=0130, Subject ID=100919, Gender=F, Race=White, Age=51 Years, Rel Day of Study Medication Discontinuance‡=96											
100919	108	1	Hydrocortisone Sodium Succinate	100	QD	Intravenous	25.00	Adrenocortical insufficiency acute	108	.	3
	110	13	Prednisolone	60	QD	Oral	60.00	Adrenocortical insufficiency acute	108	.	3
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
Trial Number=3475-010, Site Number=0085, Subject ID=312745, Gender=M, Race=White, Age=53 Years, Rel Day of Study Medication Discontinuance‡=113											
312745	143	28	Fludrocortisone	50	QD	Oral	10.00	Adrenal insufficiency	64	170	2
	143	28	Hydrocortisone	30	BID	Oral	7.50	Adrenal insufficiency	64	170	2
Trial Number=3475-010, Site Number=0183, Subject ID=301027, Gender=M, Race=White, Age=64 Years, Rel Day of Study Medication Discontinuance‡=											
301027	245	.	Prednisolone	5	QD	Oral	5.00	Adrenal insufficiency	237	.	2
Trial Number=3475-010, Site Number=1424, Subject ID=301369, Gender=F, Race=Asian, Age=74 Years, Rel Day of Study Medication Discontinuance‡=											
301369	353	1	Hydrocortisone	5	QD	Oral	1.25	Adrenal insufficiency	323	.	3
	354	3	Hydrocortisone	10	QD	Oral	2.50	Adrenal insufficiency	323	.	3

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Listing of Concomitant Systemic Corticosteroid Use for AEOSI - Adrenal Insufficiency Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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
	356	2	Prednisolone	40	QD	Oral	40.00	Adrenal insufficiency	323	.	3
	358	15	Prednisolone	35	QD	Oral	35.00	Adrenal insufficiency	323	.	3
	373	13	Prednisolone	30	QD	Oral	30.00	Adrenal insufficiency	323	.	3
	386	14	Prednisolone	20	QD	Oral	20.00	Adrenal insufficiency	323	.	3
	400	13	Prednisolone	10	QD	Oral	10.00	Adrenal insufficiency	323	.	3
	414	7	Prednisolone	30	QD	Oral	30.00	Adrenal insufficiency	323	.	3
	421	8	Prednisolone	18	QD	Oral	17.50	Adrenal insufficiency	323	.	3
	435	7	Prednisolone	15	QD	Oral	15.00	Adrenal insufficiency	323	.	3
	442	7	Prednisolone	10	QD	Oral	10.00	Adrenal insufficiency	323	.	3
	442	7	Prednisolone	4	QD	Oral	3.50	Adrenal insufficiency	323	.	3
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											

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Listing of Concomitant Systemic Corticosteroid Use for AEOSI - Adrenal Insufficiency Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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
360742	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
	245	.	Hydrocortisone	15	QD	Oral	3.75	Adrenal insufficiency	83	.	3
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
	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
	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
	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
	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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Listing of Concomitant Systemic Corticosteroid Use for AEOSI - Adrenal Insufficiency Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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
	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

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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Subjects With Adverse Events by Outcome
(Incidence > 0% in One or More Treatment Groups)
AEOSI- Adrenal Insufficiency
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

		P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	Outcome	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population		682		1,232		1,567		2,799	
With one or more adverse events	Overall	5	(0.7)	9	(0.7)	13	(0.8)	22	(0.8)
	Fatal	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
	Not Resolved	3	(0.4)	7	(0.6)	10	(0.6)	17	(0.6)
	Resolved	2	(0.3)	2	(0.2)	3	(0.2)	5	(0.2)
	Unknown	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

Outcome: Resolved = RECOVERED/RESOLVED, Not resolved = NOT RECOVERED/NOT RESOLVED.
Every subject is counted once for the AE outcome, with the order: Fatal>Not Resolved>Resolving>Unknown>Sequelae>Resolved.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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付録 2.7.4- 66　　免疫関連の甲状腺機能障害（甲状腺機能低下症及び甲状腺機能亢進症）の AEOSI 解析

001 試験＋002 試験＋006 試験＋010 試験

MK-3475 を投与された悪性黒色腫及び非小細胞肺癌患者（安全性解析対象集団）

Adverse Event Summary
AEOSI - Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1,232		1,567		2,799	
with one or more adverse events	56	(8.2)	98	(8.0)	139	(8.9)	237	(8.5)
with no adverse event	626	(91.8)	1,134	(92.0)	1,428	(91.1)	2,562	(91.5)
with drug-related† adverse events	48	(7.0)	88	(7.1)	126	(8.0)	214	(7.6)
with Grade 3- 5 adverse events	0	(0.0)	1	(0.1)	2	(0.1)	3	(0.1)
with Grade 3- 5 drug-related adverse events	0	(0.0)	1	(0.1)	2	(0.1)	3	(0.1)
with serious adverse events	2	(0.3)	4	(0.3)	1	(0.1)	5	(0.2)
with serious drug-related adverse events	2	(0.3)	4	(0.3)	1	(0.1)	5	(0.2)
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	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
discontinued due to a drug-related adverse event	1	(0.1)	1	(0.1)	0	(0.0)	1	(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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of AEOSI - Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1232		1567		2799	
Subjects with Hypothyroidism	56	(8.2)	98	(8.0)	139	(8.9)	237	(8.5)
Time to Onset of First Hypothyroidism (days)†								
Mean (Std)	108.1 (78.1)		122.6 (75.4)		124.9 (97.0)		123.9 (88.6)	
Median	105.0		107.0		106.0		106.0	
Range	19 to 457		19 to 457		1 to 576		1 to 576	
Total episodes of Hypothyroidism	61		105		142		247	
Average Episodes per subject	1.09		1.07		1.02		1.04	
Episode duration (days)‡								

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Summary of AEOSI - Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Median	Not reached		Not reached		Not reached		Not reached	
Range	2 to 538+		2 to 842+		2 to 740+		2 to 842+	

(%) = Number of subjects with Hypothyroidism / Number of subjects in population.
† Time to onset statistics are based on number of subjects with Hypothyroidism.
‡ From product-limit (Kaplan-Meier) method for censored data. 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.
+ indicates the AE episode is not recovered/resolved by the time of the cutoff date or date of death.
Std = Standard Deviation.
Grades are based on NCI CTCAE version 4.0.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Subjects With Adverse Events by Maximum Toxicity Grade
(Incidence >0% in One or More Treatment Groups)
AEOSI- Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1,232		1,567		2,799	
with one or more adverse events	56	(8.2)	98	(8.0)	139	(8.9)	237	(8.5)
Grade 1	21	(3.1)	28	(2.3)	32	(2.0)	60	(2.1)
Grade 2	35	(5.1)	69	(5.6)	105	(6.7)	174	(6.2)
Grade 3	0	(0.0)	1	(0.1)	2	(0.1)	3	(0.1)
with no adverse events	626	(91.8)	1,134	(92.0)	1,428	(91.1)	2,562	(91.5)
Endocrine disorders	**56**	**(8.2)**	**98**	**(8.0)**	**139**	**(8.9)**	**237**	**(8.5)**
Grade 1	21	(3.1)	28	(2.3)	32	(2.0)	60	(2.1)
Grade 2	35	(5.1)	69	(5.6)	105	(6.7)	174	(6.2)
Grade 3	0	(0.0)	1	(0.1)	2	(0.1)	3	(0.1)
Hypothyroidism	56	(8.2)	98	(8.0)	138	(8.8)	236	(8.4)
Grade 1	21	(3.1)	28	(2.3)	32	(2.0)	60	(2.1)
Grade 2	35	(5.1)	69	(5.6)	104	(6.6)	173	(6.2)
Grade 3	0	(0.0)	1	(0.1)	2	(0.1)	3	(0.1)
Myxoedema	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
Grade 2	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
Primary hypothyroidism	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)

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Subjects With Adverse Events by Maximum Toxicity Grade
(Incidence >0% in One or More Treatment Groups)
AEOSI- Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Primary hypothyroidism	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Grade 2	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)

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 for MEL: [redacted]).

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

(MK-3475 PN002 Database Cutoff Date: [redacted]).

(MK-3475 PN006 Database Cutoff Date: 03MAR2015).

(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of Concomitant Corticosteroid Use for AEOSI - Hypothyroidism PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475 (APaT Population)

	P010 (N=682)		PN001 Lung, PN010 (N=1232)		PN001 Mel, PN002, PN006 (N=1567)		PN001,PN002, PN006, PN010 (N=2799)	
	n	%	n	%	n	%	n	%
Subjects with one or more Hypothyroidism	56		98		139		237	
Treated with systemic corticosteroid	0	0	1	1.0	3	2.2	4	1.7
High starting dose†	0	0	0	0	1	0.7	1	0.4
Low starting dose‡	0	0	1	1.0	2	1.4	3	1.3
Not treated with systemic corticosteroid	56	100.0	97	99.0	136	97.8	233	98.3

The number of Subjects with one or more Hypothyroidism is used as the denominator for the percentage calculation.
† 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.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of Concomitant Corticosteroid Use for AEOSI - Hypothyroidism Episodes PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475 (APaT Population)

	P010	PN001 Lung, PN010	PN001 Mel, PN002, PN006	PN001,PN002, PN006, PN010
Total Episodes	61	105	142	247
High Starting Dose (%) †	**0 (0.0)**	**0 (0.0)**	**1 (0.7)**	**1 (0.4)**
Starting dose (mg/day)				
Mean (Std)	0 (0)	0 (0)	60 (.)	60 (.)
Median (Range)	0 (0-0)	0 (0-0)	60 (60-60)	60 (60-60)
Duration (days)§				
Mean (Std)	0 (0)	0 (0)	4 (.)	4 (.)
Median (Range)	0 (0-0)	0 (0-0)	4 (4-4)	4 (4-4)
Low Starting Dose (%) ‡	**0 (0.0)**	**1 (1.0)**	**2 (1.4)**	**3 (1.2)**
Starting dose (mg/day)				
Mean (Std)	0 (0)	3 (.)	16 (12)	12 (12)
Median (Range)	0 (0-0)	3 (3-3)	16 (8-25)	8 (3-25)
Duration (days)§				
Mean (Std)	0 (0)	1 (.)	48 (66)	32 (54)
Median (Range)	0 (0-0)	1 (1-1)	48 (1-94)	1 (1-94)
Not Treated with Systemic Corticosteroid (%)	**61 (100.0)**	**104 (99.0)**	**139 (97.9)**	**243 (98.4)**

† 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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Listing of Subjects With Adverse Events
AEOSI- Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=000157, Gender=M, Race=White, Age=32 Years, Rel Day of Study Medication Discontinuance†=147										
000157	Treatment Cycle 4	68	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0010, Subject ID=000282, Gender=M, Race=White, Age=55 Years, Rel Day of Study Medication Discontinuance†=315										
000282	Treatment Cycle 10	189	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0010, Subject ID=000295, Gender=M, Race=White, Age=47 Years, Rel Day of Study Medication Discontinuance†=64										
000295	Safety Follow-up	70	Hypothyroidism	2 Weeks	Moderate	2		Y		Resolved
Trial Number=3475-001, Site Number=0010, Subject ID=000457, Gender=M, Race=White, Age=61 Years, Rel Day of Study Medication Discontinuance†=43										
000457	Safety Follow-up	48	Hypothyroidism	6 Days	Mild	1		Y	N/A	Resolved
		54	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0011, Subject ID=000307, Gender=M, Race=White, Age=88 Years, Rel Day of Study Medication Discontinuance†=										
000307	Treatment Cycle 17	362	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0011, Subject ID=000498, Gender=M, Race=White, Age=54 Years, Rel Day of Study Medication Discontinuance†=										
000498	Treatment Cycle 4	65	Hypothyroidism	Continuing	Mild	1		Y		Not Resolved
Trial Number=3475-001, Site Number=0015, Subject ID=000491, Gender=M, Race=White, Age=65 Years, Rel Day of Study Medication Discontinuance†=										
000491	Treatment Cycle 4	62	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved

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Listing of Subjects With Adverse Events
AEOSI- Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=000602, Gender=M, Race=White, Age=75 Years, Rel Day of Study Medication Discontinuance†=400										
000602	Treatment Cycle 10	208	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0018, Subject ID=000409, Gender=M, Race=White, Age=80 Years, Rel Day of Study Medication Discontinuance†=272										
000409	Treatment Cycle 4	62	Hypothyroidism	Continuing	Moderate	2		Y		Not 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	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0019, Subject ID=003008, Gender=F, Race=White, Age=57 Years, Rel Day of Study Medication Discontinuance†=										
003008	Treatment Cycle 6	104	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0020, Subject ID=000550, Gender=F, Race=White, Age=52 Years, Rel Day of Study Medication Discontinuance†=176										
000550	Treatment Cycle 6	106	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0021, Subject ID=000528, Gender=F, Race=White, Age=55 Years, Rel Day of Study Medication Discontinuance†=										
000528	Treatment Cycle 2	38	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0021, Subject ID=000538, Gender=F, Race=White, Age=36 Years, Rel Day of Study Medication Discontinuance†=64										
000538	Treatment Cycle 2	22	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0021, Subject ID=000545, Gender=M, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=										

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Listing of Subjects With Adverse Events
AEOSI- Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=000545, Gender=M, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=										
000545	Treatment Cycle 10	189	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0023, Subject ID=000320, Gender=F, Race=White, Age=57 Years, Rel Day of Study Medication Discontinuance†=										
000320	Treatment Cycle 13	253	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0023, Subject ID=003001, Gender=F, Race=White, Age=48 Years, Rel Day of Study Medication Discontinuance†=43										
003001	Treatment Cycle 1	20	Hypothyroidism	Continuing	Mild	1		Y	N/A	Not Resolved
Trial Number=3475-001, Site Number=0121, Subject ID=003026, Gender=M, Race=White, Age=65 Years, Rel Day of Study Medication Discontinuance†=										
003026	Treatment Cycle 12	229	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-002, Site Number=0007, Subject ID=100105, Gender=M, Race=White, Age=67 Years, Rel Day of Study Medication Discontinuance†=										
100105	Treatment Cycle 24	484	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-002, Site Number=0007, Subject ID=101234, Gender=M, Race=White, Age=78 Years, Rel Day of Study Medication Discontinuance†=										
101234	Treatment Cycle 14	296	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-002, Site Number=0010, Subject ID=100677, Gender=F, Race=White, Age=76 Years, Rel Day of Study Medication Discontinuance†=252										
100677	Treatment Cycle 1	22	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-002, Site Number=0016, Subject ID=100619, Gender=M, Race=White, Age=75 Years, Rel Day of Study Medication Discontinuance†=255										

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Listing of Subjects With Adverse Events
AEOSI- Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=0016, Subject ID=100619, Gender=M, Race=White, Age=75 Years, Rel Day of Study Medication Discontinuance†=255										
100619	Treatment Cycle 6	106	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-002, Site Number=0025, Subject ID=101226, Gender=F, Race=White, Age=76 Years, Rel Day of Study Medication Discontinuance†=169										
101226	Safety Follow-up	198	Hypothyroidism	Continuing		1	N	Y	None	Not Resolved
Trial Number=3475-002, Site Number=0031, Subject ID=101270, Gender=M, Race=White, Age=77 Years, Rel Day of Study Medication Discontinuance†=85										
101270	Safety Follow-up	115	Hypothyroidism	Continuing		2	N	Y	N/A	Not Resolved
Trial Number=3475-002, Site Number=0033, Subject ID=100325, Gender=F, Race=White, Age=49 Years, Rel Day of Study Medication Discontinuance†=415										
100325	Treatment Cycle 5	106	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-002, Site Number=0058, Subject ID=100041, Gender=F, Race=White, Age=39 Years, Rel Day of Study Medication Discontinuance†=609										
100041	Treatment Cycle 4	84	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-002, Site Number=0061, Subject ID=101204, Gender=F, Race=White, Age=43 Years, Rel Day of Study Medication Discontinuance†=728										
101204	Treatment Cycle 18	371	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-002, Site Number=0081, Subject ID=100664, Gender=M, Race=White, Age=15 Years, Rel Day of Study Medication Discontinuance†=148										
100664	Treatment Cycle 3	42	Hypothyroidism	3.14 Weeks		1	N	N	None	Resolved
Trial Number=3475-002, Site Number=0087, Subject ID=102107, Gender=M, Race=White, Age=34 Years, Rel Day of Study Medication Discontinuance†=70										

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Listing of Subjects With Adverse Events
AEOSI- Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=0087, Subject ID=102107, Gender=M, Race=White, Age=34 Years, Rel Day of Study Medication Discontinuance†=70										
102107	Treatment Cycle 2	26	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
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 16	406	Hypothyroidism	Continuing		1	N	N	None	Not Resolved
Trial Number=3475-002, Site Number=0090, Subject ID=100630, Gender=F, Race=White, Age=50 Years, Rel Day of Study Medication Discontinuance†=169										
100630	Treatment Cycle 3	62	Hypothyroidism	3.48 Months		1	N	Y	None	Resolved
Trial Number=3475-002, Site Number=0151, Subject ID=100088, Gender=M, Race=White, Age=55 Years, Rel Day of Study Medication Discontinuance†=										
100088	Treatment Cycle 10	192	Hypothyroidism	3 Weeks		1	N	Y	None	Resolved
Trial Number=3475-010, Site Number=0006, Subject ID=312907, Gender=M, Race=White, Age=59 Years, Rel Day of Study Medication Discontinuance†=										
312907	Treatment Cycle 6	107	Hypothyroidism	4.86 Months		1	N	Y	None	Resolved
	Treatment Cycle 13	275	Hypothyroidism	Continuing		1	N	Y	None	Not Resolved
Trial Number=3475-010, Site Number=0006, Subject ID=314200, Gender=M, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance†=107										
314200	Treatment Cycle 6	107	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-010, Site Number=0028, Subject ID=310007, Gender=M, Race=Black Or African American, Age=75 Years, Rel Day of Study Medication Discontinuance†=										
310007	Treatment Cycle 4	105	Hypothyroidism	Continuing		2	N	Y	Reduced	Not Resolved

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Listing of Subjects With Adverse Events
AEOSI- Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=3475-010, Site Number=0037, Subject ID=310781, Gender=F, Race=White, Age=76 Years, Rel Day of Study Medication Discontinuance†=43										
310781	Treatment Cycle 2	22	Hypothyroidism	Continuing		1	N	Y	None	Not Resolved
Trial Number=3475-010, Site Number=0050, Subject ID=300004, Gender=F, Race=White, Age=55 Years, Rel Day of Study Medication Discontinuance†=										
300004	Treatment Cycle 6	105	Hypothyroidism	Continuing		1	N	Y	None	Not Resolved
Trial Number=3475-010, Site Number=0050, Subject ID=306601, Gender=F, Race=White, Age=75 Years, Rel Day of Study Medication Discontinuance†=169										
306601	Treatment Cycle 2	22	Hypothyroidism	Continuing		1	N	Y	None	Not Resolved
Trial Number=3475-010, Site Number=0058, Subject ID=309570, Gender=M, Race=Black Or African American, Age=64 Years, Rel Day of Study Medication Discontinuance†=										
309570	Treatment Cycle 4	61	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-010, Site Number=0062, Subject ID=300417, Gender=M, Race=White, Age=51 Years, Rel Day of Study Medication Discontinuance†=106										
300417	Treatment Cycle 3	46	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-010, Site Number=0122, Subject ID=313512, Gender=F, Race=White, Age=53 Years, Rel Day of Study Medication Discontinuance†=106										
313512	Treatment Cycle 5	85	Hypothyroidism	1.68 Months		1	N	N	None	Resolved
Trial Number=3475-010, Site Number=0167, Subject ID=308717, Gender=M, Race=White, Age=76 Years, Rel Day of Study Medication Discontinuance†=										
308717	Treatment Cycle 12	249	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-010, Site Number=0181, Subject ID=304856, Gender=F, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=										

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Listing of Subjects With Adverse Events
AEOSI- Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=3475-010, Site Number=0181, Subject ID=304856, Gender=F, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=										
304856	Treatment Cycle 1	19	Hypothyroidism	Continuing		1	N	Y	None	Not Resolved
Trial Number=3475-010, Site Number=0184, Subject ID=311208, Gender=F, Race=White, Age=59 Years, Rel Day of Study Medication Discontinuance†=										
311208	Treatment Cycle 6	126	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-010, Site Number=0201, Subject ID=312217, Gender=M, Race=White, Age=62 Years, Rel Day of Study Medication Discontinuance†=										
312217	Treatment Cycle 9	187	Hypothyroidism	Continuing		1	N	Y	None	Not Resolved
Trial Number=3475-010, Site Number=0205, Subject ID=301281, Gender=M, Race=White, Age=52 Years, Rel Day of Study Medication Discontinuance†=360										
301281	Treatment Cycle 8	148	Hypothyroidism	Continuing		2	N	Y	None	Resolving
Trial Number=3475-010, Site Number=0208, Subject ID=308277, Gender=M, Race=White, Age=68 Years, Rel Day of Study Medication Discontinuance†=85										
308277	Treatment Cycle 1	21	Hypothyroidism	3.09 Months		1	N	Y	None	Resolved
Trial Number=3475-010, Site Number=0209, Subject ID=313318, Gender=F, Race=White, Age=64 Years, Rel Day of Study Medication Discontinuance†=279										
313318	Treatment Cycle 6	112	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-010, Site Number=0284, Subject ID=302744, Gender=F, Race=White, Age=58 Years, Rel Day of Study Medication Discontinuance†=										
302744	Treatment Cycle 8	148	Hypothyroidism	3.94 Months		2	N	Y	None	Sequelae
Trial Number=3475-010, Site Number=0404, Subject ID=311494, Gender=M, Race=White, Age=75 Years, Rel Day of Study Medication Discontinuance†=										

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Listing of Subjects With Adverse Events
AEOSI- Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=3475-010, Site Number=0404, Subject ID=311494, Gender=M, Race=White, Age=75 Years, Rel Day of Study Medication Discontinuance†=										
311494	Treatment Cycle 6	107	Hypothyroidism	7.16 Months		2	N	N	None	Unknown
Trial Number=3475-010, Site Number=0407, Subject ID=306573, Gender=M, Race=White, Age=72 Years, Rel Day of Study Medication Discontinuance†=										
306573	Treatment Cycle 11	241	Hypothyroidism	Continuing		2	Y	Y	Interrupted	Not Resolved
Trial Number=3475-010, Site Number=0440, Subject ID=310818, Gender=M, Race=White, Age=63 Years, Rel Day of Study Medication Discontinuance†=296										
310818	Treatment Cycle 6	106	Hypothyroidism	Continuing		1	N	N	None	Not Resolved
Trial Number=3475-010, Site Number=0800, Subject ID=312186, Gender=M, Race=White, Age=61 Years, Rel Day of Study Medication Discontinuance†=43										
312186	Treatment Cycle 2	22	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-010, Site Number=0926, Subject ID=307528, Gender=F, Race=White, Age=68 Years, Rel Day of Study Medication Discontinuance†=407										
307528	Treatment Cycle 13	322	Hypothyroidism	Unknown		2	N	Y	None	Unknown
Trial Number=3475-010, Site Number=0968, Subject ID=313103, Gender=F, Race=White, Age=75 Years, Rel Day of Study Medication Discontinuance†=										
313103	Treatment Cycle 8	150	Hypothyroidism	Continuing		1	N	Y	None	Not Resolved
Trial Number=3475-010, Site Number=1004, Subject ID=312177, Gender=M, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance†=148										
312177	Treatment Cycle 4	64	Hypothyroidism	7.23 Months		1	N	Y	None	Unknown
Trial Number=3475-010, Site Number=1245, Subject ID=308648, Gender=M, Race=Asian, Age=53 Years, Rel Day of Study Medication Discontinuance†=147										

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Listing of Subjects With Adverse Events
AEOSI- Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=3475-010, Site Number=1245, Subject ID=308648, Gender=M, Race=Asian, Age=53 Years, Rel Day of Study Medication Discontinuance†=147										
308648	Treatment Cycle 4	64	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-010, Site Number=1322, Subject ID=306739, Gender=M, Race=Asian, Age=75 Years, Rel Day of Study Medication Discontinuance†=234										
306739	Treatment Cycle 9	191	Hypothyroidism	3.45 Months		1	N	Y	None	Resolved
Trial Number=3475-010, Site Number=1366, Subject ID=310223, Gender=M, Race=American Indian Or Alaska Native, Age=57 Years, Rel Day of Study Medication Discontinuance†=385										
310223	Treatment Cycle 6	125	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-010, Site Number=1411, Subject ID=301875, Gender=M, Race=Asian, Age=70 Years, Rel Day of Study Medication Discontinuance†=64										
301875	Safety Follow-up	82	Hypothyroidism	Continuing		1	N	Y	None	Not Resolved
MK-3475 10 mg/kg Q3W										
Trial Number=3475-001, Site Number=0001, Subject ID=001436, Gender=M, Race=White, Age=65 Years, Rel Day of Study Medication Discontinuance†=										
001436	Treatment Cycle 5	106	Hypothyroidism	Continuing	Moderate	2		Y	Interrupted	Not Resolved
Trial Number=3475-001, Site Number=0001, Subject ID=001525, Gender=M, Race=White, Age=71 Years, Rel Day of Study Medication Discontinuance†=176										
001525	Treatment Cycle 9	176	Hypothyroidism	Continuing	Moderate	2		Y	N/A	Not Resolved
Trial Number=3475-001, Site Number=0003, Subject ID=001258, Gender=M, Race=White, Age=42 Years, Rel Day of Study Medication Discontinuance†=65										
001258	Treatment Cycle 4	65	Hypothyroidism	Continuing	Mild	1		N		Not Resolved

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Listing of Subjects With Adverse Events
AEOSI- Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=0008, Subject ID=001170, Gender=F, Race=White, Age=78 Years, Rel Day of Study Medication Discontinuance†=										
001170	Treatment Cycle 6	126	Hypothyroidism	4.63 Months	Moderate	2		Y	Interrupted	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	Safety Follow-up	240	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0010, Subject ID=000499, Gender=F, Race=White, Age=60 Years, Rel Day of Study Medication Discontinuance†=190										
000499	Treatment Cycle 2	22	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0010, Subject ID=000818, Gender=M, Race=White, Age=65 Years, Rel Day of Study Medication Discontinuance†=										
000818	Treatment Cycle 14 Treatment Cycle 15	340 361	Hypothyroidism Hypothyroidism	3 Weeks Continuing	Moderate Mild	2 1		Y Y	 N/A	Resolved Not Resolved
Trial Number=3475-001, Site Number=0010, Subject ID=000910, Gender=F, Race=Multiracial, Age=69 Years, Rel Day of Study Medication Discontinuance†=170										
000910	Treatment Cycle 6	110	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0010, Subject ID=001073, Gender=F, Race=White, Age=49 Years, Rel Day of Study Medication Discontinuance†=210										
001073	Safety Follow-up	212	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0010, Subject ID=001220, Gender=M, Race=White, Age=73 Years, Rel Day of Study Medication Discontinuance†=										
001220	Treatment Cycle 12 Treatment Cycle 16	231 329	Hypothyroidism Hypothyroidism	3.22 Months Continuing	Moderate Mild	2 1		Y Y	 N/A	Resolved Not Resolved

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Listing of Subjects With Adverse Events
AEOSI- Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=000068, Gender=M, Race=White, Age=46 Years, Rel Day of Study Medication Discontinuance†=83										
000068	Extended Safety Follow-up	160	Hypothyroidism	1.41 Months	Severe	3	Y	Y		Resolved
Trial Number=3475-001, Site Number=0012, Subject ID=001095, Gender=M, Race=White, Age=79 Years, Rel Day of Study Medication Discontinuance†=										
001095	Treatment Cycle 8	148	Hypothyroidism	3 Weeks	Mild	1		Y	N/A	Resolved
	Treatment Cycle 9	169	Hypothyroidism	1.45 Months	Moderate	2		Y		Resolved
Trial Number=3475-001, Site Number=0015, Subject ID=000383, Gender=F, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance†=										
000383	Treatment Cycle 6	106	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0015, Subject ID=000519, Gender=M, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance†=										
000519	Treatment Cycle 9	187	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0016, Subject ID=001502, Gender=M, Race=White, Age=83 Years, Rel Day of Study Medication Discontinuance†=547										
001502	Treatment Cycle 6	148	Hypothyroidism	Continuing	Mild	1		Y	N/A	Not Resolved
Trial Number=3475-001, Site Number=0019, Subject ID=000190, Gender=F, Race=White, Age=41 Years, Rel Day of Study Medication Discontinuance†=43										
000190	Safety Follow-up	64	Hypothyroidism	1.14 Weeks	Mild	1		N		Resolved
		72	Hypothyroidism	Continuing	Moderate	2		N		Not Resolved
Trial Number=3475-001, Site Number=0019, Subject ID=000367, Gender=F, Race=White, Age=63 Years, Rel Day of Study Medication Discontinuance†=168										

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Listing of Subjects With Adverse Events
AEOSI- Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q3W										
Trial Number=3475-001, Site Number=0019, Subject ID=000367, Gender=F, Race=White, Age=63 Years, Rel Day of Study Medication Discontinuance†=168										
000367	Treatment Cycle 1	5	Hypothyroidism	Continuing	Moderate	2		N		Not Resolved
Trial Number=3475-001, Site Number=0019, Subject ID=001505, Gender=F, Race=White, Age=75 Years, Rel Day of Study Medication Discontinuance†=211										
001505	Treatment Cycle 6	106	Hypothyroidism	Continuing	Moderate	2		N		Not Resolved
Trial Number=3475-001, Site Number=0019, Subject ID=001562, Gender=M, Race=White, Age=59 Years, Rel Day of Study Medication Discontinuance†=										
001562	Treatment Cycle 12	232	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
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 3	57	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0020, Subject ID=001350, Gender=M, Race=White, Age=44 Years, Rel Day of Study Medication Discontinuance†=85										
001350	Treatment Cycle 5	85	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0020, Subject ID=001353, Gender=F, Race=White, Age=81 Years, Rel Day of Study Medication Discontinuance†=85										
001353	Treatment Cycle 3	42	Hypothyroidism	Continuing	Mild	1		Y	N/A	Not Resolved
Trial Number=3475-001, Site Number=0020, Subject ID=001543, Gender=M, Race=White, Age=69 Years, Rel Day of Study Medication Discontinuance†=63										
001543	Safety Follow-up	91	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0020, Subject ID=001566, Gender=F, Race=White, Age=60 Years, Rel Day of Study Medication Discontinuance†=300										

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Listing of Subjects With Adverse Events
AEOSI- Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=001566, Gender=F, Race=White, Age=60 Years, Rel Day of Study Medication Discontinuance†=300										
001566	Treatment Cycle 1	21	Hypothyroidism	2.86 Weeks	Moderate	2		Y		Resolved
	Treatment Cycle 4	111	Myxoedema	3.43 Weeks	Moderate	2		Y	Interrupted	Resolved
		135	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0021, Subject ID=000132, Gender=F, Race=White, Age=38 Years, Rel Day of Study Medication Discontinuance†=153										
000132	Safety Follow-up	171	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0021, Subject ID=000484, Gender=F, Race=White, Age=67 Years, Rel Day of Study Medication Discontinuance†=106										
000484	Treatment Cycle 3	44	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0021, Subject ID=001408, Gender=M, Race=White, Age=38 Years, Rel Day of Study Medication Discontinuance†=										
001408	Treatment Cycle 7	127	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0021, Subject ID=001412, Gender=M, Race=White, Age=57 Years, Rel Day of Study Medication Discontinuance†=										
001412	Treatment Cycle 4	85	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0021, Subject ID=001448, Gender=F, Race=White, Age=50 Years, Rel Day of Study Medication Discontinuance†=										
001448	Treatment Cycle 6	106	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0023, Subject ID=000161, Gender=M, Race=White, Age=67 Years, Rel Day of Study Medication Discontinuance†=										
000161	Treatment Cycle 9	191	Hypothyroidism	5.72 Months	Mild	1		Y	N/A	Resolved

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Listing of Subjects With Adverse Events
AEOSI- Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q3W										
Trial Number=3475-001, Site Number=0023, Subject ID=000161, Gender=M, Race=White, Age=67 Years, Rel Day of Study Medication Discontinuance†=										
000161	Treatment Cycle 18	365	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0023, Subject ID=000953, Gender=F, Race=Asian, Age=52 Years, Rel Day of Study Medication Discontinuance†=64										
000953	Safety Follow-up	84	Hypothyroidism	1.43 Weeks	Severe	3	Y	Y		Resolved
		94	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0024, Subject ID=000121, Gender=M, Race=White, Age=51 Years, Rel Day of Study Medication Discontinuance†=56										
000121	Treatment Cycle 2	41	Hypothyroidism	1.44 Years	Moderate	2		Y	Interrupted	Resolved
Trial Number=3475-001, Site Number=0036, Subject ID=001143, Gender=M, Race=White, Age=56 Years, Rel Day of Study Medication Discontinuance†=										
001143	Treatment Cycle 12	232	Hypothyroidism	2.76 Months	Moderate	2		Y		Resolved
Trial Number=3475-001, Site Number=0073, Subject ID=001578, Gender=F, Race=Asian, Age=76 Years, Rel Day of Study Medication Discontinuance†=										
001578	Treatment Cycle 5	106	Hypothyroidism	Continuing	Moderate	2	Y	Y	Interrupted	Not Resolved
Trial Number=3475-001, Site Number=0083, Subject ID=001025, Gender=F, Race=Asian, Age=63 Years, Rel Day of Study Medication Discontinuance†=169										
001025	Treatment Cycle 8	149	Hypothyroidism	Continuing	Mild	1		Y		Not Resolved
Trial Number=3475-001, Site Number=0134, Subject ID=001140, Gender=F, Race=White, Age=65 Years, Rel Day of Study Medication Discontinuance†=										
001140	Treatment Cycle 6	104	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved

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Listing of Subjects With Adverse Events
AEOSI- Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=0016, Subject ID=100627, Gender=M, Race=White, Age=56 Years, Rel Day of Study Medication Discontinuance†=127										
100627	Treatment Cycle 2	22	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-002, Site Number=0021, Subject ID=101218, Gender=F, Race=White, Age=56 Years, Rel Day of Study Medication Discontinuance†=106										
101218	Treatment Cycle 5	105	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-002, Site Number=0028, Subject ID=102124, Gender=M, Race=White, Age=59 Years, Rel Day of Study Medication Discontinuance†=162										
102124	Treatment Cycle 5	105	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-002, Site Number=0033, Subject ID=101504, Gender=F, Race=White, Age=43 Years, Rel Day of Study Medication Discontinuance†=112										
101504	Treatment Cycle 4	64	Hypothyroidism	Continuing		1	N	N	N/A	Not Resolved
Trial Number=3475-002, Site Number=0061, Subject ID=100091, Gender=M, Race=White, Age=78 Years, Rel Day of Study Medication Discontinuance†=190										
100091	Treatment Cycle 7	127	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-002, Site Number=0080, Subject ID=100022, Gender=M, Race=White, Age=45 Years, Rel Day of Study Medication Discontinuance†=										
100022	Treatment Cycle 6	126	Hypothyroidism	2.04 Months		2	N	Y	None	Resolved
Trial Number=3475-002, Site Number=0080, Subject ID=100313, Gender=F, Race=White, Age=68 Years, Rel Day of Study Medication Discontinuance†=421										
100313	Treatment Cycle 10	213	Hypothyroidism	1.41 Months		2	N	Y	None	Resolved
Trial Number=3475-002, Site Number=0080, Subject ID=100652, Gender=F, Race=White, Age=62 Years, Rel Day of Study Medication Discontinuance†=422										

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Listing of Subjects With Adverse Events
AEOSI- Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=100652, Gender=F, Race=White, Age=62 Years, Rel Day of Study Medication Discontinuance†=422										
100652	Treatment Cycle 3	63	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-002, Site Number=0088, Subject ID=102142, Gender=M, Race=White, Age=53 Years, Rel Day of Study Medication Discontinuance†=43										
102142	Treatment Cycle 1	8	Hypothyroidism	6 Days		2	N	Y	None	Resolved
		14	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-002, Site Number=0090, Subject ID=100045, Gender=M, Race=White, Age=62 Years, Rel Day of Study Medication Discontinuance†=										
100045	Treatment Cycle 10	204	Hypothyroidism	1.09 Years		2	N	Y	None	Resolved
Trial Number=3475-002, Site Number=0101, Subject ID=101833, Gender=F, Race=White, Age=80 Years, Rel Day of Study Medication Discontinuance†=65										
101833	Safety Follow-up	85	Hypothyroidism	Continuing		1	N	Y	None	Not Resolved
Trial Number=3475-002, Site Number=0111, Subject ID=100329, Gender=F, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=										
100329	Treatment Cycle 5	105	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-002, Site Number=0151, Subject ID=100002, Gender=F, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance†=212										
100002	Treatment Cycle 2	63	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-002, Site Number=0151, Subject ID=100312, Gender=F, Race=White, Age=54 Years, Rel Day of Study Medication Discontinuance†=485										
100312	Treatment Cycle 5	86	Hypothyroidism	Continuing		2	N	N	None	Not Resolved

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Listing of Subjects With Adverse Events
AEOSI- Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=0170, Subject ID=100622, Gender=M, Race=White, Age=76 Years, Rel Day of Study Medication Discontinuance†=1										
100622	Safety Follow-up	29	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=0001, Subject ID=361997, Gender=M, Race=White, Age=60 Years, Rel Day of Study Medication Discontinuance†=211										
361997	Treatment Cycle 9	189	Hypothyroidism	1.41 Months		1	N	Y	None	Resolved
Trial Number=3475-006, Site Number=0002, Subject ID=363240, Gender=M, Race=White, Age=68 Years, Rel Day of Study Medication Discontinuance†=										
363240	Treatment Cycle 12	241	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=0300, Subject ID=361650, Gender=M, Race=White, Age=74 Years, Rel Day of Study Medication Discontinuance†=										
361650	Treatment Cycle 4	70	Hypothyroidism	Continuing		1	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=0312, Subject ID=364060, Gender=M, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance†=										
364060	Treatment Cycle 3	42	Hypothyroidism	Unknown		2	N	Y	None	Unknown
Trial Number=3475-006, Site Number=0312, Subject ID=369039, Gender=M, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=										
369039	Treatment Cycle 6	106	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=0501, Subject ID=362675, Gender=F, Race=White, Age=51 Years, Rel Day of Study Medication Discontinuance†=22										
362675	Treatment Cycle 1	1	Hypothyroidism	1.02 Months		2	N	N	N/A	Unknown
Trial Number=3475-006, Site Number=0507, Subject ID=366988, Gender=M, Race=Multiple, Age=34 Years, Rel Day of Study Medication Discontinuance†=										

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Listing of Subjects With Adverse Events
AEOSI- Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=0507, Subject ID=366988, Gender=M, Race=Multiple, Age=34 Years, Rel Day of Study Medication Discontinuance†=										
366988	Treatment Cycle 7	147	Hypothyroidism	Continuing		1	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=0605, Subject ID=360489, Gender=F, Race=White, Age=61 Years, Rel Day of Study Medication Discontinuance†=54										
360489	Treatment Cycle 3	54	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=0605, Subject ID=362662, Gender=F, Race=White, Age=38 Years, Rel Day of Study Medication Discontinuance†=232										
362662	Treatment Cycle 2	20	Hypothyroidism	9.72 Months		2	N	Y	None	Resolved
Trial Number=3475-006, Site Number=0605, Subject ID=367085, Gender=M, Race=White, Age=64 Years, Rel Day of Study Medication Discontinuance†=147										
367085	Treatment Cycle 6	105	Hypothyroidism	3.14 Weeks		1	N	Y	None	Resolved
Trial Number=3475-006, Site Number=0607, Subject ID=364455, Gender=M, Race=White, Age=77 Years, Rel Day of Study Medication Discontinuance†=										
364455	Treatment Cycle 10	197	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=0611, Subject ID=361610, Gender=F, Race=White, Age=40 Years, Rel Day of Study Medication Discontinuance†=127										
361610	Treatment Cycle 3	43	Hypothyroidism	Continuing		1	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=0612, Subject ID=361134, Gender=F, Race=White, Age=53 Years, Rel Day of Study Medication Discontinuance†=										
361134	Treatment Cycle 5	94	Hypothyroidism	1.45 Months		1	N	Y	None	Resolved
Trial Number=3475-006, Site Number=0612, Subject ID=363119, Gender=F, Race=White, Age=59 Years, Rel Day of Study Medication Discontinuance†=173										

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Listing of Subjects With Adverse Events
AEOSI- Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=0612, Subject ID=363119, Gender=F, Race=White, Age=59 Years, Rel Day of Study Medication Discontinuance†=173										
363119	Treatment Cycle 7	131	Hypothyroidism	1.41 Months		1	N	Y	None	Resolved
Trial Number=3475-006, Site Number=0702, Subject ID=367414, Gender=F, Race=White, Age=62 Years, Rel Day of Study Medication Discontinuance†=359										
367414	Treatment Cycle 6	107	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=0901, Subject ID=365724, Gender=F, Race=White, Age=63 Years, Rel Day of Study Medication Discontinuance†=										
365724	Treatment Cycle 6	106	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=1500, Subject ID=363996, Gender=M, Race=White, Age=42 Years, Rel Day of Study Medication Discontinuance†=22										
363996	Safety Follow-up	43	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=1502, Subject ID=369150, Gender=F, Race=White, Age=84 Years, Rel Day of Study Medication Discontinuance†=107										
369150	Treatment Cycle 4	65	Primary hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=1504, Subject ID=365695, Gender=M, Race=White, Age=65 Years, Rel Day of Study Medication Discontinuance†=										
365695	Treatment Cycle 7	143	Hypothyroidism	Continuing		2	N	Y	None	Resolving
Trial Number=3475-006, Site Number=1603, Subject ID=360612, Gender=M, Race=White, Age=65 Years, Rel Day of Study Medication Discontinuance†=										
360612	Treatment Cycle 7	127	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=1703, Subject ID=363479, Gender=M, Race=White, Age=64 Years, Rel Day of Study Medication Discontinuance†=										

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Listing of Subjects With Adverse Events
AEOSI- Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=1703, Subject ID=363479, Gender=M, Race=White, Age=64 Years, Rel Day of Study Medication Discontinuance†=										
363479	Treatment Cycle 7	148	Hypothyroidism	4.93 Months		2	N	Y	Interrupted	Resolved
Trial Number=3475-006, Site Number=1707, Subject ID=362376, Gender=F, Race=White, Age=68 Years, Rel Day of Study Medication Discontinuance†=										
362376	Treatment Cycle 4	83	Hypothyroidism	1.68 Months		2	N	Y	Interrupted	Resolved
Trial Number=3475-006, Site Number=1711, Subject ID=366346, Gender=F, Race=White, Age=55 Years, Rel Day of Study Medication Discontinuance†=65										
366346	Treatment Cycle 1	11	Hypothyroidism	Continuing		2	N	N	None	Not Resolved
Trial Number=3475-006, Site Number=1804, Subject ID=363862, Gender=M, Race=White, Age=71 Years, Rel Day of Study Medication Discontinuance†=41										
363862	Treatment Cycle 2	18	Hypothyroidism	3.43 Weeks		1	N	N	None	Resolved
Trial Number=3475-006, Site Number=1810, Subject ID=365529, Gender=M, Race=White, Age=52 Years, Rel Day of Study Medication Discontinuance†=										
365529	Treatment Cycle 14	294	Hypothyroidism	1.97 Months		1	N	Y	None	Resolved
	Treatment Cycle 17	354	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=1810, Subject ID=369578, Gender=F, Race=White, Age=62 Years, Rel Day of Study Medication Discontinuance†=										
369578	Treatment Cycle 4	64	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=1814, Subject ID=367816, Gender=M, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance†=										
367816	Treatment Cycle 14	270	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved

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Listing of Subjects With Adverse Events
AEOSI- Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=1818, Subject ID=364877, Gender=M, Race=White, Age=80 Years, Rel Day of Study Medication Discontinuance†=										
364877	Treatment Cycle 8	148	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=1820, Subject ID=367788, Gender=M, Race=White, Age=33 Years, Rel Day of Study Medication Discontinuance†=										
367788	Treatment Cycle 6	107	Hypothyroidism	Continuing		1	N	Y	None	Not Resolved
Trial Number=3475-010, Site Number=0006, Subject ID=306565, Gender=M, Race=White, Age=54 Years, Rel Day of Study Medication Discontinuance†=107										
306565	Treatment Cycle 3	44	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-010, Site Number=0014, Subject ID=302077, Gender=M, Race=White, Age=65 Years, Rel Day of Study Medication Discontinuance†=141										
302077	Treatment Cycle 3	86	Hypothyroidism	Continuing		2	N	Y	Discontinued	Not Resolved
Trial Number=3475-010, Site Number=0027, Subject ID=312104, Gender=M, Race=White, Age=62 Years, Rel Day of Study Medication Discontinuance†=										
312104	Treatment Cycle 6	107	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-010, Site Number=0037, Subject ID=302733, Gender=F, Race=Asian, Age=61 Years, Rel Day of Study Medication Discontinuance†=244										
302733	Treatment Cycle 2	21	Hypothyroidism	4.83 Months		1	N	Y	None	Resolved
	Treatment Cycle 8	168	Hypothyroidism	1.58 Months		2	N	Y	None	Resolved
	Treatment Cycle 11	244	Hypothyroidism	Unknown		2	N	Y	None	Unknown
Trial Number=3475-010, Site Number=0045, Subject ID=300012, Gender=M, Race=White, Age=63 Years, Rel Day of Study Medication Discontinuance†=45										
300012	Treatment Cycle 2	22	Hypothyroidism	1.68 Months		1	N	Y	None	Resolved

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Listing of Subjects With Adverse Events
AEOSI- Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=3475-010, Site Number=0055, Subject ID=311446, Gender=F, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=										
311446	Treatment Cycle 3	65	Hypothyroidism	7.1 Months		2	N	Y	None	Resolved
Trial Number=3475-010, Site Number=0081, Subject ID=305369, Gender=F, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance†=130										
305369	Treatment Cycle 2	39	Hypothyroidism	Continuing		1	N	N	None	Not Resolved
Trial Number=3475-010, Site Number=0089, Subject ID=300809, Gender=M, Race=White, Age=67 Years, Rel Day of Study Medication Discontinuance†=										
300809	Treatment Cycle 9	189	Hypothyroidism	1.41 Months		1	N	Y	None	Resolved
Trial Number=3475-010, Site Number=0096, Subject ID=300751, Gender=F, Race=, Age=60 Years, Rel Day of Study Medication Discontinuance†=232										
300751	Treatment Cycle 2	43	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-010, Site Number=0122, Subject ID=310300, Gender=M, Race=White, Age=55 Years, Rel Day of Study Medication Discontinuance†=248										
310300	Treatment Cycle 3	64	Hypothyroidism	2.27 Months		2	N	N	None	Resolved
	Treatment Cycle 7	161	Hypothyroidism	2 Days		2	N	N	None	Resolved
	Treatment Cycle 8	165	Hypothyroidism	Continuing		2	N	N	None	Not Resolved
Trial Number=3475-010, Site Number=0180, Subject ID=311829, Gender=F, Race=White, Age=61 Years, Rel Day of Study Medication Discontinuance†=526										
311829	Treatment Cycle 5	104	Hypothyroidism	2.56 Months		2	N	Y	Reduced	Resolved
Trial Number=3475-010, Site Number=0181, Subject ID=313988, Gender=M, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=										
313988	Treatment Cycle 6	137	Hypothyroidism	Continuing		2	Y	Y	None	Not Resolved

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Listing of Subjects With Adverse Events
AEOSI- Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=3475-010, Site Number=0183, Subject ID=301027, Gender=M, Race=White, Age=64 Years, Rel Day of Study Medication Discontinuance†=										
301027	Treatment Cycle 6	107	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-010, Site Number=0282, Subject ID=304866, Gender=M, Race=White, Age=78 Years, Rel Day of Study Medication Discontinuance†=										
304866	Treatment Cycle 7	129	Hypothyroidism	2.1 Months		1	N	Y	None	Resolved
Trial Number=3475-010, Site Number=0282, Subject ID=306612, Gender=M, Race=White, Age=60 Years, Rel Day of Study Medication Discontinuance†=										
306612	Treatment Cycle 7	143	Hypothyroidism	2.79 Months		2	N	N	None	Resolved
Trial Number=3475-010, Site Number=0443, Subject ID=301469, Gender=F, Race=White, Age=61 Years, Rel Day of Study Medication Discontinuance†=										
301469	Treatment Cycle 7	126	Hypothyroidism	Continuing		1	N	N	None	Resolving
Trial Number=3475-010, Site Number=0452, Subject ID=308756, Gender=F, Race=White, Age=58 Years, Rel Day of Study Medication Discontinuance†=211										
308756	Treatment Cycle 6	107	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-010, Site Number=0560, Subject ID=300343, Gender=F, Race=White, Age=72 Years, Rel Day of Study Medication Discontinuance†=266										
300343	Treatment Cycle 3	64	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-010, Site Number=0560, Subject ID=307270, Gender=M, Race=White, Age=60 Years, Rel Day of Study Medication Discontinuance†=										
307270	Treatment Cycle 20	457	Hypothyroidism	Continuing		1	N	Y	None	Not Resolved
Trial Number=3475-010, Site Number=0560, Subject ID=309361, Gender=M, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=										

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Listing of Subjects With Adverse Events
AEOSI- Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=3475-010, Site Number=0560, Subject ID=309361, Gender=M, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=										
309361	Treatment Cycle 9	189	Hypothyroidism	8.02 Months		2	N	Y	Reduced	Sequelae
Trial Number=3475-010, Site Number=0920, Subject ID=308160, Gender=M, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=120										
308160	Treatment Cycle 3	76	Hypothyroidism	3.14 Weeks		1	N	Y	None	Resolved
Trial Number=3475-010, Site Number=1004, Subject ID=302223, Gender=F, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=46										
302223	Safety Follow-up	67	Hypothyroidism	Unknown		1	N	Y	None	Unknown
Trial Number=3475-010, Site Number=1242, Subject ID=309419, Gender=M, Race=Asian, Age=49 Years, Rel Day of Study Medication Discontinuance†=										
309419	Treatment Cycle 6	106	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-010, Site Number=1243, Subject ID=313473, Gender=F, Race=Asian, Age=55 Years, Rel Day of Study Medication Discontinuance†=										
313473	Treatment Cycle 7	155	Hypothyroidism	Continuing		2	N	N	Interrupted	Resolving
Trial Number=3475-010, Site Number=1243, Subject ID=313501, Gender=M, Race=Asian, Age=68 Years, Rel Day of Study Medication Discontinuance†=										
313501	Treatment Cycle 4	64	Hypothyroidism	Continuing		2	N	Y	Interrupted	Resolving
Trial Number=3475-010, Site Number=1244, Subject ID=309645, Gender=F, Race=Asian, Age=53 Years, Rel Day of Study Medication Discontinuance†=169										
309645	Treatment Cycle 3	63	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-010, Site Number=1405, Subject ID=312141, Gender=M, Race=Asian, Age=74 Years, Rel Day of Study Medication Discontinuance†=40										

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Listing of Subjects With Adverse Events
AEOSI- Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=3475-010, Site Number=1405, Subject ID=312141, Gender=M, Race=Asian, Age=74 Years, Rel Day of Study Medication Discontinuance†=40										
312141	Safety Follow-up	69	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-010, Site Number=1421, Subject ID=311479, Gender=M, Race=Asian, Age=49 Years, Rel Day of Study Medication Discontinuance†=										
311479	Treatment Cycle 3	64	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
MK-3475 10 mg/kg Q2W										
Trial Number=3475-001, Site Number=0001, Subject ID=001209, Gender=M, Race=White, Age=69 Years, Rel Day of Study Medication Discontinuance†=										
001209	Treatment Cycle 13	184	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0002, Subject ID=000057, Gender=F, Race=White, Age=72 Years, Rel Day of Study Medication Discontinuance†=										
000057	Treatment Cycle 6	143	Hypothyroidism	3.42 Months	Mild	1		Y	N/A	Resolved
	Treatment Cycle 11	247	Hypothyroidism	1.78 Years	Moderate	2		Y		Resolved
Trial Number=3475-001, Site Number=0002, Subject ID=001014, Gender=F, Race=White, Age=73 Years, Rel Day of Study Medication Discontinuance†=155										
001014	Treatment Cycle 6	71	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0002, Subject ID=001294, Gender=M, Race=White, Age=52 Years, Rel Day of Study Medication Discontinuance†=										
001294	Treatment Cycle 15	195	Hypothyroidism	1.41 Months	Mild	1		Y	N/A	Resolved
	Treatment Cycle 18	238	Hypothyroidism	2.3 Months	Moderate	2		Y		Resolved

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Listing of Subjects With Adverse Events
AEOSI- Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q2W										
Trial Number=3475-001, Site Number=0003, Subject ID=000067, Gender=F, Race=White, Age=51 Years, Rel Day of Study Medication Discontinuance†=										
000067	Treatment Cycle 8	106	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0003, Subject ID=000098, Gender=M, Race=White, Age=59 Years, Rel Day of Study Medication Discontinuance†=										
000098	Treatment Cycle 6	81	Hypothyroidism	1.02 Months	Severe	3		Y	Interrupted	Resolved
	Treatment Cycle 8	134	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
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 10	141	Hypothyroidism	Continuing	Moderate	2		Y	Interrupted	Not Resolved
Trial Number=3475-001, Site Number=0010, Subject ID=000031, Gender=M, Race=White, Age=77 Years, Rel Day of Study Medication Discontinuance†=										
000031	Treatment Cycle 10	126	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0010, Subject ID=000033, Gender=F, Race=White, Age=61 Years, Rel Day of Study Medication Discontinuance†=										
000033	Treatment Cycle 10	141	Hypothyroidism	Continuing	Moderate	2		N		Not Resolved
Trial Number=3475-001, Site Number=0010, Subject ID=000045, Gender=M, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance†=441										
000045	Treatment Cycle 8	99	Hypothyroidism	Continuing	Moderate	2		Y	Interrupted	Not Resolved
Trial Number=3475-001, Site Number=0010, Subject ID=001104, Gender=F, Race=White, Age=57 Years, Rel Day of Study Medication Discontinuance†=73										
001104	Treatment Cycle 6	73	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved

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Listing of Subjects With Adverse Events
AEOSI- Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q2W										
Trial Number=3475-001, Site Number=0010, Subject ID=001211, Gender=M, Race=White, Age=65 Years, Rel Day of Study Medication Discontinuance†=										
001211	Treatment Cycle 5	84	Hypothyroidism	4.14 Weeks	Mild	1		Y		Resolved
	Treatment Cycle 7	113	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0010, Subject ID=001221, Gender=M, Race=White, Age=51 Years, Rel Day of Study Medication Discontinuance†=										
001221	Treatment Cycle 8	99	Hypothyroidism	Continuing	Mild	1		Y		Not Resolved
Trial Number=3475-001, Site Number=0015, Subject ID=000038, Gender=F, Race=White, Age=89 Years, Rel Day of Study Medication Discontinuance†=313										
000038	Treatment Cycle 10	130	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0015, Subject ID=000909, Gender=M, Race=White, Age=53 Years, Rel Day of Study Medication Discontinuance†=223										
000909	Treatment Cycle 12	153	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0015, Subject ID=000939, Gender=M, Race=White, Age=74 Years, Rel Day of Study Medication Discontinuance†=										
000939	Treatment Cycle 16	210	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0015, Subject ID=000946, Gender=M, Race=White, Age=54 Years, Rel Day of Study Medication Discontinuance†=										
000946	Treatment Cycle 13	178	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0015, Subject ID=001285, Gender=M, Race=White, Age=38 Years, Rel Day of Study Medication Discontinuance†=										
001285	Treatment Cycle 9	113	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved

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Listing of Subjects With Adverse Events
AEOSI- Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=001553, Gender=M, Race=White, Age=65 Years, Rel Day of Study Medication Discontinuance†=225										
001553	Treatment Cycle 12	155	Hypothyroidism	Continuing	Mild	1		Y		Not Resolved
Trial Number=3475-001, Site Number=0015, Subject ID=001708, Gender=M, Race=White, Age=59 Years, Rel Day of Study Medication Discontinuance†=463										
001708	Treatment Cycle 10	127	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0016, Subject ID=001738, Gender=M, Race=White, Age=76 Years, Rel Day of Study Medication Discontinuance†=438										
001738	Treatment Cycle 20	270	Hypothyroidism	1.91 Months	Mild	1		Y	N/A	Resolved
Trial Number=3475-001, Site Number=0016, Subject ID=001740, Gender=F, Race=White, Age=62 Years, Rel Day of Study Medication Discontinuance†=351										
001740	Treatment Cycle 10	137	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0019, Subject ID=000040, Gender=F, Race=White, Age=44 Years, Rel Day of Study Medication Discontinuance†=										
000040	Treatment Cycle 17	230	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0019, Subject ID=001066, Gender=M, Race=White, Age=55 Years, Rel Day of Study Medication Discontinuance†=										
001066	Treatment Cycle 12	154	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0019, Subject ID=001291, Gender=F, Race=White, Age=67 Years, Rel Day of Study Medication Discontinuance†=										
001291	Treatment Cycle 8	106	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0019, Subject ID=001516, Gender=F, Race=White, Age=59 Years, Rel Day of Study Medication Discontinuance†=267										

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Listing of Subjects With Adverse Events
AEOSI- Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=001516, Gender=F, Race=White, Age=59 Years, Rel Day of Study Medication Discontinuance†=267										
001516	Treatment Cycle 8	107	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0020, Subject ID=000904, Gender=F, Race=White, Age=51 Years, Rel Day of Study Medication Discontinuance†=99										
000904	Treatment Cycle 6	71	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0020, Subject ID=000921, Gender=M, Race=White, Age=53 Years, Rel Day of Study Medication Discontinuance†=256										
000921	Treatment Cycle 6	72	Hypothyroidism	8.74 Months	Moderate	2		Y		Resolved
Trial Number=3475-001, Site Number=0020, Subject ID=001390, Gender=F, Race=White, Age=48 Years, Rel Day of Study Medication Discontinuance†=85										
001390	Safety Follow-up	111	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0020, Subject ID=001404, Gender=F, Race=White, Age=42 Years, Rel Day of Study Medication Discontinuance†=71										
001404	Treatment Cycle 4	56	Hypothyroidism	Continuing	Moderate	2		Y		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 38	576	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0023, Subject ID=001509, Gender=M, Race=White, Age=56 Years, Rel Day of Study Medication Discontinuance†=										
001509	Treatment Cycle 8	127	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0027, Subject ID=001515, Gender=M, Race=Black Or African American, Age=72 Years, Rel Day of Study Medication Discontinuance†=253										

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Listing of Subjects With Adverse Events
AEOSI- Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=0027, Subject ID=001515, Gender=M, Race=Black Or African American, Age=72 Years, Rel Day of Study Medication Discontinuance†=253										
001515	Treatment Cycle 10	129	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0028, Subject ID=001507, Gender=M, Race=White, Age=83 Years, Rel Day of Study Medication Discontinuance†=										
001507	Treatment Cycle 14	225	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0036, Subject ID=001116, Gender=M, Race=White, Age=56 Years, Rel Day of Study Medication Discontinuance†=										
001116	Treatment Cycle 6	72	Hypothyroidism	5.98 Months	Moderate	2		Y		Resolved
Trial Number=3475-001, Site Number=0040, Subject ID=001107, Gender=M, Race=White, Age=41 Years, Rel Day of Study Medication Discontinuance†=181										
001107	Treatment Cycle 13	167	Hypothyroidism	3 Weeks	Mild	1		Y	N/A	Resolved
Trial Number=3475-001, Site Number=0090, Subject ID=001051, Gender=M, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance†=										
001051	Treatment Cycle 5	71	Hypothyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0134, Subject ID=001582, Gender=F, Race=White, Age=50 Years, Rel Day of Study Medication Discontinuance†=219										
001582	Treatment Cycle 13	189	Hypothyroidism	2.43 Weeks	Mild	1		Y	N/A	Resolved
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	Treatment Cycle 3	40	Hypothyroidism	1.64 Months		1	N	Y	None	Resolved
Trial Number=3475-006, Site Number=0002, Subject ID=360490, Gender=F, Race=White, Age=57 Years, Rel Day of Study Medication Discontinuance†=99										

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Listing of Subjects With Adverse Events
AEOSI- Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=0002, Subject ID=360490, Gender=F, Race=White, Age=57 Years, Rel Day of Study Medication Discontinuance†=99										
360490	Safety Follow-up	113	Hypothyroidism	Continuing		2	N	Y	N/A	Not Resolved
Trial Number=3475-006, Site Number=0003, Subject ID=362014, Gender=M, Race=White, Age=78 Years, Rel Day of Study Medication Discontinuance†=										
362014	Treatment Cycle 6	84	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=0005, Subject ID=362871, Gender=M, Race=White, Age=36 Years, Rel Day of Study Medication Discontinuance†=279										
362871	Treatment Cycle 12	153	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=0102, Subject ID=365853, Gender=F, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=										
365853	Treatment Cycle 11	143	Hypothyroidism	Continuing		1	N	N	None	Not Resolved
Trial Number=3475-006, Site Number=0300, Subject ID=369262, Gender=M, Race=White, Age=54 Years, Rel Day of Study Medication Discontinuance†=										
369262	Treatment Cycle 8	106	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=0400, Subject ID=363379, Gender=M, Race=White, Age=54 Years, Rel Day of Study Medication Discontinuance†=										
363379	Treatment Cycle 24	336	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=0400, Subject ID=369352, Gender=F, Race=White, Age=26 Years, Rel Day of Study Medication Discontinuance†=99										
369352	Treatment Cycle 6	71	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=0600, Subject ID=368594, Gender=F, Race=White, Age=72 Years, Rel Day of Study Medication Discontinuance†=										

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Listing of Subjects With Adverse Events
AEOSI- Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=0600, Subject ID=368594, Gender=F, Race=White, Age=72 Years, Rel Day of Study Medication Discontinuance†=										
368594	Treatment Cycle 14	186	Hypothyroidism	2.56 Months		2	N	Y	None	Resolved
Trial Number=3475-006, Site Number=0601, Subject ID=366173, Gender=F, Race=White, Age=63 Years, Rel Day of Study Medication Discontinuance†=										
366173	Treatment Cycle 2	39	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=0605, Subject ID=366008, Gender=F, Race=White, Age=74 Years, Rel Day of Study Medication Discontinuance†=100										
366008	Treatment Cycle 8	100	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=0605, Subject ID=366351, Gender=F, Race=White, Age=46 Years, Rel Day of Study Medication Discontinuance†=365										
366351	Treatment Cycle 5	58	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=0612, Subject ID=365175, Gender=M, Race=White, Age=72 Years, Rel Day of Study Medication Discontinuance†=										
365175	Treatment Cycle 25	355	Hypothyroidism	2.43 Months		1	N	Y	None	Resolved
Trial Number=3475-006, Site Number=0700, Subject ID=363097, Gender=F, Race=White, Age=71 Years, Rel Day of Study Medication Discontinuance†=										
363097	Treatment Cycle 5	70	Hypothyroidism	3.25 Months		2	N	Y	None	Resolved
Trial Number=3475-006, Site Number=0704, Subject ID=360742, Gender=F, Race=White, Age=83 Years, Rel Day of Study Medication Discontinuance†=154										
360742	Treatment Cycle 4	42	Hypothyroidism	Continuing		2	N	Y	Interrupted	Not Resolved
Trial Number=3475-006, Site Number=0706, Subject ID=369101, Gender=M, Race=White, Age=44 Years, Rel Day of Study Medication Discontinuance†=										

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Listing of Subjects With Adverse Events
AEOSI- Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=0706, Subject ID=369101, Gender=M, Race=White, Age=44 Years, Rel Day of Study Medication Discontinuance†=										
369101	Treatment Cycle 9	140	Hypothyroidism	2.14 Weeks		1	N	N	None	Resolved
Trial Number=3475-006, Site Number=0900, Subject ID=361895, Gender=F, Race=White, Age=37 Years, Rel Day of Study Medication Discontinuance†=										
361895	Treatment Cycle 11	142	Hypothyroidism	3.86 Weeks		1	N	Y	None	Resolved
Trial Number=3475-006, Site Number=0902, Subject ID=364274, Gender=M, Race=White, Age=34 Years, Rel Day of Study Medication Discontinuance†=										
364274	Treatment Cycle 16	211	Hypothyroidism	Continuing		1	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=0902, Subject ID=369337, Gender=M, Race=White, Age=56 Years, Rel Day of Study Medication Discontinuance†=										
369337	Treatment Cycle 7	96	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=1301, Subject ID=368724, Gender=M, Race=White, Age=73 Years, Rel Day of Study Medication Discontinuance†=204										
368724	Treatment Cycle 6	71	Hypothyroidism	Continuing		2	N	Y	None	Resolving
Trial Number=3475-006, Site Number=1502, Subject ID=361180, Gender=M, Race=White, Age=76 Years, Rel Day of Study Medication Discontinuance†=436										
361180	Treatment Cycle 31	435	Hypothyroidism	Continuing		1	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=1502, Subject ID=361305, Gender=F, Race=White, Age=62 Years, Rel Day of Study Medication Discontinuance†=100										
361305	Safety Follow-up	114	Hypothyroidism	Continuing		1	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=1504, Subject ID=366969, Gender=M, Race=White, Age=71 Years, Rel Day of Study Medication Discontinuance†=										

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Listing of Subjects With Adverse Events
AEOSI- Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=1504, Subject ID=366969, Gender=M, Race=White, Age=71 Years, Rel Day of Study Medication Discontinuance†=										
366969	Treatment Cycle 16	224	Hypothyroidism	2.14 Weeks		1	N	N	None	Resolved
Trial Number=3475-006, Site Number=1600, Subject ID=361918, Gender=F, Race=White, Age=58 Years, Rel Day of Study Medication Discontinuance†=										
361918	Treatment Cycle 7	96	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=1708, Subject ID=363322, Gender=M, Race=White, Age=52 Years, Rel Day of Study Medication Discontinuance†=281										
363322	Treatment Cycle 6	70	Hypothyroidism	1.87 Months		1	N	Y	None	Resolved
Trial Number=3475-006, Site Number=1808, Subject ID=366961, Gender=F, Race=White, Age=79 Years, Rel Day of Study Medication Discontinuance†=141										
366961	Treatment Cycle 6	72	Hypothyroidism	Continuing		1	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=1818, Subject ID=367651, Gender=M, Race=White, Age=75 Years, Rel Day of Study Medication Discontinuance†=309										
367651	Treatment Cycle 8	99	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=1819, Subject ID=365965, Gender=M, Race=White, Age=40 Years, Rel Day of Study Medication Discontinuance†=										
365965	Treatment Cycle 10	127	Hypothyroidism	8.31 Months		2	N	Y	None	Resolved
Trial Number=3475-006, Site Number=1819, Subject ID=367668, Gender=M, Race=White, Age=47 Years, Rel Day of Study Medication Discontinuance†=85										
367668	Treatment Cycle 4	43	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=1823, Subject ID=360915, Gender=M, Race=White, Age=60 Years, Rel Day of Study Medication Discontinuance†=146										

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Listing of Subjects With Adverse Events
AEOSI- Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=1823, Subject ID=360915, Gender=M, Race=White, Age=60 Years, Rel Day of Study Medication Discontinuance†=146										
360915	Treatment Cycle 6	69	Hypothyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=1901, Subject ID=365696, Gender=M, Race=White, Age=65 Years, Rel Day of Study Medication Discontinuance†=71										
365696	Treatment Cycle 4	43	Hypothyroidism	Continuing		1	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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Listing of Concomitant Systemic Corticosteroid Use for AEOSI - Hypothyroidism Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=0021, Subject ID=000484, Gender=F, Race=White, Age=67 Years, Rel Day of Study Medication Discontinuance[‡]=106											
000484	86	.	Hydrocortisone	30	QD	Oral Administration	7.50	Hypothyroidism	44	.	2
	75	4	Prednisone	60	QD	Oral Administration	60.00	Hypothyroidism	44	.	2
Trial Number=3475-001, Site Number=0073, Subject ID=001578, Gender=F, Race=Asian, Age=76 Years, Rel Day of Study Medication Discontinuance[‡]=											

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Listing of Concomitant Systemic Corticosteroid Use for AEOSI - Hypothyroidism Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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
001578	106	1	Hydrocortisone	10	QD	Oral Administration	2.50	Hypothyroidism	106	.	2
	107	.	Hydrocortisone	30	QD	Oral Administration	7.50	Hypothyroidism	106	.	2
Trial Number=3475-002, Site Number=0080, Subject ID=100022, Gender=M, Race=White, Age=45 Years, Rel Day of Study Medication Discontinuance‡=											
100022	156	94	Hydrocortisone	30	QD	Oral	7.50	Hypothyroidism	126	187	2
	156	94	Hydrocortisone	30	QD	Oral	7.50	Hypothyroidism	126	187	2

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Listing of Concomitant Systemic Corticosteroid Use for AEOSI - Hypothyroidism Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=0700, Subject ID=363097, Gender=F, Race=White, Age=71 Years, Rel Day of Study Medication Discontinuance[‡]=											
363097	71	1	Hydrocortisone	100	ONCE	Intravenous	25.00	Hypothyroidism	70	168	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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Subjects With Adverse Events by Outcome
(Incidence > 0% in One or More Treatment Groups)
AEOSI- Hypothyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

		P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	Outcome	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population		682		1,232		1,567		2,799	
With one or more adverse events	Overall	56	(8.2)	98	(8.0)	139	(8.9)	237	(8.5)
	Fatal	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
	Not Resolved	35	(5.1)	69	(5.6)	107	(6.8)	176	(6.3)
	Resolved	10	(1.5)	18	(1.5)	28	(1.8)	46	(1.6)
	Resolving	4	(0.6)	4	(0.3)	2	(0.1)	6	(0.2)
	Sequelae	2	(0.3)	2	(0.2)	0	(0.0)	2	(0.1)
	Unknown	5	(0.7)	5	(0.4)	2	(0.1)	7	(0.3)

Outcome: Resolved = RECOVERED/RESOLVED, Not resolved = NOT RECOVERED/NOT RESOLVED.
Every subject is counted once for the AE outcome, with the order: Fatal>Not Resolved>Resolving>Unknown>Sequelae>Resolved.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Adverse Event Summary
AEOSI - Hyperthyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1,232		1,567		2,799	
with one or more adverse events	32	(4.7)	43	(3.5)	53	(3.4)	96	(3.4)
with no adverse event	650	(95.3)	1,189	(96.5)	1,514	(96.6)	2,703	(96.6)
with drug-related† adverse events	25	(3.7)	35	(2.8)	47	(3.0)	82	(2.9)
with Grade 3- 5 adverse events	1	(0.1)	2	(0.2)	2	(0.1)	4	(0.1)
with Grade 3- 5 drug-related adverse events	1	(0.1)	2	(0.2)	2	(0.1)	4	(0.1)
with serious adverse events	2	(0.3)	3	(0.2)	3	(0.2)	6	(0.2)
with serious drug-related adverse events	2	(0.3)	3	(0.2)	3	(0.2)	6	(0.2)
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)	2	(0.1)	2	(0.1)
discontinued due to a drug-related adverse event	0	(0.0)	0	(0.0)	2	(0.1)	2	(0.1)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	2	(0.1)	2	(0.1)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	2	(0.1)	2	(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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of AEOSI - Hyperthyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1232		1567		2799	
Subjects with Hyperthyroidism	32	(4.7)	43	(3.5)	53	(3.4)	96	(3.4)
Time to Onset of First Hyperthyroidism (days)†								
Mean (Std)	55.9 (40.9)		59.8 (59.5)		78.2 (105.5)		69.9 (88.0)	
Median	43.5		44.0		44.0		44.0	
Range	17 to 209		2 to 356		1 to 665		1 to 665	
Total episodes of Hyperthyroidism	32		44		61		105	
Average Episodes per subject	1.00		1.02		1.15		1.09	
Episode duration (days)‡								

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Summary of AEOSI - Hyperthyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Median	64.0		78.0		62.0		64.0	
Range	14 to 456+		14 to 456+		3 to 447+		3 to 456+	

(%) = Number of subjects with Hyperthyroidism / Number of subjects in population.
† Time to onset statistics are based on number of subjects with Hyperthyroidism.
‡ From product-limit (Kaplan-Meier) method for censored data. 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.
+ indicates the AE episode is not recovered/resolved by the time of the cutoff date or date of death.
Std = Standard Deviation.
Grades are based on NCI CTCAE version 4.0.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted].
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted].
(MK-3475 PN002 Database Cutoff Date: [redacted].
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Subjects With Adverse Events by Maximum Toxicity Grade
(Incidence >0% in One or More Treatment Groups)
AEOSI- Hyperthyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1,232		1,567		2,799	
with one or more adverse events	32	(4.7)	43	(3.5)	53	(3.4)	96	(3.4)
Grade 1	22	(3.2)	28	(2.3)	42	(2.7)	70	(2.5)
Grade 2	9	(1.3)	13	(1.1)	9	(0.6)	22	(0.8)
Grade 3	1	(0.1)	2	(0.2)	2	(0.1)	4	(0.1)
with no adverse events	650	(95.3)	1,189	(96.5)	1,514	(96.6)	2,703	(96.6)
Endocrine disorders	**32**	**(4.7)**	**43**	**(3.5)**	**53**	**(3.4)**	**96**	**(3.4)**
Grade 1	22	(3.2)	28	(2.3)	42	(2.7)	70	(2.5)
Grade 2	9	(1.3)	13	(1.1)	9	(0.6)	22	(0.8)
Grade 3	1	(0.1)	2	(0.2)	2	(0.1)	4	(0.1)
Hyperthyroidism	32	(4.7)	43	(3.5)	53	(3.4)	96	(3.4)
Grade 1	22	(3.2)	28	(2.3)	42	(2.7)	70	(2.5)
Grade 2	9	(1.3)	13	(1.1)	9	(0.6)	22	(0.8)

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Subjects With Adverse Events by Maximum Toxicity Grade
(Incidence >0% in One or More Treatment Groups)
AEOSI- Hyperthyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Hyperthyroidism	32	(4.7)	43	(3.5)	53	(3.4)	96	(3.4)
Grade 3	1	(0.1)	2	(0.2)	2	(0.1)	4	(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 for MEL: [redacted].

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

(MK-3475 PN002 Database Cutoff Date: [redacted]).

(MK-3475 PN006 Database Cutoff Date: 03MAR2015).

(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of Concomitant Corticosteroid Use for AEOSI - Hyperthyroidism PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475 (APaT Population)

	P010 (N=682)		PN001 Lung, PN010 (N=1232)		PN001 Mel, PN002, PN006 (N=1567)		PN001,PN002, PN006, PN010 (N=2799)	
	n	%	n	%	n	%	n	%
Subjects with one or more Hyperthyroidism	32		43		53		96	
Treated with systemic corticosteroid	1	3.1	1	2.3	2	3.8	3	3.1
High starting dose[†]	1	3.1	1	2.3	2	3.8	3	3.1
Low starting dose[‡]	0	0	0	0	0	0	0	0
Not treated with systemic corticosteroid	31	96.9	42	97.7	51	96.2	93	96.9

The number of Subjects with one or more Hyperthyroidism is used as the denominator for the percentage calculation.
[†] 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.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of Concomitant Corticosteroid Use for AEOSI - Hyperthyroidism Episodes PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475 (APaT Population)

	P010	PN001 Lung, PN010	PN001 Mel, PN002, PN006	PN001,PN002, PN006, PN010
Total Episodes	32	44	61	105
High Starting Dose (%) †	**1 (3.1)**	**1 (2.3)**	**2 (3.3)**	**3 (2.9)**
Starting dose (mg/day)				
Mean (Std)	40 (.)	40 (.)	75 (0)	63 (20)
Median (Range)	40 (40-40)	40 (40-40)	75 (75-75)	75 (40-75)
Duration (days)§				
Mean (Std)	41 (.)	41 (.)	5 (4)	17 (21)
Median (Range)	41 (41-41)	41 (41-41)	5 (2-8)	8 (2-41)
Low Starting Dose (%) ‡	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**
Not Treated with Systemic Corticosteroid (%)	**31 (96.9)**	**43 (97.7)**	**59 (96.7)**	**102 (97.1)**

† 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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Listing of Subjects With Adverse Events
AEOSI- Hyperthyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=0012, Subject ID=000389, Gender=F, Race=White, Age=68 Years, Rel Day of Study Medication Discontinuance†=22										
000389	Safety Follow-up	40	Hyperthyroidism	6.08 Months	Moderate	2	Y	Y	Discontinued	Resolved
Trial Number=3475-001, Site Number=0021, Subject ID=000542, Gender=M, Race=White, Age=74 Years, Rel Day of Study Medication Discontinuance†=515										
000542	Treatment Cycle 3	43	Hyperthyroidism	2.76 Months	Mild	1		Y	N/A	Resolved
Trial Number=3475-002, Site Number=0010, Subject ID=100334, Gender=F, Race=White, Age=33 Years, Rel Day of Study Medication Discontinuance†=127										
100334	Treatment Cycle 1	22	Hyperthyroidism	2.83 Months		1	N	Y	None	Resolved
Trial Number=3475-002, Site Number=0033, Subject ID=100325, Gender=F, Race=White, Age=49 Years, Rel Day of Study Medication Discontinuance†=415										
100325	Treatment Cycle 2	43	Hyperthyroidism	2.1 Months		1	N	Y	None	Resolved
Trial Number=3475-002, Site Number=0088, Subject ID=101506, Gender=M, Race=White, Age=57 Years, Rel Day of Study Medication Discontinuance†=126										
101506	Treatment Cycle 1 Treatment Cycle 5 Treatment Cycle 6	1 81 104	Hyperthyroidism Hyperthyroidism Hyperthyroidism	3.86 Weeks 1.43 Weeks 1.68 Months		1 1 1	N N N	N Y Y	None None None	Resolved Resolved Resolved
Trial Number=3475-002, Site Number=0140, Subject ID=100109, Gender=M, Race=White, Age=33 Years, Rel Day of Study Medication Discontinuance†=232										
100109	Treatment Cycle 6	106	Hyperthyroidism	Continuing		1	N	Y	None	Not Resolved
Trial Number=3475-002, Site Number=0150, Subject ID=101223, Gender=F, Race=White, Age=84 Years, Rel Day of Study Medication Discontinuance†=435										
101223	Treatment Cycle 12	253	Hyperthyroidism	Unknown		1	N	Y	None	Unknown

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Listing of Subjects With Adverse Events
AEOSI- Hyperthyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=0151, Subject ID=100007, Gender=M, Race=White, Age=65 Years, Rel Day of Study Medication Discontinuance†=737										
100007	Treatment Cycle 2	25	Hyperthyroidism	5.91 Months		2	N	Y	None	Resolved
	Treatment Cycle 18	492	Hyperthyroidism	3 Weeks		1	N	Y	None	Resolved
	Treatment Cycle 20	534	Hyperthyroidism	Continuing		1	N	Y	None	Not Resolved
Trial Number=3475-002, Site Number=0151, Subject ID=100088, Gender=M, Race=White, Age=55 Years, Rel Day of Study Medication Discontinuance†=										
100088	Treatment Cycle 5	88	Hyperthyroidism	1.35 Months		1	N	Y	None	Resolved
	Treatment Cycle 12	234	Hyperthyroidism	2.83 Months		1	N	Y	None	Resolved
Trial Number=3475-010, Site Number=0006, Subject ID=312285, Gender=F, Race=White, Age=52 Years, Rel Day of Study Medication Discontinuance†=134										
312285	Treatment Cycle 3	43	Hyperthyroidism	Continuing		1	N	Y	None	Not Resolved
Trial Number=3475-010, Site Number=0006, Subject ID=314200, Gender=M, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance†=107										
314200	Treatment Cycle 3	44	Hyperthyroidism	1.41 Months		1	N	N	None	Resolved
Trial Number=3475-010, Site Number=0028, Subject ID=310007, Gender=M, Race=Black Or African American, Age=75 Years, Rel Day of Study Medication Discontinuance†=										
310007	Treatment Cycle 3	64	Hyperthyroidism	1.18 Months		2	N	Y	Interrupted	Resolved
Trial Number=3475-010, Site Number=0050, Subject ID=300004, Gender=F, Race=White, Age=55 Years, Rel Day of Study Medication Discontinuance†=										
300004	Treatment Cycle 4	64	Hyperthyroidism	1.38 Months		1	N	Y	None	Resolved
Trial Number=3475-010, Site Number=0094, Subject ID=307713, Gender=F, Race=White, Age=39 Years, Rel Day of Study Medication Discontinuance†=										

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Listing of Subjects With Adverse Events
AEOSI- Hyperthyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=3475-010, Site Number=0094, Subject ID=307713, Gender=F, Race=White, Age=39 Years, Rel Day of Study Medication Discontinuance†=										
307713	Treatment Cycle 2	42	Hyperthyroidism	8.54 Months		1	N	Y	None	Resolved
Trial Number=3475-010, Site Number=0162, Subject ID=305766, Gender=M, Race=White, Age=72 Years, Rel Day of Study Medication Discontinuance†=169										
305766	Treatment Cycle 7	147	Hyperthyroidism	1.41 Months		1	N	N	None	Resolved
Trial Number=3475-010, Site Number=0205, Subject ID=301281, Gender=M, Race=White, Age=52 Years, Rel Day of Study Medication Discontinuance†=360										
301281	Treatment Cycle 6	106	Hyperthyroidism	1.38 Months		1	N	Y	None	Resolved
Trial Number=3475-010, Site Number=1245, Subject ID=301979, Gender=M, Race=Asian, Age=71 Years, Rel Day of Study Medication Discontinuance†=										
301979	Treatment Cycle 6	106	Hyperthyroidism	2.79 Months		2	N	Y	None	Resolved
Trial Number=3475-010, Site Number=1245, Subject ID=308648, Gender=M, Race=Asian, Age=53 Years, Rel Day of Study Medication Discontinuance†=147										
308648	Treatment Cycle 2	22	Hyperthyroidism	1.41 Months		1	N	Y	None	Resolved
Trial Number=3475-010, Site Number=1322, Subject ID=312348, Gender=M, Race=Asian, Age=57 Years, Rel Day of Study Medication Discontinuance†=230										
312348	Treatment Cycle 5	103	Hyperthyroidism	4.21 Months		1	N	Y	None	Resolved
Trial Number=3475-010, Site Number=1420, Subject ID=302578, Gender=F, Race=Asian, Age=48 Years, Rel Day of Study Medication Discontinuance†=90										
302578	Treatment Cycle 2	43	Hyperthyroidism	2.3 Months		1	N	Y	None	Resolved
Trial Number=3475-010, Site Number=1428, Subject ID=307204, Gender=F, Race=Asian, Age=78 Years, Rel Day of Study Medication Discontinuance†=										

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Listing of Subjects With Adverse Events
AEOSI- Hyperthyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=3475-010, Site Number=1428, Subject ID=307204, Gender=F, Race=Asian, Age=78 Years, Rel Day of Study Medication Discontinuance†=										
307204	Treatment Cycle 1	21	Hyperthyroidism	1.41 Months		1	N	Y	None	Resolved
MK-3475 10 mg/kg Q3W										
Trial Number=3475-001, Site Number=0010, Subject ID=001073, Gender=F, Race=White, Age=49 Years, Rel Day of Study Medication Discontinuance†=210										
001073	Treatment Cycle 3	63	Hyperthyroidism	1.41 Months	Mild	1		Y	N/A	Resolved
Trial Number=3475-001, Site Number=0011, Subject ID=001396, Gender=F, Race=White, Age=71 Years, Rel Day of Study Medication Discontinuance†=										
001396	Treatment Cycle 2	22	Hyperthyroidism	1.38 Months	Mild	1		Y	N/A	Resolved
Trial Number=3475-001, Site Number=0015, Subject ID=000905, Gender=F, Race=White, Age=69 Years, Rel Day of Study Medication Discontinuance†=189										
000905	Treatment Cycle 1	2	Hyperthyroidism	Continuing	Mild	1		N	N/A	Not Resolved
Trial Number=3475-001, Site Number=0016, Subject ID=000327, Gender=F, Race=White, Age=48 Years, Rel Day of Study Medication Discontinuance†=358										
000327	Treatment Cycle 4	64	Hyperthyroidism	4.11 Months	Mild	1		Y	N/A	Resolved
Trial Number=3475-001, Site Number=0019, Subject ID=001108, Gender=F, Race=White, Age=75 Years, Rel Day of Study Medication Discontinuance†=85										
001108	Treatment Cycle 2	22	Hyperthyroidism	Continuing	Mild	1		Y		Not Resolved
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 1	15	Hyperthyroidism	1.41 Months	Moderate	2		Y		Resolved

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Listing of Subjects With Adverse Events
AEOSI- Hyperthyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q3W										
Trial Number=3475-001, Site Number=0020, Subject ID=001350, Gender=M, Race=White, Age=44 Years, Rel Day of Study Medication Discontinuance†=85										
001350	Treatment Cycle 3	43	Hyperthyroidism	1.41 Months	Mild	1		Y	N/A	Resolved
Trial Number=3475-001, Site Number=0021, Subject ID=001405, Gender=M, Race=White, Age=57 Years, Rel Day of Study Medication Discontinuance†=										
001405	Treatment Cycle 5	84	Hyperthyroidism	Continuing	Mild	1		Y	N/A	Not Resolved
Trial Number=3475-001, Site Number=0021, Subject ID=001408, Gender=M, Race=White, Age=38 Years, Rel Day of Study Medication Discontinuance†=										
001408	Treatment Cycle 3	43	Hyperthyroidism	2.76 Months	Mild	1		Y	N/A	Resolved
Trial Number=3475-001, Site Number=0021, Subject ID=001412, Gender=M, Race=White, Age=57 Years, Rel Day of Study Medication Discontinuance†=										
001412	Treatment Cycle 2	37	Hyperthyroidism	4 Weeks	Severe	3	Y	Y	Interrupted	Resolved
Trial Number=3475-001, Site Number=0023, Subject ID=000161, Gender=M, Race=White, Age=67 Years, Rel Day of Study Medication Discontinuance†=										
000161	Treatment Cycle 4	64	Hyperthyroidism	4.17 Months	Mild	1		Y	N/A	Resolved
Trial Number=3475-001, Site Number=0023, Subject ID=000953, Gender=F, Race=Asian, Age=52 Years, Rel Day of Study Medication Discontinuance†=64										
000953	Treatment Cycle 2	28	Hyperthyroidism	2 Days	Severe	3	Y	Y		Resolved
		30	Hyperthyroidism	1.81 Months	Moderate	2		Y		Resolved
Trial Number=3475-001, Site Number=0023, Subject ID=000955, Gender=F, Race=White, Age=68 Years, Rel Day of Study Medication Discontinuance†=341										
000955	Treatment Cycle 3	63	Hyperthyroidism	4.14 Months	Mild	1		Y	N/A	Resolved

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Listing of Subjects With Adverse Events
AEOSI- Hyperthyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=0070, Subject ID=001035, Gender=F, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=287										
001035	Treatment Cycle 3	84	Hyperthyroidism	Continuing	Mild	1		Y	N/A	Not Resolved
Trial Number=3475-002, Site Number=0033, Subject ID=100609, Gender=M, Race=White, Age=43 Years, Rel Day of Study Medication Discontinuance†=										
100609	Treatment Cycle 1	23	Hyperthyroidism	2.04 Months		1	N	N	N/A	Resolved
Trial Number=3475-002, Site Number=0070, Subject ID=100108, Gender=M, Race=White, Age=51 Years, Rel Day of Study Medication Discontinuance†=148										
100108	Treatment Cycle 3	64	Hyperthyroidism	1.41 Months		1	N	Y	None	Resolved
Trial Number=3475-006, Site Number=0003, Subject ID=361013, Gender=F, Race=White, Age=33 Years, Rel Day of Study Medication Discontinuance†=										
361013	Treatment Cycle 1	1	Hyperthyroidism	2.86 Months		1	N	Y	None	Resolved
Trial Number=3475-006, Site Number=0003, Subject ID=365319, Gender=M, Race=White, Age=81 Years, Rel Day of Study Medication Discontinuance†=										
365319	Treatment Cycle 3	43	Hyperthyroidism	Continuing		1	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=0301, Subject ID=364220, Gender=F, Race=White, Age=56 Years, Rel Day of Study Medication Discontinuance†=188										
364220	Treatment Cycle 3	41	Hyperthyroidism	Continuing		1	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=0601, Subject ID=362914, Gender=M, Race=White, Age=39 Years, Rel Day of Study Medication Discontinuance†=										
362914	Treatment Cycle 11	225	Hyperthyroidism	1.41 Months		1	N	N	None	Resolved
Trial Number=3475-006, Site Number=0605, Subject ID=360080, Gender=M, Race=White, Age=61 Years, Rel Day of Study Medication Discontinuance†=274										

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Listing of Subjects With Adverse Events
AEOSI- Hyperthyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=0605, Subject ID=360080, Gender=M, Race=White, Age=61 Years, Rel Day of Study Medication Discontinuance†=274										
360080	Treatment Cycle 8	148	Hyperthyroidism	3.48 Months		2	N	Y	None	Resolved
Trial Number=3475-006, Site Number=0605, Subject ID=364113, Gender=F, Race=White, Age=52 Years, Rel Day of Study Medication Discontinuance†=										
364113	Treatment Cycle 3	44	Hyperthyroidism	Continuing		1	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=0612, Subject ID=361134, Gender=F, Race=White, Age=53 Years, Rel Day of Study Medication Discontinuance†=										
361134	Treatment Cycle 1	26	Hyperthyroidism	3.86 Weeks		2	N	Y	Interrupted	Resolved
Trial Number=3475-006, Site Number=0902, Subject ID=362669, Gender=M, Race=White, Age=62 Years, Rel Day of Study Medication Discontinuance†=127										
362669	Treatment Cycle 3	43	Hyperthyroidism	2.04 Months		1	N	Y	None	Resolved
Trial Number=3475-006, Site Number=1819, Subject ID=362629, Gender=M, Race=White, Age=62 Years, Rel Day of Study Medication Discontinuance†=										
362629	Treatment Cycle 16	315	Hyperthyroidism	1.45 Months		1	N	Y	None	Resolved
Trial Number=3475-006, Site Number=1820, Subject ID=367788, Gender=M, Race=White, Age=33 Years, Rel Day of Study Medication Discontinuance†=										
367788	Treatment Cycle 3	46	Hyperthyroidism	2.04 Months		2	N	N	None	Resolved
Trial Number=3475-006, Site Number=1900, Subject ID=362368, Gender=F, Race=White, Age=32 Years, Rel Day of Study Medication Discontinuance†=										
362368	Treatment Cycle 7	125	Hyperthyroidism	Unknown		1	N	Y	None	Unknown
Trial Number=3475-010, Site Number=0006, Subject ID=306565, Gender=M, Race=White, Age=54 Years, Rel Day of Study Medication Discontinuance†=107										

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Listing of Subjects With Adverse Events
AEOSI- Hyperthyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=3475-010, Site Number=0006, Subject ID=306565, Gender=M, Race=White, Age=54 Years, Rel Day of Study Medication Discontinuance†=107										
306565	Treatment Cycle 2	23	Hyperthyroidism	3.14 Weeks		1	N	Y	None	Resolved
Trial Number=3475-010, Site Number=0055, Subject ID=311446, Gender=F, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=										
311446	Treatment Cycle 3	44	Hyperthyroidism	2 Weeks		1	Y	Y	None	Resolved
Trial Number=3475-010, Site Number=0081, Subject ID=304345, Gender=M, Race=White, Age=57 Years, Rel Day of Study Medication Discontinuance†=										
304345	Treatment Cycle 1	17	Hyperthyroidism	3.65 Months		1	N	N	N/A	Resolved
Trial Number=3475-010, Site Number=0081, Subject ID=305939, Gender=M, Race=Asian, Age=57 Years, Rel Day of Study Medication Discontinuance†=471										
305939	Treatment Cycle 2	22	Hyperthyroidism	9.53 Months		2	N	N	None	Resolved
Trial Number=3475-010, Site Number=0092, Subject ID=307409, Gender=M, Race=White, Age=47 Years, Rel Day of Study Medication Discontinuance†=22										
307409	Safety Follow-up	40	Hyperthyroidism	3.86 Weeks		3	Y	Y	N/A	Resolved
Trial Number=3475-010, Site Number=0096, Subject ID=313712, Gender=M, Race=White, Age=61 Years, Rel Day of Study Medication Discontinuance†=253										
313712	Treatment Cycle 10	209	Hyperthyroidism	1.45 Months		1	N	Y	None	Resolved
Trial Number=3475-010, Site Number=0122, Subject ID=307816, Gender=F, Race=White, Age=74 Years, Rel Day of Study Medication Discontinuance†=106										
307816	Treatment Cycle 4	64	Hyperthyroidism	3.14 Weeks		2	N	N	None	Resolved
Trial Number=3475-010, Site Number=0136, Subject ID=301907, Gender=M, Race=White, Age=52 Years, Rel Day of Study Medication Discontinuance†=64										

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Listing of Subjects With Adverse Events
AEOSI- Hyperthyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=3475-010, Site Number=0136, Subject ID=301907, Gender=M, Race=White, Age=52 Years, Rel Day of Study Medication Discontinuance†=64										
301907	Treatment Cycle 3	43	Hyperthyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-010, Site Number=0136, Subject ID=305862, Gender=M, Race=White, Age=44 Years, Rel Day of Study Medication Discontinuance†=237										
305862	Treatment Cycle 3	56	Hyperthyroidism	Continuing		1	N	Y	None	Not Resolved
Trial Number=3475-010, Site Number=0137, Subject ID=313391, Gender=F, Race=White, Age=75 Years, Rel Day of Study Medication Discontinuance†=										
313391	Treatment Cycle 3	57	Hyperthyroidism	1.64 Months		1	N	Y	None	Resolved
Trial Number=3475-010, Site Number=0138, Subject ID=305038, Gender=M, Race=White, Age=62 Years, Rel Day of Study Medication Discontinuance†=106										
305038	Treatment Cycle 3	44	Hyperthyroidism	1.38 Months		1	N	Y	None	Resolved
Trial Number=3475-010, Site Number=0183, Subject ID=301027, Gender=M, Race=White, Age=64 Years, Rel Day of Study Medication Discontinuance†=										
301027	Treatment Cycle 2	41	Hyperthyroidism	2.6 Months		2	N	Y	None	Resolved
Trial Number=3475-010, Site Number=0200, Subject ID=308329, Gender=M, Race=White, Age=79 Years, Rel Day of Study Medication Discontinuance†=469										
308329	Treatment Cycle 2	22	Hyperthyroidism	2.1 Months		1	N	Y	Interrupted	Resolved
Trial Number=3475-010, Site Number=0201, Subject ID=306439, Gender=M, Race=White, Age=53 Years, Rel Day of Study Medication Discontinuance†=43										
306439	Treatment Cycle 2	42	Hyperthyroidism	Continuing		1	N	Y	None	Not Resolved
Trial Number=3475-010, Site Number=0282, Subject ID=306612, Gender=M, Race=White, Age=60 Years, Rel Day of Study Medication Discontinuance†=										

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Listing of Subjects With Adverse Events
AEOSI- Hyperthyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=3475-010, Site Number=0282, Subject ID=306612, Gender=M, Race=White, Age=60 Years, Rel Day of Study Medication Discontinuance†=										
306612	Treatment Cycle 4	66	Hyperthyroidism	2.56 Months		2	N	N	None	Resolved
Trial Number=3475-010, Site Number=0443, Subject ID=301469, Gender=F, Race=White, Age=61 Years, Rel Day of Study Medication Discontinuance†=										
301469	Treatment Cycle 4	63	Hyperthyroidism	2.1 Months		2	N	Y	None	Resolved
Trial Number=3475-010, Site Number=0452, Subject ID=309774, Gender=M, Race=White, Age=63 Years, Rel Day of Study Medication Discontinuance†=170										
309774	Treatment Cycle 2	27	Hyperthyroidism	1.41 Months		1	N	N	None	Resolved
Trial Number=3475-010, Site Number=0452, Subject ID=313980, Gender=F, Race=White, Age=56 Years, Rel Day of Study Medication Discontinuance†=20										
313980	Treatment Cycle 1	19	Hyperthyroidism	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-010, Site Number=1080, Subject ID=300935, Gender=M, Race=White, Age=57 Years, Rel Day of Study Medication Discontinuance†=										
300935	Treatment Cycle 3	62	Hyperthyroidism	Continuing		1	N	Y	None	Not Resolved
Trial Number=3475-010, Site Number=1243, Subject ID=313473, Gender=F, Race=Asian, Age=55 Years, Rel Day of Study Medication Discontinuance†=										
313473	Treatment Cycle 2	22	Hyperthyroidism	4.37 Months		1	N	Y	Interrupted	Resolved
MK-3475 10 mg/kg Q2W										
Trial Number=3475-001, Site Number=0010, Subject ID=000031, Gender=M, Race=White, Age=77 Years, Rel Day of Study Medication Discontinuance†=										
000031	Treatment Cycle 46	665	Hyperthyroidism	Continuing	Mild	1		N	N/A	Not Resolved

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Listing of Subjects With Adverse Events
AEOSI- Hyperthyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q2W										
Trial Number=3475-001, Site Number=0010, Subject ID=000031, Gender=M, Race=White, Age=77 Years, Rel Day of Study Medication Discontinuance†=										
000031	Treatment Cycle 59	835	Hyperthyroidism	Continuing	Mild	1		N	N/A	Not 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 16	239	Hyperthyroidism	3.42 Months	Mild	1		Y	N/A	Resolved
	Treatment Cycle 23	343	Hyperthyroidism	2.56 Months	Moderate	2		Y	Interrupted	Resolved
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	Safety Follow-up	51	Hyperthyroidism	4.14 Weeks	Severe	3	Y	Y	Discontinued	Resolved
Trial Number=3475-001, Site Number=0013, Subject ID=001134, Gender=F, Race=White, Age=52 Years, Rel Day of Study Medication Discontinuance†=										
001134	Treatment Cycle 24	356	Hyperthyroidism	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0015, Subject ID=000946, Gender=M, Race=White, Age=54 Years, Rel Day of Study Medication Discontinuance†=										
000946	Treatment Cycle 3	29	Hyperthyroidism	4.93 Months	Moderate	2		Y		Resolved
Trial Number=3475-001, Site Number=0019, Subject ID=001247, Gender=M, Race=White, Age=61 Years, Rel Day of Study Medication Discontinuance†=337										
001247	Treatment Cycle 1	6	Hyperthyroidism	2.83 Months	Mild	1		N	N/A	Resolved
Trial Number=3475-001, Site Number=0020, Subject ID=001390, Gender=F, Race=White, Age=48 Years, Rel Day of Study Medication Discontinuance†=85										
001390	Treatment Cycle 5	57	Hyperthyroidism	1.77 Months	Mild	1		Y		Resolved

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Listing of Subjects With Adverse Events
AEOSI- Hyperthyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=0020, Subject ID=001404, Gender=F, Race=White, Age=42 Years, Rel Day of Study Medication Discontinuance†=71										
001404	Treatment Cycle 2	15	Hyperthyroidism	4.14 Weeks	Mild	1		Y	N/A	Resolved
Trial Number=3475-001, Site Number=0036, Subject ID=001116, Gender=M, Race=White, Age=56 Years, Rel Day of Study Medication Discontinuance†=										
001116	Treatment Cycle 4	44	Hyperthyroidism	4 Weeks	Moderate	2		Y		Resolved
	Treatment Cycle 23	310	Hyperthyroidism	Continuing	Mild	1		Y	N/A	Not Resolved
Trial Number=3475-001, Site Number=0040, Subject ID=001107, Gender=M, Race=White, Age=41 Years, Rel Day of Study Medication Discontinuance†=181										
001107	Treatment Cycle 3	27	Hyperthyroidism	2 Weeks	Mild	1		Y	N/A	Resolved
	Treatment Cycle 4	41	Hyperthyroidism	1.38 Months	Moderate	2		Y		Resolved
	Treatment Cycle 7	83	Hyperthyroidism	4 Weeks	Mild	1		Y		Resolved
Trial Number=3475-006, Site Number=0003, Subject ID=362014, Gender=M, Race=White, Age=78 Years, Rel Day of Study Medication Discontinuance†=										
362014	Treatment Cycle 2	28	Hyperthyroidism	1.84 Months		1	N	Y	None	Resolved
Trial Number=3475-006, Site Number=0300, Subject ID=369262, Gender=M, Race=White, Age=54 Years, Rel Day of Study Medication Discontinuance†=										
369262	Treatment Cycle 4	50	Hyperthyroidism	1.84 Months		2	N	Y	None	Resolved
Trial Number=3475-006, Site Number=0312, Subject ID=364603, Gender=M, Race=White, Age=47 Years, Rel Day of Study Medication Discontinuance†=										
364603	Treatment Cycle 14	183	Hyperthyroidism	Continuing		1	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=0601, Subject ID=366173, Gender=F, Race=White, Age=63 Years, Rel Day of Study Medication Discontinuance†=										

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Listing of Subjects With Adverse Events
AEOSI- Hyperthyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=0601, Subject ID=366173, Gender=F, Race=White, Age=63 Years, Rel Day of Study Medication Discontinuance†=										
366173	Treatment Cycle 2	24	Hyperthyroidism	2.29 Weeks		1	N	Y	None	Resolved
Trial Number=3475-006, Site Number=0605, Subject ID=360483, Gender=F, Race=White, Age=22 Years, Rel Day of Study Medication Discontinuance†=71										
360483	Treatment Cycle 5	57	Hyperthyroidism	Continuing		1	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=0605, Subject ID=366008, Gender=F, Race=White, Age=74 Years, Rel Day of Study Medication Discontinuance†=100										
366008	Treatment Cycle 5	57	Hyperthyroidism	1.41 Months		1	N	Y	None	Resolved
Trial Number=3475-006, Site Number=0605, Subject ID=366351, Gender=F, Race=White, Age=46 Years, Rel Day of Study Medication Discontinuance†=365										
366351	Treatment Cycle 3	29	Hyperthyroidism	4.14 Weeks		1	N	Y	None	Resolved
Trial Number=3475-006, Site Number=0605, Subject ID=367764, Gender=F, Race=White, Age=61 Years, Rel Day of Study Medication Discontinuance†=										
367764	Treatment Cycle 2	15	Hyperthyroidism	2.14 Weeks		1	N	Y	None	Resolved
Trial Number=3475-006, Site Number=0701, Subject ID=364182, Gender=M, Race=White, Age=78 Years, Rel Day of Study Medication Discontinuance†=										
364182	Treatment Cycle 2	15	Hyperthyroidism	4 Weeks		1	N	Y	None	Resolved
	Treatment Cycle 9	125	Hyperthyroidism	4.29 Weeks		1	N	Y	None	Resolved
	Treatment Cycle 15	209	Hyperthyroidism	Continuing		1	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=0900, Subject ID=361895, Gender=F, Race=White, Age=37 Years, Rel Day of Study Medication Discontinuance†=										
361895	Treatment Cycle 2	16	Hyperthyroidism	3.25 Months		1	N	Y	None	Resolved

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Listing of Subjects With Adverse Events
AEOSI- Hyperthyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=0902, Subject ID=369337, Gender=M, Race=White, Age=56 Years, Rel Day of Study Medication Discontinuance†=										
369337	Treatment Cycle 3	44	Hyperthyroidism	3.43 Weeks		1	N	Y	Interrupted	Resolved
Trial Number=3475-006, Site Number=1300, Subject ID=360246, Gender=M, Race=White, Age=18 Years, Rel Day of Study Medication Discontinuance†=										
360246	Treatment Cycle 6	85	Hyperthyroidism	1.41 Months		1	N	N	None	Resolved
Trial Number=3475-006, Site Number=1600, Subject ID=361918, Gender=F, Race=White, Age=58 Years, Rel Day of Study Medication Discontinuance†=										
361918	Treatment Cycle 5	68	Hyperthyroidism	2.14 Weeks		1	N	Y	None	Resolved
Trial Number=3475-006, Site Number=1603, Subject ID=369113, Gender=M, Race=White, Age=56 Years, Rel Day of Study Medication Discontinuance†=										
369113	Treatment Cycle 8	99	Hyperthyroidism	Continuing		1	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=1708, Subject ID=363322, Gender=M, Race=White, Age=52 Years, Rel Day of Study Medication Discontinuance†=281										
363322	Treatment Cycle 3	29	Hyperthyroidism	1.38 Months		2	N	Y	None	Resolved
Trial Number=3475-006, Site Number=1804, Subject ID=368450, Gender=M, Race=, Age=38 Years, Rel Day of Study Medication Discontinuance†=149										
368450	Treatment Cycle 6	71	Hyperthyroidism	6.01 Months		1	N	Y	None	Resolved
Trial Number=3475-006, Site Number=1807, Subject ID=366429, Gender=M, Race=White, Age=43 Years, Rel Day of Study Medication Discontinuance†=										
366429	Treatment Cycle 8	98	Hyperthyroidism	Continuing		1	N	Y	None	Not Resolved
Trial Number=3475-006, Site Number=1819, Subject ID=365965, Gender=M, Race=White, Age=40 Years, Rel Day of Study Medication Discontinuance†=										

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Listing of Subjects With Adverse Events
AEOSI- Hyperthyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=365965, Gender=M, Race=White, Age=40 Years, Rel Day of Study Medication Discontinuance[†]=										
365965	Treatment Cycle 6	71	Hyperthyroidism	1.87 Months		1	N	Y	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 for MEL: [redacted]).

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

(MK-3475 PN002 Database Cutoff Date: [redacted]).

(MK-3475 PN006 Database Cutoff Date: 03MAR2015).

(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Listing of Concomitant Systemic Corticosteroid Use for AEOSI - Hyperthyroidism Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=0021, Subject ID=000484, Gender=F, Race=White, Age=67 Years, Rel Day of Study Medication Discontinuance[‡]=106											
000484	86	.	Hydrocortisone	30	QD	Oral Administration	7.50	Hypothyroidism	44	.	2
	75	4	Prednisone	60	QD	Oral Administration	60.00	Hypothyroidism	44	.	2
Trial Number=3475-001, Site Number=0073, Subject ID=001578, Gender=F, Race=Asian, Age=76 Years, Rel Day of Study Medication Discontinuance[‡]=											

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Listing of Concomitant Systemic Corticosteroid Use for AEOSI - Hyperthyroidism Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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
001578	106	1	Hydrocortisone	10	QD	Oral Administration	2.50	Hypothyroidism	106	.	2
	107	.	Hydrocortisone	30	QD	Oral Administration	7.50	Hypothyroidism	106	.	2
Trial Number=3475-002, Site Number=0080, Subject ID=100022, Gender=M, Race=White, Age=45 Years, Rel Day of Study Medication Discontinuance‡=											
100022	156	94	Hydrocortisone	30	QD	Oral	7.50	Hypothyroidism	126	187	2
	156	94	Hydrocortisone	30	QD	Oral	7.50	Hypothyroidism	126	187	2

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Listing of Concomitant Systemic Corticosteroid Use for AEOSI - Hyperthyroidism Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=0700, Subject ID=363097, Gender=F, Race=White, Age=71 Years, Rel Day of Study Medication Discontinuance‡=											
363097	71	1	Hydrocortisone	100	ONCE	Intravenous	25.00	Hypothyroidism	70	168	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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Subjects With Adverse Events by Outcome
(Incidence > 0% in One or More Treatment Groups)
AEOSI- Hyperthyroidism
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

		P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	Outcome	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population		682		1,232		1,567		2,799	
With one or more adverse events	Overall	32	(4.7)	43	(3.5)	53	(3.4)	96	(3.4)
	Fatal	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
	Not Resolved	6	(0.9)	11	(0.9)	12	(0.8)	23	(0.8)
	Resolved	26	(3.8)	32	(2.6)	39	(2.5)	71	(2.5)
	Unknown	0	(0.0)	0	(0.0)	2	(0.1)	2	(0.1)

Outcome: Resolved = RECOVERED/RESOLVED, Not resolved = NOT RECOVERED/NOT RESOLVED.
Every subject is counted once for the AE outcome, with the order: Fatal>Not Resolved>Resolving>Unknown>Sequelae>Resolved.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Adverse Event Summary
AEOSI - Thyroiditis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1,232		1,567		2,799	
with one or more adverse events	3	(0.4)	3	(0.2)	13	(0.8)	16	(0.6)
with no adverse event	679	(99.6)	1,229	(99.8)	1,554	(99.2)	2,783	(99.4)
with drug-related† adverse events	3	(0.4)	3	(0.2)	13	(0.8)	16	(0.6)
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)	1	(0.1)	1	(0.0)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	1	(0.1)	1	(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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of AEOSI - Thyroiditis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1232		1567		2799	
Subjects with Thyroiditis	3	(0.4)	3	(0.2)	13	(0.8)	16	(0.6)
Time to Onset of First Thyroiditis (days)†								
Mean (Std)	56.3 (42.6)		56.3 (42.6)		45.3 (28.8)		47.4 (30.4)	
Median	43.0		43.0		29.0		36.0	
Range	22 to 104		22 to 104		15 to 106		15 to 106	
Total episodes of Thyroiditis	3		3		13		16	
Average Episodes per subject	1.00		1.00		1.00		1.00	
Episode duration (days)‡								

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Summary of AEOSI - Thyroiditis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Median	65.0		65.0		Not reached		Not reached	
Range	50 to 549+		50 to 549+		43 to 580+		43 to 580+	

(%) = Number of subjects with Thyroiditis / Number of subjects in population.
† Time to onset statistics are based on number of subjects with Thyroiditis.
‡ From product-limit (Kaplan-Meier) method for censored data. 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.
+ indicates the AE episode is not recovered/resolved by the time of the cutoff date or date of death.
Std = Standard Deviation.
Grades are based on NCI CTCAE version 4.0.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Subjects With Adverse Events by Maximum Toxicity Grade
(Incidence >0% in One or More Treatment Groups)
AEOSI- Thyroiditis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1,232		1,567		2,799	
with one or more adverse events	3	(0.4)	3	(0.2)	13	(0.8)	16	(0.6)
Grade 1	3	(0.4)	3	(0.2)	6	(0.4)	9	(0.3)
Grade 2	0	(0.0)	0	(0.0)	7	(0.4)	7	(0.3)
with no adverse events	679	(99.6)	1,229	(99.8)	1,554	(99.2)	2,783	(99.4)
Endocrine disorders	**3**	**(0.4)**	**3**	**(0.2)**	**13**	**(0.8)**	**16**	**(0.6)**
Grade 1	3	(0.4)	3	(0.2)	6	(0.4)	9	(0.3)
Grade 2	0	(0.0)	0	(0.0)	7	(0.4)	7	(0.3)
Autoimmune thyroiditis	1	(0.1)	1	(0.1)	4	(0.3)	5	(0.2)
Grade 1	1	(0.1)	1	(0.1)	1	(0.1)	2	(0.1)
Grade 2	0	(0.0)	0	(0.0)	3	(0.2)	3	(0.1)
Thyroiditis	2	(0.3)	2	(0.2)	9	(0.6)	11	(0.4)
Grade 1	2	(0.3)	2	(0.2)	5	(0.3)	7	(0.3)

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Subjects With Adverse Events by Maximum Toxicity Grade
(Incidence >0% in One or More Treatment Groups)
AEOSI- Thyroiditis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Thyroiditis	2	(0.3)	2	(0.2)	9	(0.6)	11	(0.4)
Grade 2	0	(0.0)	0	(0.0)	4	(0.3)	4	(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 for MEL: [redacted]).

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

(MK-3475 PN002 Database Cutoff Date: [redacted]).

(MK-3475 PN006 Database Cutoff Date: 03MAR2015).

(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of Concomitant Corticosteroid Use for AEOSI - Thyroiditis PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475 (APaT Population)

	P010 (N=682)		PN001 Lung, PN010 (N=1232)		PN001 Mel, PN002, PN006 (N=1567)		PN001,PN002, PN006, PN010 (N=2799)	
	n	%	n	%	n	%	n	%
Subjects with one or more Thyroiditis	3		3		13		16	
Treated with systemic corticosteroid	0	0	0	0	0	0	0	0
High starting dose†	0	0	0	0	0	0	0	0
Low starting dose‡	0	0	0	0	0	0	0	0
Not treated with systemic corticosteroid	3	100.0	3	100.0	13	100.0	16	100.0

The number of Subjects with one or more Thyroiditis is used as the denominator for the percentage calculation.
† 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.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of Concomitant Corticosteroid Use for AEOSI - Thyroiditis Episodes
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010	PN001 Lung, PN010	PN001 Mel, PN002, PN006	PN001,PN002, PN006, PN010
Total Episodes	3	3	13	16
High Starting Dose (%) †	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**
Low Starting Dose (%) ‡	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**
Not Treated with Systemic Corticosteroid (%)	**3 (100.0)**	**3 (100.0)**	**13 (100.0)**	**16 (100.0)**

† 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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Listing of Subjects With Adverse Events
AEOSI- Thyroiditis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=000491, Gender=M, Race=White, Age=65 Years, Rel Day of Study Medication Discontinuance†=										
000491	Treatment Cycle 2	20	Thyroiditis	1.41 Months	Mild	1		Y	N/A	Resolved
Trial Number=3475-001, Site Number=0020, Subject ID=000547, Gender=M, Race=White, Age=49 Years, Rel Day of Study Medication Discontinuance†=										
000547	Treatment Cycle 2	29	Thyroiditis	1.87 Months	Mild	1		Y		Resolved
Trial Number=3475-001, Site Number=0021, Subject ID=000483, Gender=F, Race=White, Age=52 Years, Rel Day of Study Medication Discontinuance†=85										
000483	Treatment Cycle 4	64	Thyroiditis	Continuing	Moderate	2		Y	N/A	Not Resolved
Trial Number=3475-010, Site Number=0006, Subject ID=314200, Gender=M, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance†=107										
314200	Treatment Cycle 1	22	Thyroiditis	2.14 Months		1	N	Y	None	Resolved
Trial Number=3475-010, Site Number=0026, Subject ID=300750, Gender=M, Race=White, Age=59 Years, Rel Day of Study Medication Discontinuance†=										
300750	Treatment Cycle 6	104	Thyroiditis	1.64 Months		1	N	Y	None	Resolved
MK-3475 10 mg/kg Q3W										
Trial Number=3475-001, Site Number=0011, Subject ID=001368, Gender=F, Race=White, Age=44 Years, Rel Day of Study Medication Discontinuance†=194										
001368	Treatment Cycle 2 Treatment Cycle 3	20 46	Thyroiditis Thyroiditis	3.86 Weeks Continuing	Mild Moderate	1 2		Y Y	N/A	Resolved Not Resolved
Trial Number=3475-001, Site Number=0011, Subject ID=001396, Gender=F, Race=White, Age=71 Years, Rel Day of Study Medication Discontinuance†=										

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Listing of Subjects With Adverse Events
AEOSI- Thyroiditis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=001396, Gender=F, Race=White, Age=71 Years, Rel Day of Study Medication Discontinuance†=										
001396	Treatment Cycle 4	64	Autoimmune thyroiditis	3 Weeks	Moderate	2		Y	N/A	Resolved
	Treatment Cycle 5	85	Autoimmune thyroiditis	Continuing	Mild	1		Y		Not Resolved
Trial Number=3475-001, Site Number=0016, Subject ID=001422, Gender=M, Race=White, Age=87 Years, Rel Day of Study Medication Discontinuance†=87										
001422	Treatment Cycle 4	64	Autoimmune thyroiditis	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0021, Subject ID=001391, Gender=M, Race=White, Age=54 Years, Rel Day of Study Medication Discontinuance†=64										
001391	Treatment Cycle 2	22	Thyroiditis	Continuing	Mild	1		Y		Not Resolved
Trial Number=3475-002, Site Number=0070, Subject ID=100108, Gender=M, Race=White, Age=51 Years, Rel Day of Study Medication Discontinuance†=148										
100108	Treatment Cycle 5	106	Thyroiditis	Continuing		2	N	Y	None	Not Resolved
Trial Number=3475-002, Site Number=0080, Subject ID=100652, Gender=F, Race=White, Age=62 Years, Rel Day of Study Medication Discontinuance†=422										
100652	Treatment Cycle 1	21	Autoimmune thyroiditis	Continuing		1	N	Y	None	Not Resolved
Trial Number=3475-002, Site Number=0142, Subject ID=100322, Gender=F, Race=White, Age=34 Years, Rel Day of Study Medication Discontinuance†=										
100322	Treatment Cycle 2	25	Autoimmune thyroiditis	3.42 Months		2	N	Y	None	Resolved
Trial Number=3475-010, Site Number=1243, Subject ID=313473, Gender=F, Race=Asian, Age=55 Years, Rel Day of Study Medication Discontinuance†=										
313473	Treatment Cycle 2	43	Autoimmune thyroiditis	Continuing		1	N	Y	None	Resolving

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Listing of Subjects With Adverse Events
AEOSI- Thyroiditis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=001247, Gender=M, Race=White, Age=61 Years, Rel Day of Study Medication Discontinuance†=337										
001247	Treatment Cycle 6	71	Thyroiditis	1.68 Months	Mild	1		Y	N/A	Resolved
Trial Number=3475-006, Site Number=1600, Subject ID=361918, Gender=F, Race=White, Age=58 Years, Rel Day of Study Medication Discontinuance†=										
361918	Treatment Cycle 5	68	Thyroiditis	1.48 Months		1	N	Y	None	Resolved
Trial Number=3475-006, Site Number=1700, Subject ID=365574, Gender=M, Race=White, Age=59 Years, Rel Day of Study Medication Discontinuance†=351										
365574	Treatment Cycle 2	15	Thyroiditis	Continuing		2	Y	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 for MEL: [redacted]).

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

(MK-3475 PN002 Database Cutoff Date: [redacted]).

(MK-3475 PN006 Database Cutoff Date: 03MAR2015).

(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Subjects With Adverse Events by Outcome
(Incidence > 0% in One or More Treatment Groups)
AEOSI- Thyroiditis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

		P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	Outcome	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population		682		1,232		1,567		2,799	
With one or more adverse events	Overall	3	(0.4)	3	(0.2)	13	(0.8)	16	(0.6)
	Fatal	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
	Not Resolved	0	(0.0)	0	(0.0)	8	(0.5)	8	(0.3)
	Resolved	2	(0.3)	2	(0.2)	5	(0.3)	7	(0.3)
	Resolving	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
	Unknown	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

Outcome: Resolved = RECOVERED/RESOLVED, Not resolved = NOT RECOVERED/NOT RESOLVED.
Every subject is counted once for the AE outcome, with the order: Fatal>Not Resolved>Resolving>Unknown>Sequelae>Resolved.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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付録 2.7.4- 67　　免疫関連の 1 型糖尿病の AEOSI 解析

001 試験＋002 試験＋006 試験＋010 試験

MK-3475 を投与された悪性黒色腫及び非小細胞肺癌患者（安全性解析対象集団）

Adverse Event Summary
AEOSI - Type 1 Diabetes Mellitus
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1,232		1,567		2,799	
with one or more adverse events	3	(0.4)	3	(0.2)	3	(0.2)	6	(0.2)
with no adverse event	679	(99.6)	1,229	(99.8)	1,564	(99.8)	2,793	(99.8)
with drug-related† adverse events	3	(0.4)	3	(0.2)	2	(0.1)	5	(0.2)
with Grade 3- 5 adverse events	3	(0.4)	3	(0.2)	2	(0.1)	5	(0.2)
with Grade 3- 5 drug-related adverse events	3	(0.4)	3	(0.2)	1	(0.1)	4	(0.1)
with serious adverse events	3	(0.4)	3	(0.2)	3	(0.2)	6	(0.2)
with serious drug-related adverse events	3	(0.4)	3	(0.2)	2	(0.1)	5	(0.2)
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)	1	(0.1)	1	(0.0)
discontinued due to a drug-related adverse event	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	1	(0.1)	1	(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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of AEOSI - Type 1 Diabetes Mellitus
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010	PN001 Lung, PN010	PN001 Mel, PN002, PN006	PN001,PN002, PN006, PN010
	n (%)	n (%)	n (%)	n (%)
Subjects in population	682	1232	1567	2799
Subjects with Type 1 Diabetes Mellitus	3 (0.4)	3 (0.2)	3 (0.2)	6 (0.2)
Time to Onset of First Type 1 Diabetes Mellitus (days)†				
Mean (Std)	106.0 (67.0)	106.0 (67.0)	176.3 (184.8)	141.2 (130.2)
Median	127.0	127.0	106.0	116.5
Range	31 to 160	31 to 160	37 to 386	31 to 386
Total episodes of Type 1 Diabetes Mellitus	4	4	3	7
Average Episodes per subject	1.33	1.33	1.00	1.17
Episode duration (days)‡				

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Summary of AEOSI - Type 1 Diabetes Mellitus
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Median	Not reached		Not reached		Not reached		Not reached	
Range	7 to 346+		7 to 346+		10+ to 336+		7 to 346+	

(%) = Number of subjects with Type 1 Diabetes Mellitus / Number of subjects in population.
† Time to onset statistics are based on number of subjects with Type 1 Diabetes Mellitus.
‡ From product-limit (Kaplan-Meier) method for censored data. 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.
+ indicates the AE episode is not recovered/resolved by the time of the cutoff date or date of death.
Std = Standard Deviation.
Grades are based on NCI CTCAE version 4.0.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Subjects With Adverse Events by Maximum Toxicity Grade
(Incidence >0% in One or More Treatment Groups)
AEOSI- Type 1 Diabetes Mellitus
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1,232		1,567		2,799	
with one or more adverse events	3	(0.4)	3	(0.2)	3	(0.2)	6	(0.2)
Grade 2	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Grade 3	2	(0.3)	2	(0.2)	1	(0.1)	3	(0.1)
Grade 4	1	(0.1)	1	(0.1)	1	(0.1)	2	(0.1)
with no adverse events	679	(99.6)	1,229	(99.8)	1,564	(99.8)	2,793	(99.8)
Metabolism and nutrition disorders	**3**	**(0.4)**	**3**	**(0.2)**	**3**	**(0.2)**	**6**	**(0.2)**
Grade 2	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Grade 3	2	(0.3)	2	(0.2)	1	(0.1)	3	(0.1)
Grade 4	1	(0.1)	1	(0.1)	1	(0.1)	2	(0.1)
Diabetic ketoacidosis	1	(0.1)	1	(0.1)	1	(0.1)	2	(0.1)
Grade 3	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Grade 4	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
Type 1 diabetes mellitus	3	(0.4)	3	(0.2)	2	(0.1)	5	(0.2)
Grade 2	1	(0.1)	1	(0.1)	1	(0.1)	2	(0.1)
Grade 3	2	(0.3)	2	(0.2)	0	(0.0)	2	(0.1)

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Subjects With Adverse Events by Maximum Toxicity Grade
(Incidence >0% in One or More Treatment Groups)
AEOSI- Type 1 Diabetes Mellitus
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Type 1 diabetes mellitus	3	(0.4)	3	(0.2)	2	(0.1)	5	(0.2)
Grade 4	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)

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 for MEL: [redacted]).

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

(MK-3475 PN002 Database Cutoff Date: [redacted]).

(MK-3475 PN006 Database Cutoff Date: 03MAR2015).

(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of Concomitant Corticosteroid Use for AEOSI - Type 1 Diabetes Mellitus PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475 (APaT Population)

	P010 (N=682)		PN001 Lung, PN010 (N=1232)		PN001 Mel, PN002, PN006 (N=1567)		PN001,PN002, PN006, PN010 (N=2799)	
	n	%	n	%	n	%	n	%
Subjects with one or more Type 1 Diabetes Mellitus	3		3		3		6	
Treated with systemic corticosteroid	0	0	0	0	0	0	0	0
High starting dose[†]	0	0	0	0	0	0	0	0
Low starting dose[‡]	0	0	0	0	0	0	0	0
Not treated with systemic corticosteroid	3	100.0	3	100.0	3	100.0	6	100.0

The number of Subjects with one or more Type 1 Diabetes Mellitus is used as the denominator for the percentage calculation.
[†] 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.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of Concomitant Corticosteroid Use for AEOSI - Type 1 Diabetes Mellitus Episodes PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475 (APaT Population)

	P010	PN001 Lung, PN010	PN001 Mel, PN002, PN006	PN001,PN002, PN006, PN010
Total Episodes	4	4	3	7
High Starting Dose (%) †	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**
Low Starting Dose (%) ‡	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**
Not Treated with Systemic Corticosteroid (%)	**4 (100.0)**	**4 (100.0)**	**3 (100.0)**	**7 (100.0)**

† 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 for MEL: [redacted].
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Listing of Subjects With Adverse Events
AEOSI- Type 1 Diabetes Mellitus
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=3475-010, Site Number=0096, Subject ID=304814, Gender=M, Race=, Age=67 Years, Rel Day of Study Medication Discontinuance†=1										
304814	Safety Follow-up	31	Type 1 diabetes mellitus	1.15 Months		3	Y	Y	None	Resolved
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
Trial Number=3475-010, Site Number=0014, Subject ID=302077, Gender=M, Race=White, Age=65 Years, Rel Day of Study Medication Discontinuance†=141										
302077	Safety Follow-up	160	Diabetic ketoacidosis	1 Weeks		4	Y	Y	N/A	Resolved
		167	Type 1 diabetes mellitus	Continuing		2	N	Y	N/A	Not Resolved
Trial Number=3475-010, Site Number=1245, Subject ID=310534, Gender=M, Race=Asian, Age=67 Years, Rel Day of Study Medication Discontinuance†=										
310534	Treatment Cycle 7	127	Type 1 diabetes mellitus	Continuing		3	Y	Y	Interrupted	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										

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Listing of Subjects With Adverse Events
AEOSI- Type 1 Diabetes Mellitus
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=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 for MEL: [redacted]).

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

(MK-3475 PN002 Database Cutoff Date: [redacted]).

(MK-3475 PN006 Database Cutoff Date: 03MAR2015).

(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Subjects With Adverse Events by Outcome
(Incidence > 0% in One or More Treatment Groups)
AEOSI- Type 1 Diabetes Mellitus
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

		P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	Outcome	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population		682		1,232		1,567		2,799	
With one or more adverse events	Overall	3	(0.4)	3	(0.2)	3	(0.2)	6	(0.2)
	Fatal	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
	Not Resolved	2	(0.3)	2	(0.2)	2	(0.1)	4	(0.1)
	Resolved	1	(0.1)	1	(0.1)	1	(0.1)	2	(0.1)
	Unknown	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

Outcome: Resolved = RECOVERED/RESOLVED, Not resolved = NOT RECOVERED/NOT RESOLVED.
Every subject is counted once for the AE outcome, with the order: Fatal>Not Resolved>Resolving>Unknown>Sequelae>Resolved.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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付録 2.7.4- 68　　免疫関連のぶどう膜炎の AEOSI 解析

001 試験＋002 試験＋006 試験＋010 試験

MK-3475 を投与された悪性黒色腫及び非小細胞肺癌患者（安全性解析対象集団）

Adverse Event Summary
AEOSI - Uveitis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1,232		1,567		2,799	
with one or more adverse events	0	(0.0)	0	(0.0)	14	(0.9)	14	(0.5)
with no adverse event	682	(100.0)	1,232	(100.0)	1,553	(99.1)	2,785	(99.5)
with drug-related† adverse events	0	(0.0)	0	(0.0)	14	(0.9)	14	(0.5)
with Grade 3- 5 adverse events	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
with Grade 3- 5 drug-related adverse events	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
with serious adverse events	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	1	(0.1)	1	(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)	1	(0.1)	1	(0.0)
discontinued due to a drug-related adverse event	0	(0.0)	0	(0.0)	1	(0.1)	1	(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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of AEOSI - Uveitis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1232		1567		2799	
Subjects with Uveitis	0		0		14	(0.9)	14	(0.5)
Time to Onset of First Uveitis (days)†								
Mean (Std)	0		0		122.4 (124.7)		122.4 (124.7)	
Median	0.0		0.0		63.0		63.0	
Range	0 to 0		0 to 0		13 to 400		13 to 400	
Total episodes of Uveitis	0		0		15		15	
Average Episodes per subject	0		0		1.07		1.07	
Episode duration (days)‡								

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Summary of AEOSI - Uveitis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Median	0		0		43.0		43.0	
Range	0 to 0		0 to 0		11 to 410+		11 to 410+	

(%) = Number of subjects with Uveitis / Number of subjects in population.
† Time to onset statistics are based on number of subjects with Uveitis.
‡ From product-limit (Kaplan-Meier) method for censored data. 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.
+ indicates the AE episode is not recovered/resolved by the time of the cutoff date or date of death.
Std = Standard Deviation.
Grades are based on NCI CTCAE version 4.0.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Subjects With Adverse Events by Maximum Toxicity Grade
(Incidence >0% in One or More Treatment Groups)
AEOSI- Uveitis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1,232		1,567		2,799	
with one or more adverse events	0	(0.0)	0	(0.0)	14	(0.9)	14	(0.5)
Grade 1	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Grade 2	0	(0.0)	0	(0.0)	12	(0.8)	12	(0.4)
Grade 3	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
with no adverse events	682	(100.0)	1,232	(100.0)	1,553	(99.1)	2,785	(99.5)
Eye disorders	**0**	**(0.0)**	**0**	**(0.0)**	**14**	**(0.9)**	**14**	**(0.5)**
Grade 1	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Grade 2	0	(0.0)	0	(0.0)	12	(0.8)	12	(0.4)
Grade 3	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Iridocyclitis	0	(0.0)	0	(0.0)	2	(0.1)	2	(0.1)
Grade 2	0	(0.0)	0	(0.0)	2	(0.1)	2	(0.1)
Iritis	0	(0.0)	0	(0.0)	2	(0.1)	2	(0.1)
Grade 1	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Grade 3	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Uveitis	0	(0.0)	0	(0.0)	10	(0.6)	10	(0.4)

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Subjects With Adverse Events by Maximum Toxicity Grade
(Incidence >0% in One or More Treatment Groups)
AEOSI- Uveitis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Uveitis	0	(0.0)	0	(0.0)	10	(0.6)	10	(0.4)
Grade 2	0	(0.0)	0	(0.0)	10	(0.6)	10	(0.4)

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.

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

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

(MK-3475 PN002 Database Cutoff Date: [redacted]).

(MK-3475 PN006 Database Cutoff Date: 03MAR2015).

(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of Concomitant Corticosteroid Use for AEOSI - Uveitis PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475 (APaT Population)

	P010 (N=682)		NSCLC (N=1232)		PN001 Mel, PN002, PN006 (N=1567)		PN001,PN002, PN006, PN010 (N=2799)	
	n	%	n	%	n	%	n	%
Subjects with one or more Uveitis	0		0		14		14	
Treated with systemic corticosteroid	0	0	0	0	1	7.1	1	7.1
High starting dose†	0	0	0	0	0	0	0	0
Low starting dose‡	0	0	0	0	1	7.1	1	7.1
Not treated with systemic corticosteroid	0	0	0	0	13	92.9	13	92.9

The number of Subjects with one or more Uveitis is used as the denominator for the percentage calculation.
† 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.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of Concomitant Corticosteroid Use for AEOSI - Uveitis Episodes PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475 (APaT Population)

	P010	PN001 Lung, PN010	PN001 Mel, PN002, PN006	PN001,PN002, PN006, PN010
Total Episodes	0	0	15	15
High Starting Dose (%) †	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**
Low Starting Dose (%) ‡	**0 (0.0)**	**0 (0.0)**	**1 (6.7)**	**1 (6.7)**
Starting dose (mg/day)				
Mean (Std)	0 (0)	0 (0)	30 (.)	30 (.)
Median (Range)	0 (0-0)	0 (0-0)	30 (30-30)	30 (30-30)
Duration (days)§				
Mean (Std)	0 (0)	0 (0)	1 (.)	1 (.)
Median (Range)	0 (0-0)	0 (0-0)	1 (1-1)	1 (1-1)
Not Treated with Systemic Corticosteroid (%)	**0 (0.0)**	**0 (0.0)**	**14 (93.3)**	**14 (93.3)**

† 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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Listing of Subjects With Adverse Events
AEOSI- Uveitis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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	Continuing		1	N	Y	None	Resolving

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Listing of Subjects With Adverse Events
AEOSI- Uveitis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=100134, Gender=F, Race=White, Age=42 Years, Rel Day of Study Medication Discontinuance†=359										
100134	Treatment Cycle 17	338	Uveitis	3.48 Months		2	N	Y	Discontinued	Resolved
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=0003, Subject ID=365596, Gender=M, Race=White, Age=74 Years, Rel Day of Study Medication Discontinuance†=										
365596	Treatment Cycle 19	400	Uveitis	2.79 Months		2	N	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†=437										
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

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Listing of Subjects With Adverse Events
AEOSI- Uveitis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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†=259										
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 for MEL: [redacted]).

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

(MK-3475 PN002 Database Cutoff Date: [redacted].

(MK-3475 PN006 Database Cutoff Date: 03MAR2015).

(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Listing of Concomitant Systemic Corticosteroid Use for AEOSI - Uveitis Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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, Rel Day of Study Medication Discontinuance[‡]=259											
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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Subjects With Adverse Events by Outcome
(Incidence > 0% in One or More Treatment Groups)
AEOSI- Uveitis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

		P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	Outcome	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population		682		1,232		1,567		2,799	
With one or more adverse events	Overall	0	(0.0)	0	(0.0)	14	(0.9)	14	(0.5)
	Fatal	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
	Not Resolved	0	(0.0)	0	(0.0)	2	(0.1)	2	(0.1)
	Resolved	0	(0.0)	0	(0.0)	11	(0.7)	11	(0.4)
	Resolving	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
	Unknown	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

Outcome: Resolved = RECOVERED/RESOLVED, Not resolved = NOT RECOVERED/NOT RESOLVED.
Every subject is counted once for the AE outcome, with the order: Fatal>Not Resolved>Resolving>Unknown>Sequelae>Resolved.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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付録 2.7.4- 69　　免疫関連の膵炎の AEOSI 解析

001 試験＋002 試験＋006 試験＋010 試験

MK-3475 を投与された悪性黒色腫及び非小細胞肺癌患者（安全性解析対象集団）

Adverse Event Summary
AEOSI - Pancreatitis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1,232		1,567		2,799	
with one or more adverse events	3	(0.4)	3	(0.2)	6	(0.4)	9	(0.3)
with no adverse event	679	(99.6)	1,229	(99.8)	1,561	(99.6)	2,790	(99.7)
with drug-related† adverse events	1	(0.1)	1	(0.1)	5	(0.3)	6	(0.2)
with Grade 3- 5 adverse events	2	(0.3)	2	(0.2)	4	(0.3)	6	(0.2)
with Grade 3- 5 drug-related adverse events	0	(0.0)	0	(0.0)	3	(0.2)	3	(0.1)
with serious adverse events	2	(0.3)	2	(0.2)	5	(0.3)	7	(0.3)
with serious drug-related adverse events	1	(0.1)	1	(0.1)	4	(0.3)	5	(0.2)
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)	4	(0.3)	4	(0.1)
discontinued due to a drug-related adverse event	0	(0.0)	0	(0.0)	4	(0.3)	4	(0.1)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	3	(0.2)	3	(0.1)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	3	(0.2)	3	(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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of AEOSI - Pancreatitis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1232		1567		2799	
Subjects with Pancreatitis	3	(0.4)	3	(0.2)	6	(0.4)	9	(0.3)
Time to Onset of First Pancreatitis (days)†								
Mean (Std)	99.0 (43.3)		99.0 (43.3)		153.8 (97.9)		135.6 (84.9)	
Median	75.0		75.0		121.0		116.0	
Range	73 to 149		73 to 149		76 to 338		73 to 338	
Total episodes of Pancreatitis	3		3		8		11	
Average Episodes per subject	1.00		1.00		1.33		1.22	
Episode duration (days)‡								

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Summary of AEOSI - Pancreatitis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Median	14.0		14.0		23.5		20.0	
Range	3 to 55		3 to 55		4 to 326+		3 to 326+	

(%) = Number of subjects with Pancreatitis / Number of subjects in population.
† Time to onset statistics are based on number of subjects with Pancreatitis.
‡ From product-limit (Kaplan-Meier) method for censored data. 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.
+ indicates the AE episode is not recovered/resolved by the time of the cutoff date or date of death.
Std = Standard Deviation.
Grades are based on NCI CTCAE version 4.0.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Subjects With Adverse Events by Maximum Toxicity Grade
(Incidence >0% in One or More Treatment Groups)
AEOSI- Pancreatitis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1,232		1,567		2,799	
with one or more adverse events	3	(0.4)	3	(0.2)	6	(0.4)	9	(0.3)
Grade 2	1	(0.1)	1	(0.1)	2	(0.1)	3	(0.1)
Grade 3	2	(0.3)	2	(0.2)	4	(0.3)	6	(0.2)
with no adverse events	679	(99.6)	1,229	(99.8)	1,561	(99.6)	2,790	(99.7)
Gastrointestinal disorders	**3**	**(0.4)**	**3**	**(0.2)**	**6**	**(0.4)**	**9**	**(0.3)**
Grade 2	1	(0.1)	1	(0.1)	2	(0.1)	3	(0.1)
Grade 3	2	(0.3)	2	(0.2)	4	(0.3)	6	(0.2)
Autoimmune pancreatitis	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Grade 3	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Pancreatitis	2	(0.3)	2	(0.2)	5	(0.3)	7	(0.3)
Grade 2	1	(0.1)	1	(0.1)	2	(0.1)	3	(0.1)
Grade 3	1	(0.1)	1	(0.1)	3	(0.2)	4	(0.1)
Pancreatitis acute	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)

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Subjects With Adverse Events by Maximum Toxicity Grade
(Incidence >0% in One or More Treatment Groups)
AEOSI- Pancreatitis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Pancreatitis acute	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
Grade 3	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)

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 for MEL: [redacted]).

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

(MK-3475 PN002 Database Cutoff Date: [redacted]).

(MK-3475 PN006 Database Cutoff Date: 03MAR2015).

(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of Concomitant Corticosteroid Use for AEOSI - Pancreatitis PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475 (APaT Population)

	P010 (N=682)		PN001 Lung, PN010 (N=1232)		PN001 Mel, PN002, PN006 (N=1567)		PN001,PN002, PN006, PN010 (N=2799)	
	n	%	n	%	n	%	n	%
Subjects with one or more Pancreatitis	3		3		6		9	
Treated with systemic corticosteroid	1	33.3	1	33.3	4	66.7	5	55.6
High starting dose†	0	0	0	0	3	50.0	3	33.3
Low starting dose‡	1	33.3	1	33.3	1	16.7	2	22.2
Not treated with systemic corticosteroid	2	66.7	2	66.7	2	33.3	4	44.4

The number of Subjects with one or more Pancreatitis is used as the denominator for the percentage calculation.
† 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.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of Concomitant Corticosteroid Use for AEOSI - Pancreatitis Episodes PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475 (APaT Population)

	P010	PN001 Lung, PN010	PN001 Mel, PN002, PN006	PN001,PN002, PN006, PN010
Total Episodes	3	3	8	11
High Starting Dose (%) †	**0 (0.0)**	**0 (0.0)**	**3 (37.5)**	**3 (27.3)**
Starting dose (mg/day)				
Mean (Std)	0 (0)	0 (0)	123 (68)	123 (68)
Median (Range)	0 (0-0)	0 (0-0)	100 (70-200)	100 (70-200)
Duration (days)§				
Mean (Std)	0 (0)	0 (0)	5 (3)	5 (3)
Median (Range)	0 (0-0)	0 (0-0)	5 (3-8)	5 (3-8)
Low Starting Dose (%) ‡	**1 (33.3)**	**1 (33.3)**	**1 (12.5)**	**2 (18.2)**
Starting dose (mg/day)				
Mean (Std)	13 (.)	13 (.)	10 (.)	12 (2)
Median (Range)	13 (13-13)	13 (13-13)	10 (10-10)	12 (10-13)
Duration (days)§				
Mean (Std)	2 (.)	2 (.)	318 (.)	160 (223)
Median (Range)	2 (2-2)	2 (2-2)	318 (318-318)	160 (2-318)
Not Treated with Systemic Corticosteroid (%)	**2 (66.7)**	**2 (66.7)**	**4 (50.0)**	**6 (54.5)**

† 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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Listing of Subjects With Adverse Events
AEOSI- Pancreatitis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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
Trial Number=3475-010, Site Number=0004, Subject ID=301679, Gender=M, Race=White, Age=67 Years, Rel Day of Study Medication Discontinuance†=49										
301679	Safety Follow-up	75	Pancreatitis acute	3 Days		3	N	N	None	Unknown
Trial Number=3475-010, Site Number=0201, Subject ID=309551, Gender=M, Race=White, Age=43 Years, Rel Day of Study Medication Discontinuance†=100										
309551	Treatment Cycle 3	73	Pancreatitis	2 Weeks		2	Y	Y	Interrupted	Resolved
Trial Number=3475-010, Site Number=1417, Subject ID=309855, Gender=M, Race=Asian, Age=64 Years, Rel Day of Study Medication Discontinuance†=110										
309855	Extended Safety Follow-up	149	Pancreatitis	1.81 Months		3	Y	N	N/A	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=3475-002, Site Number=0111, Subject ID=100335, Gender=M, Race=White, Age=56 Years, Rel Day of Study Medication Discontinuance†=378										
100335	Treatment Cycle 17 Safety Follow-up	338 393	Pancreatitis Pancreatitis	2.86 Weeks 4 Weeks		3 3	Y Y	Y Y	None Discontinued	Resolved Resolved

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Listing of Subjects With Adverse Events
AEOSI- Pancreatitis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=0111, Subject ID=100335, Gender=M, Race=White, Age=56 Years, Rel Day of Study Medication Discontinuance†=378										
100335	Extended Safety Follow-up	468	Pancreatitis	1.14 Weeks		3	Y	Y	N/A	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	Discontinued	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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Listing of Subjects With Adverse Events
AEOSI- Pancreatitis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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 for MEL: [redacted]).

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

(MK-3475 PN002 Database Cutoff Date: [redacted]).

(MK-3475 PN006 Database Cutoff Date: 03MAR2015).

(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Listing of Concomitant Systemic Corticosteroid Use for AEOSI - Pancreatitis Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=0088, Subject ID=101285, Gender=F, Race=White, Age=64 Years, Rel Day of Study Medication Discontinuance‡=											
101285	126	8	Prednisolone	70	QD	Intravenous	70.00	Pancreatitis	126	132	2
Trial Number=3475-010, Site Number=0201, Subject ID=309551, Gender=M, Race=White, Age=43 Years, Rel Day of Study Medication Discontinuance‡=100											
309551	76	2	Dexamethasone	2	QD	Oral	13.34	Pancreatitis	73	86	2
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

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Listing of Concomitant Systemic Corticosteroid Use for AEOSI - Pancreatitis Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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
	137	19	Prednisolone	50	QD	Oral	50.00	Autoimmune pancreatitis	116	142	3
	156	6	Prednisolone	40	QD	Oral	40.00	Autoimmune pancreatitis	116	142	3
	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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Subjects With Adverse Events by Outcome
(Incidence > 0% in One or More Treatment Groups)
AEOSI- Pancreatitis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

		P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	Outcome	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population		682		1,232		1,567		2,799	
With one or more adverse events	Overall	3	(0.4)	3	(0.2)	6	(0.4)	9	(0.3)
	Fatal	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
	Not Resolved	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
	Resolved	2	(0.3)	2	(0.2)	4	(0.3)	6	(0.2)
	Sequelae	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
	Unknown	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)

Outcome: Resolved = RECOVERED/RESOLVED, Not resolved = NOT RECOVERED/NOT RESOLVED.
Every subject is counted once for the AE outcome, with the order: Fatal>Not Resolved>Resolving>Unknown>Sequelae>Resolved.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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付録 2.7.4- 70　　免疫関連の筋炎の AEOSI 解析

001 試験＋002 試験＋006 試験＋010 試験

MK-3475 を投与された悪性黒色腫及び非小細胞肺癌患者（安全性解析対象集団）

Adverse Event Summary
AEOSI - Myositis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1,232		1,567		2,799	
with one or more adverse events	3	(0.4)	3	(0.2)	8	(0.5)	11	(0.4)
with no adverse event	679	(99.6)	1,229	(99.8)	1,559	(99.5)	2,788	(99.6)
with drug-related† adverse events	1	(0.1)	1	(0.1)	6	(0.4)	7	(0.3)
with Grade 3- 5 adverse events	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
with Grade 3- 5 drug-related adverse events	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
with serious adverse events	1	(0.1)	1	(0.1)	3	(0.2)	4	(0.1)
with serious drug-related adverse events	1	(0.1)	1	(0.1)	3	(0.2)	4	(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)	5	(0.3)	5	(0.2)
discontinued due to a drug-related adverse event	0	(0.0)	0	(0.0)	5	(0.3)	5	(0.2)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	3	(0.2)	3	(0.1)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	3	(0.2)	3	(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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of AEOSI - Myositis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1232		1567		2799	
Subjects with Myositis	3	(0.4)	3	(0.2)	8	(0.5)	11	(0.4)
Time to Onset of First Myositis (days)†								
Mean (Std)	73.3 (63.9)		73.3 (63.9)		186.5 (151.6)		155.6 (140.4)	
Median	86.0		86.0		146.5		101.0	
Range	4 to 130		4 to 130		20 to 459		4 to 459	
Total episodes of Myositis	3		3		9		12	
Average Episodes per subject	1.00		1.00		1.13		1.09	
Episode duration (days)‡								

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Summary of AEOSI - Myositis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Median	Not reached		Not reached		137.0		137.0	
Range	52+ to 71+		52+ to 71+		8 to 381+		8 to 381+	

(%) = Number of subjects with Myositis / Number of subjects in population.
† Time to onset statistics are based on number of subjects with Myositis.
‡ From product-limit (Kaplan-Meier) method for censored data. 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.
+ indicates the AE episode is not recovered/resolved by the time of the cutoff date or date of death.
Std = Standard Deviation.
Grades are based on NCI CTCAE version 4.0.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted].
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted].
(MK-3475 PN002 Database Cutoff Date: [redacted].
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Subjects With Adverse Events by Maximum Toxicity Grade
(Incidence >0% in One or More Treatment Groups)
AEOSI- Myositis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1,232		1,567		2,799	
with one or more adverse events	3	(0.4)	3	(0.2)	8	(0.5)	11	(0.4)
Grade 1	2	(0.3)	2	(0.2)	2	(0.1)	4	(0.1)
Grade 2	1	(0.1)	1	(0.1)	5	(0.3)	6	(0.2)
Grade 3	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
with no adverse events	679	(99.6)	1,229	(99.8)	1,559	(99.5)	2,788	(99.6)
Musculoskeletal and connective tissue disorders	**3**	**(0.4)**	**3**	**(0.2)**	**8**	**(0.5)**	**11**	**(0.4)**
Grade 1	2	(0.3)	2	(0.2)	2	(0.1)	4	(0.1)
Grade 2	1	(0.1)	1	(0.1)	5	(0.3)	6	(0.2)
Grade 3	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Myopathy	2	(0.3)	2	(0.2)	1	(0.1)	3	(0.1)
Grade 1	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
Grade 2	1	(0.1)	1	(0.1)	1	(0.1)	2	(0.1)
Myositis	1	(0.1)	1	(0.1)	6	(0.4)	7	(0.3)
Grade 1	1	(0.1)	1	(0.1)	2	(0.1)	3	(0.1)
Grade 2	0	(0.0)	0	(0.0)	4	(0.3)	4	(0.1)
Rhabdomyolysis	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)

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Subjects With Adverse Events by Maximum Toxicity Grade
(Incidence >0% in One or More Treatment Groups)
AEOSI- Myositis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Rhabdomyolysis	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Grade 3	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)

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 for MEL: [redacted]).

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

(MK-3475 PN002 Database Cutoff Date: [redacted]).

(MK-3475 PN006 Database Cutoff Date: 03MAR2015).

(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of Concomitant Corticosteroid Use for AEOSI - Myositis PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475 (APaT Population)

	P010 (N=682)		PN001 Lung, PN010 (N=1232)		PN001 Mel, PN002, PN006 (N=1567)		PN001,PN002, PN006, PN010 (N=2799)	
	n	%	n	%	n	%	n	%
Subjects with one or more Myositis	3		3		8		11	
Treated with systemic corticosteroid	1	33.3	1	33.3	2	25.0	3	27.3
High starting dose†	1	33.3	1	33.3	2	25.0	3	27.3
Low starting dose‡	0	0	0	0	0	0	0	0
Not treated with systemic corticosteroid	2	66.7	2	66.7	6	75.0	8	72.7

The number of Subjects with one or more Myositis is used as the denominator for the percentage calculation.
† 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.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of Concomitant Corticosteroid Use for AEOSI - Myositis Episodes PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475 (APaT Population)

	P010	PN001 Lung, PN010	PN001 Mel, PN002, PN006	PN001,PN002, PN006, PN010
Total Episodes	3	3	9	12
High Starting Dose (%) †	**1 (33.3)**	**1 (33.3)**	**2 (22.2)**	**3 (25.0)**
Starting dose (mg/day)				
Mean (Std)	53 (.)	53 (.)	530 (665)	371 (545)
Median (Range)	53 (53-53)	53 (53-53)	530 (60-1000)	60 (53-1000)
Duration (days)§				
Mean (Std)	47 (.)	47 (.)	5 (3)	19 (24)
Median (Range)	47 (47-47)	47 (47-47)	5 (3-7)	7 (3-47)
Low Starting Dose (%) ‡	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**
Not Treated with Systemic Corticosteroid (%)	**2 (66.7)**	**2 (66.7)**	**7 (77.8)**	**9 (75.0)**

† 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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Listing of Subjects With Adverse Events
AEOSI- Myositis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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
Trial Number=3475-010, Site Number=0003, Subject ID=300001, Gender=F, Race=White, Age=69 Years, Rel Day of Study Medication Discontinuance†=113										
300001	Safety Follow-up	130	Myositis	Continuing		1	N	N	None	Not Resolved
Trial Number=3475-010, Site Number=1080, Subject ID=312970, Gender=F, Race=White, Age=62 Years, Rel Day of Study Medication Discontinuance†=94										
312970	Treatment Cycle 4	86	Myopathy	Continuing		2	Y	Y	Interrupted	Resolving
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=000110, Gender=M, Race=White, Age=61 Years, Rel Day of Study Medication Discontinuance†=23										
000110	Extended Safety Follow-up	54	Myositis	Continuing	Moderate	2	Y	Y	Discontinued	Not Resolved
Trial Number=3475-001, Site Number=0024, Subject ID=000482, Gender=M, Race=White, Age=49 Years, Rel Day of Study Medication Discontinuance†=570										
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										

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Listing of Subjects With Adverse Events
AEOSI- Myositis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=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
Trial Number=3475-010, Site Number=0088, Subject ID=314103, Gender=F, Race=White, Age=57 Years, Rel Day of Study Medication Discontinuance†=22										
314103	Treatment Cycle 1	4	Myopathy	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
	Safety Follow-up	365	Myopathy	4.5 Months	Moderate	2	Y	Y	Discontinued	Resolved
Trial Number=3475-006, Site Number=1818, Subject ID=367651, Gender=M, Race=White, Age=75 Years, Rel Day of Study Medication Discontinuance†=309										

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Listing of Subjects With Adverse Events
AEOSI- Myositis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=1818, Subject ID=367651, Gender=M, Race=White, Age=75 Years, Rel Day of Study Medication Discontinuance[†]=309										
367651	Safety Follow-up	323	Myositis	1.14 Weeks		2	N	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 for MEL: [redacted].

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

(MK-3475 PN002 Database Cutoff Date: [redacted].

(MK-3475 PN006 Database Cutoff Date: 03MAR2015).

(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Listing of Concomitant Systemic Corticosteroid Use for AEOSI - Myositis Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=3475-010, Site Number=1080, Subject ID=312970, Gender=F, Race=White, Age=62 Years, Rel Day of Study Medication Discontinuance‡=94											
312970	110	.	Dexamethasone	8	QD	Oral	53.36	Myopathy	86	.	2
MK-3475 10 mg/kg Q3W											
Trial Number=3475-001, Site Number=0024, Subject ID=000110, Gender=M, Race=White, Age=61 Years, Rel Day of Study Medication Discontinuance‡=23											

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Listing of Concomitant Systemic Corticosteroid Use for AEOSI - Myositis Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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
000110	66	3	Meprednisone	1000	QD	Intravenous Administration	1000.00	Myositis	54	.	2
MK-3475 10 mg/kg Q2W											
Trial Number=3475-006, Site Number=1818, Subject ID=367651, Gender=M, Race=White, Age=75 Years, Rel Day of Study Medication Discontinuance‡=309											
367651	323	7	Prednisone	60	QD	Oral	60.00	Myositis	323	330	2
	330	7	Prednisone	40	QD	Oral	40.00	Myositis	323	330	2

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Listing of Concomitant Systemic Corticosteroid Use for AEOSI - Myositis Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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
	347	4	Prednisone	10	QD	Oral	10.00	Myositis	323	330	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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Subjects With Adverse Events by Outcome
(Incidence > 0% in One or More Treatment Groups)
AEOSI- Myositis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

		P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	Outcome	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population		682		1,232		1,567		2,799	
With one or more adverse events	Overall	3	(0.4)	3	(0.2)	8	(0.5)	11	(0.4)
	Fatal	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
	Not Resolved	2	(0.3)	2	(0.2)	4	(0.3)	6	(0.2)
	Resolved	0	(0.0)	0	(0.0)	4	(0.3)	4	(0.1)
	Resolving	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
	Unknown	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

Outcome: Resolved = RECOVERED/RESOLVED, Not resolved = NOT RECOVERED/NOT RESOLVED.
Every subject is counted once for the AE outcome, with the order: Fatal>Not Resolved>Resolving>Unknown>Sequelae>Resolved.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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付録 2.7.4- 71　　免疫関連の重度の皮膚反応の AEOSI 解析

001 試験＋002 試験＋006 試験＋010 試験

MK-3475 を投与された悪性黒色腫及び非小細胞肺癌患者（安全性解析対象集団）

Adverse Event Summary
AEOSI - Skin
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1,232		1,567		2,799	
with one or more adverse events	11	(1.6)	18	(1.5)	28	(1.8)	46	(1.6)
with no adverse event	671	(98.4)	1,214	(98.5)	1,539	(98.2)	2,753	(98.4)
with drug-related† adverse events	9	(1.3)	13	(1.1)	19	(1.2)	32	(1.1)
with Grade 3- 5 adverse events	8	(1.2)	13	(1.1)	25	(1.6)	38	(1.4)
with Grade 3- 5 drug-related adverse events	7	(1.0)	10	(0.8)	17	(1.1)	27	(1.0)
with serious adverse events	3	(0.4)	7	(0.6)	8	(0.5)	15	(0.5)
with serious drug-related adverse events	2	(0.3)	4	(0.3)	4	(0.3)	8	(0.3)
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	1	(0.1)	2	(0.2)	3	(0.2)	5	(0.2)
discontinued due to a drug-related adverse event	1	(0.1)	2	(0.2)	2	(0.1)	4	(0.1)
discontinued due to a serious adverse event	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)
discontinued due to a serious drug-related adverse event	0	(0.0)	1	(0.1)	1	(0.1)	2	(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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of AEOSI - Skin
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1232		1567		2799	
Subjects with Skin	11	(1.6)	18	(1.5)	28	(1.8)	46	(1.6)
Time to Onset of First Skin (days)†								
Mean (Std)	91.8 (94.5)		114.2 (117.4)		167.1 (172.2)		146.4 (153.9)	
Median	63.0		86.0		115.0		106.5	
Range	8 to 332		8 to 453		4 to 653		4 to 653	
Total episodes of Skin	12		19		32		51	
Average Episodes per subject	1.09		1.06		1.14		1.11	
Episode duration (days)‡								

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Summary of AEOSI - Skin
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Median	76.5		40.0		23.0		37.0	
Range	8 to 325		4 to 420+		3 to 463+		3 to 463+	

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

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

‡ From product-limit (Kaplan-Meier) method for censored data. 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.

+ indicates the AE episode is not recovered/resolved by the time of the cutoff date or date of death.

Std = Standard Deviation.

Grades are based on NCI CTCAE version 4.0.

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

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

(MK-3475 PN002 Database Cutoff Date: [redacted]).

(MK-3475 PN006 Database Cutoff Date: 03MAR2015).

(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Subjects With Adverse Events by Maximum Toxicity Grade
(Incidence >0% in One or More Treatment Groups)
AEOSI- Skin
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1,232		1,567		2,799	
with one or more adverse events	11	(1.6)	18	(1.5)	28	(1.8)	46	(1.6)
Grade 1	1	(0.1)	2	(0.2)	3	(0.2)	5	(0.2)
Grade 2	2	(0.3)	3	(0.2)	0	(0.0)	3	(0.1)
Grade 3	8	(1.2)	13	(1.1)	25	(1.6)	38	(1.4)
with no adverse events	671	(98.4)	1,214	(98.5)	1,539	(98.2)	2,753	(98.4)
Hepatobiliary disorders	**0**	**(0.0)**	**0**	**(0.0)**	**1**	**(0.1)**	**1**	**(0.0)**
Grade 3	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Jaundice	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Grade 3	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Infections and infestations	**1**	**(0.1)**	**1**	**(0.1)**	**0**	**(0.0)**	**1**	**(0.0)**
Grade 3	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
Rash pustular	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
Grade 3	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
Injury, poisoning and procedural complications	**1**	**(0.1)**	**1**	**(0.1)**	**0**	**(0.0)**	**1**	**(0.0)**
Grade 3	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
Contusion	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
Grade 3	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)

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Subjects With Adverse Events by Maximum Toxicity Grade
(Incidence >0% in One or More Treatment Groups)
AEOSI- Skin
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Reproductive system and breast disorders	**1**	**(0.1)**	**1**	**(0.1)**	**0**	**(0.0)**	**1**	**(0.0)**
Grade 3	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
Pruritus genital	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
Grade 3	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
Skin and subcutaneous tissue disorders	**9**	**(1.3)**	**16**	**(1.3)**	**27**	**(1.7)**	**43**	**(1.5)**
Grade 1	1	(0.1)	2	(0.2)	3	(0.2)	5	(0.2)
Grade 2	2	(0.3)	3	(0.2)	0	(0.0)	3	(0.1)
Grade 3	6	(0.9)	11	(0.9)	24	(1.5)	35	(1.3)
Dermatitis	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
Grade 3	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
Dermatitis bullous	1	(0.1)	1	(0.1)	1	(0.1)	2	(0.1)
Grade 1	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Grade 2	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
Dermatitis exfoliative	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)
Grade 1	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
Grade 2	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Drug eruption	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
Grade 3	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
Erythema	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Grade 3	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Erythema multiforme	2	(0.3)	3	(0.2)	0	(0.0)	3	(0.1)
Grade 1	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)

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Subjects With Adverse Events by Maximum Toxicity Grade
(Incidence >0% in One or More Treatment Groups)
AEOSI- Skin
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Erythema multiforme	2	(0.3)	3	(0.2)	0	(0.0)	3	(0.1)
Grade 2	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
Grade 3	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
Exfoliative rash	0	(0.0)	0	(0.0)	2	(0.1)	2	(0.1)
Grade 1	0	(0.0)	0	(0.0)	2	(0.1)	2	(0.1)
Lichen planus	1	(0.1)	1	(0.1)	1	(0.1)	2	(0.1)
Grade 3	1	(0.1)	1	(0.1)	1	(0.1)	2	(0.1)
Pemphigoid	0	(0.0)	0	(0.0)	2	(0.1)	2	(0.1)
Grade 3	0	(0.0)	0	(0.0)	2	(0.1)	2	(0.1)
Pruritus	0	(0.0)	0	(0.0)	4	(0.3)	4	(0.1)
Grade 3	0	(0.0)	0	(0.0)	4	(0.3)	4	(0.1)
Psoriasis	1	(0.1)	1	(0.1)	1	(0.1)	2	(0.1)
Grade 3	1	(0.1)	1	(0.1)	1	(0.1)	2	(0.1)
Rash	2	(0.3)	4	(0.3)	5	(0.3)	9	(0.3)
Grade 3	2	(0.3)	4	(0.3)	5	(0.3)	9	(0.3)
Rash erythematous	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Grade 3	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Rash generalised	0	(0.0)	0	(0.0)	2	(0.1)	2	(0.1)
Grade 3	0	(0.0)	0	(0.0)	2	(0.1)	2	(0.1)
Rash maculo-papular	1	(0.1)	2	(0.2)	5	(0.3)	7	(0.3)
Grade 3	1	(0.1)	2	(0.2)	5	(0.3)	7	(0.3)
Rash pruritic	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Grade 3	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Skin lesion	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Grade 3	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)

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Subjects With Adverse Events by Maximum Toxicity Grade
(Incidence >0% in One or More Treatment Groups)
AEOSI- Skin
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Stevens-Johnson syndrome	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Grade 3	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Toxic skin eruption	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
Grade 2	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)

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 for MEL: [redacted]).

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

(MK-3475 PN002 Database Cutoff Date: [redacted]).

(MK-3475 PN006 Database Cutoff Date: 03MAR2015).

(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of Concomitant Corticosteroid Use for AEOSI - Skin
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010 (N=682)		PN001 Lung, PN010 (N=1232)		PN001 Mel, PN002, PN006 (N=1567)		PN001,PN002, PN006, PN010 (N=2799)	
	n	%	n	%	n	%	n	%
Subjects with one or more Skin	11		18		28		46	
Treated with systemic corticosteroid	5	45.5	8	44.4	12	42.9	20	43.5
High starting dose†	1	9.1	2	11.1	6	21.4	8	17.4
Low starting dose‡	4	36.4	6	33.3	6	21.4	12	26.1
Not treated with systemic corticosteroid	6	54.5	10	55.6	16	57.1	26	56.5

The number of Subjects with one or more Skin is used as the denominator for the percentage calculation.
† 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.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of Concomitant Corticosteroid Use for AEOSI - Skin Episodes PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475 (APaT Population)

	P010	PN001 Lung, PN010	PN001 Mel, PN002, PN006	PN001,PN002, PN006, PN010
Total Episodes	12	19	32	51
High Starting Dose (%) †	**1 (8.3)**	**2 (10.5)**	**6 (18.8)**	**8 (15.7)**
Starting dose (mg/day)				
Mean (Std)	75 (.)	68 (11)	80 (42)	77 (36)
Median (Range)	75 (75-75)	68 (60-75)	70 (40-160)	68 (40-160)
Duration (days)§				
Mean (Std)	1 (.)	9 (11)	5 (2)	6 (5)
Median (Range)	1 (1-1)	9 (1-17)	5 (3-8)	5 (1-17)
Low Starting Dose (%) ‡	**4 (33.3)**	**6 (31.6)**	**6 (18.8)**	**12 (23.5)**
Starting dose (mg/day)				
Mean (Std)	23 (13)	24 (11)	19 (15)	21 (13)
Median (Range)	25 (5-38)	25 (5-38)	18 (1-38)	25 (1-38)
Duration (days)§				
Mean (Std)	6 (6)	7 (7)	43 (76)	25 (55)
Median (Range)	3 (2-15)	3 (1-16)	14 (2-198)	7 (1-198)
Not Treated with Systemic Corticosteroid (%)	**7 (58.3)**	**11 (57.9)**	**20 (62.5)**	**31 (60.8)**

† 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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Listing of Subjects With Adverse Events
AEOSI- Skin
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=0004, Subject ID=003042, Gender=F, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=83										
003042	Treatment Cycle 1	19	Dermatitis exfoliative	Continuing	Mild	1		N	N/A	Not Resolved
Trial Number=3475-001, Site Number=0008, Subject ID=000422, Gender=F, Race=White, Age=49 Years, Rel Day of Study Medication Discontinuance†=1										
000422	Safety Follow-up	9	Jaundice	3 Days	Severe	3		N		Resolved
		22	Jaundice	Continuing	Severe	3		N	N/A	Not Resolved
Trial Number=3475-002, Site Number=0054, Subject ID=101278, Gender=M, Race=White, Age=73 Years, Rel Day of Study Medication Discontinuance†=281										
101278	Treatment Cycle 4	85	Rash maculo-papular	1.86 Weeks		3	Y	Y	Interrupted	Resolved
Trial Number=3475-002, Site Number=0110, Subject ID=102128, Gender=F, Race=White, Age=51 Years, Rel Day of Study Medication Discontinuance†=22										
102128	Treatment Cycle 1	18	Erythema	Continuing		3	N	N	None	Not 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
Trial Number=3475-010, Site Number=0209, Subject ID=314106, Gender=F, Race=White, Age=58 Years, Rel Day of Study Medication Discontinuance†=133										
314106	Safety Follow-up	142	Rash	1.86 Weeks		3	N	Y	None	Resolved
Trial Number=3475-010, Site Number=1081, Subject ID=307871, Gender=M, Race=Asian, Age=74 Years, Rel Day of Study Medication Discontinuance†=22										
307871	Treatment Cycle 1	14	Psoriasis	Continuing		3	N	Y	None	Not Resolved

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Listing of Subjects With Adverse Events
AEOSI- Skin
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=3475-010, Site Number=1245, Subject ID=308516, Gender=M, Race=Asian, Age=55 Years, Rel Day of Study Medication Discontinuance†=113										
308516	Treatment Cycle 1	26	Rash maculo-papular	1.43 Weeks		3	Y	Y	Interrupted	Resolved
Trial Number=3475-010, Site Number=1405, Subject ID=304574, Gender=M, Race=Asian, Age=66 Years, Rel Day of Study Medication Discontinuance†=										
304574	Treatment Cycle 4	137	Erythema multiforme	1.14 Weeks		2	N	N	N/A	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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Listing of Subjects With Adverse Events
AEOSI- Skin
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=3475-001, Site Number=0019, Subject ID=000928, Gender=F, Race=White, Age=63 Years, Rel Day of Study Medication Discontinuance†=428										
000928	Safety Follow-up	453	Rash	1.43 Weeks	Severe	3	Y	Y	Discontinued	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=0151, Subject ID=101217, Gender=M, Race=White, Age=80 Years, Rel Day of Study Medication Discontinuance†=632										
101217	Safety Follow-up	653	Skin lesion	Continuing		3	N	N	Discontinued	Not Resolved
Trial Number=3475-006, Site Number=0612, Subject ID=365859, Gender=M, Race=White, Age=32 Years, Rel Day of Study Medication Discontinuance†=316										
365859	Safety Follow-up	328	Rash	1.51 Months		3	Y	N	None	Resolved
Trial Number=3475-006, Site Number=1503, Subject ID=360532, Gender=F, Race=White, Age=57 Years, Rel Day of Study Medication Discontinuance†=400										
360532	Treatment Cycle 3	58	Dermatitis bullous	1.29 Weeks		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†=										

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Listing of Subjects With Adverse Events
AEOSI- Skin
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=1703, Subject ID=363479, Gender=M, Race=White, Age=64 Years, Rel Day of Study Medication Discontinuance†=										
363479	Treatment Cycle 7	148	Pruritus	7.62 Months		3	N	N	Interrupted	Resolved
Trial Number=3475-006, Site Number=1711, Subject ID=368193, Gender=F, Race=Asian, Age=30 Years, Rel Day of Study Medication Discontinuance†=43										
368193	Safety Follow-up	67	Rash	3.14 Weeks		3	Y	N	N/A	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=1810, Subject ID=364795, Gender=M, Race=White, Age=78 Years, Rel Day of Study Medication Discontinuance†=357										
364795	Safety Follow-up	360	Pemphigoid	2 Months		3	Y	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										
362113	Treatment Cycle 4	64	Exfoliative rash	3.14 Weeks		1	N	Y	None	Resolved
Trial Number=3475-010, Site Number=0005, Subject ID=303231, Gender=F, Race=White, Age=76 Years, Rel Day of Study Medication Discontinuance†=232										
303231	Treatment Cycle 2	25	Rash	1.31 Months		3	N	Y	Reduced	Resolved
Trial Number=3475-010, Site Number=0014, Subject ID=302077, Gender=M, Race=White, Age=65 Years, Rel Day of Study Medication Discontinuance†=141										
302077	Treatment Cycle 3	63	Rash pustular	4.29 Weeks		3	N	Y	Interrupted	Resolved
Trial Number=3475-010, Site Number=0037, Subject ID=305210, Gender=F, Race=Black Or African American, Age=60 Years, Rel Day of Study Medication Discontinuance†=										

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Listing of Subjects With Adverse Events
AEOSI- Skin
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=3475-010, Site Number=0037, Subject ID=305210, Gender=F, Race=Black Or African American, Age=60 Years, Rel Day of Study Medication Discontinuance†=										
305210	Treatment Cycle 7	127	Erythema multiforme	3.71 Months		1	N	Y	None	Resolved
Trial Number=3475-010, Site Number=0361, Subject ID=305971, Gender=M, Race=White, Age=62 Years, Rel Day of Study Medication Discontinuance†=169										
305971	Treatment Cycle 1	8	Pruritus genital	6.21 Months		3	N	Y	None	Resolved
	Treatment Cycle 5	105	Lichen planus	10.68 Months		3	N	Y	Discontinued	Resolved
Trial Number=3475-010, Site Number=1244, Subject ID=305539, Gender=M, Race=Asian, Age=73 Years, Rel Day of Study Medication Discontinuance†=										
305539	Treatment Cycle 16	332	Contusion	1.57 Weeks		3	Y	N	None	Resolved
Trial Number=3475-010, Site Number=1411, Subject ID=300216, Gender=M, Race=Asian, Age=60 Years, Rel Day of Study Medication Discontinuance†=										
300216	Treatment Cycle 5	100	Dermatitis bullous	4.4 Months		2	N	Y	None	Resolved
Trial Number=3475-010, Site Number=1430, Subject ID=304201, Gender=F, Race=Asian, Age=54 Years, Rel Day of Study Medication Discontinuance†=29										
304201	Safety Follow-up	36	Drug eruption	Continuing		3	Y	Y	Interrupted	Resolving
MK-3475 10 mg/kg Q2W										
Trial Number=3475-001, Site Number=0001, Subject ID=001530, Gender=M, Race=White, Age=83 Years, Rel Day of Study Medication Discontinuance†=134										
001530	Safety Follow-up	145	Dermatitis	4 Days	Severe	3	Y	N	Interrupted	Resolved
Trial Number=3475-001, Site Number=0010, Subject ID=000030, Gender=F, Race=White, Age=81 Years, Rel Day of Study Medication Discontinuance†=309										

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Listing of Subjects With Adverse Events
AEOSI- Skin
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q2W										
Trial Number=3475-001, Site Number=0010, Subject ID=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	113	Rash erythematous	2.14 Weeks	Severe	3		Y	Interrupted	Resolved
		128	Dermatitis exfoliative	1.22 Months	Moderate	2		Y	N/A	Resolved
Trial Number=3475-001, Site Number=0019, Subject ID=000924, Gender=F, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=										
000924	Treatment Cycle 11	148	Rash maculo-papular	1.71 Weeks	Severe	3		Y		Resolved
Trial Number=3475-001, Site Number=0019, Subject ID=001119, Gender=M, Race=White, Age=78 Years, Rel Day of Study Medication Discontinuance†=15										
001119	Safety Follow-up	29	Rash	3.29 Weeks	Severe	3	Y	Y		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										
001352	Treatment Cycle 1	8	Rash pruritic	3.14 Weeks	Severe	3		Y		Resolved
	Safety Follow-up	71	Pruritus	Continuing	Severe	3		N	N/A	Not Resolved
Trial Number=3475-001, Site Number=0031, Subject ID=000996, Gender=M, Race=White, Age=73 Years, Rel Day of Study Medication Discontinuance†=										

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Listing of Subjects With Adverse Events
AEOSI- Skin
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=0031, Subject ID=000996, Gender=M, Race=White, Age=73 Years, Rel Day of Study Medication Discontinuance†=										
000996	Treatment Cycle 6	72	Toxic skin eruption	Continuing	Moderate	2		Y		Not Resolved
Trial Number=3475-001, Site Number=0134, Subject ID=001182, Gender=M, Race=Black Or African American, Age=59 Years, Rel Day of Study Medication Discontinuance†=292										
001182	Treatment Cycle 13	180	Erythema multiforme	2.43 Weeks	Severe	3	Y	N	Interrupted	Resolved
		196	Erythema multiforme	1.71 Weeks	Mild	1		N		Resolved
	Treatment Cycle 14	207	Erythema multiforme	2.29 Weeks	Moderate	2		N		Resolved
	Treatment Cycle 16	222	Erythema multiforme	Continuing	Mild	1		N		Not Resolved
Trial Number=3475-006, Site Number=0002, Subject ID=361797, Gender=F, Race=White, Age=48 Years, Rel Day of Study Medication Discontinuance†=15										
361797	Safety Follow-up	18	Lichen planus	Continuing		3	Y	Y	Interrupted	Resolving
Trial Number=3475-006, Site Number=0002, Subject ID=362392, Gender=M, Race=White, Age=71 Years, Rel Day of Study Medication Discontinuance†=253										
362392	Treatment Cycle 1	8	Pemphigoid	Continuing		3	N	Y	Interrupted	Not Resolved
Trial Number=3475-006, Site Number=0102, Subject ID=362687, Gender=M, Race=White, Age=52 Years, Rel Day of Study Medication Discontinuance†=										
362687	Treatment Cycle 28	389	Rash maculo-papular	6 Days		3	N	Y	Interrupted	Resolved
Trial Number=3475-006, Site Number=1804, Subject ID=364814, Gender=F, Race=White, Age=84 Years, Rel Day of Study Medication Discontinuance†=196										

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Listing of Subjects With Adverse Events
AEOSI- Skin
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=1804, Subject ID=364814, Gender=F, Race=White, Age=84 Years, Rel Day of Study Medication Discontinuance†=196										
364814	Treatment Cycle 3	48	Psoriasis	Continuing		3	N	Y	Discontinued	Resolving

†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 for MEL: [redacted]).

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

(MK-3475 PN002 Database Cutoff Date: [redacted].

(MK-3475 PN006 Database Cutoff Date: 03MAR2015).

(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Listing of Concomitant Systemic Corticosteroid Use for AEOSI -Skin Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=0054, Subject ID=101278, Gender=M, Race=White, Age=73 Years, Rel Day of Study Medication Discontinuance‡=281											
101278	85	4	Prednisone	40	QD	Oral	40.00	Rash maculo-papular	85	97	3
	89	.	Prednisone	20	QD	Oral	20.00	Rash maculo-papular	85	97	3
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
Trial Number=3475-010, Site Number=1081, Subject ID=307871, Gender=M, Race=Asian, Age=74 Years, Rel Day of Study Medication Discontinuance‡=22											
307871	21	2	Prednisolone	25	QD	Oral	25.00	Psoriasis	14	.	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											

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Listing of Concomitant Systemic Corticosteroid Use for AEOSI -Skin Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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
000297	232	6	Methylprednisolone	128	QID	Oral Administration	160.00	Rash maculo-papular	232	253	3
Trial Number=3475-001, Site Number=0019, Subject ID=000928, Gender=F, Race=White, Age=63 Years, Rel Day of Study Medication Discontinuance‡=428											
000928	453	17	Prednisone	60	QD	Oral Administration	60.00	Rash	453	462	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
	98	3	Prednisone	10	QD	Oral	10.00	Rash maculo-papular	43	109	3
	101	3	Prednisone	5	QD	Oral	5.00	Rash maculo-papular	43	109	3
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
Trial Number=3475-006, Site Number=1810, Subject ID=364795, Gender=M, Race=White, Age=78 Years, Rel Day of Study Medication Discontinuance‡=357											
364795	362	3	Prednisone	80	QD	Oral	80.00	Pemphigoid	360	420	3
	365	3	Prednisone	60	QD	Oral	60.00	Pemphigoid	360	420	3
	368	3	Prednisone	40	QD	Oral	40.00	Pemphigoid	360	420	3
	393	7	Prednisone	40	QD	Oral	40.00	Pemphigoid	360	420	3
	400	7	Prednisone	30	QD	Oral	30.00	Pemphigoid	360	420	3
	407	7	Prednisone	20	QD	Oral	20.00	Pemphigoid	360	420	3

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Listing of Concomitant Systemic Corticosteroid Use for AEOSI -Skin Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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
	414	7	Prednisone	10	QD	Oral	10.00	Pemphigoid	360	420	3
Trial Number=3475-010, Site Number=0005, Subject ID=303231, Gender=F, Race=White, Age=76 Years, Rel Day of Study Medication Discontinuance‡=232											
303231	30	2	Methylprednisolone	4	ONCE	Oral	5.00	Rash	25	64	3
	31	12	Prednisone	60	QD	Oral	60.00	Rash	25	64	3
Trial Number=3475-010, Site Number=0014, Subject ID=302077, Gender=M, Race=White, Age=65 Years, Rel Day of Study Medication Discontinuance‡=141											
302077	64	1	Triamcinolone Acetonide	60	ONCE	Intramuscular	75.00	Rash pustular	63	92	3
Trial Number=3475-010, Site Number=0361, Subject ID=305971, Gender=M, Race=White, Age=62 Years, Rel Day of Study Medication Discontinuance‡=169											
305971	188	15	Prednisolone	38	QD	Oral	37.50	Lichen planus	105	429	3
Trial Number=3475-010, Site Number=1430, Subject ID=304201, Gender=F, Race=Asian, Age=54 Years, Rel Day of Study Medication Discontinuance‡=29											
304201	52	3	Methylprednisolone	500	UNKNOWN	Intravenous	625.00	Drug eruption	36	.	3
	48	4	Prednisolone	25	UNKNOWN	Oral	25.00	Drug eruption	36	.	3
	55	3	Prednisolone	40	UNKNOWN	Oral	40.00	Drug eruption	36	.	3
	58	4	Prednisolone	30	UNKNOWN	Oral	30.00	Drug eruption	36	.	3
	62	4	Prednisolone	20	UNKNOWN	Oral	20.00	Drug eruption	36	.	3
	66	4	Prednisolone	15	UNKNOWN	Oral	15.00	Drug eruption	36	.	3
	70	4	Prednisolone	10	UNKNOWN	Oral	10.00	Drug eruption	36	.	3
	74	4	Prednisolone	5	UNKNOWN	Oral	5.00	Drug eruption	36	.	3

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Listing of Concomitant Systemic Corticosteroid Use for AEOSI -Skin Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=3475-001, 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
Trial Number=3475-001, Site Number=0019, Subject ID=000924, Gender=F, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance‡=											
000924	153	1	Methylprednisolone	24	QD	Oral Administration	30.00	Rash maculo-papular	148	159	3
	154	1	Methylprednisolone	20	ONCE	Oral Administration	25.00	Rash maculo-papular	148	159	3
	155	1	Methylprednisolone	16	ONCE	Oral Administration	20.00	Rash maculo-papular	148	159	3
	156	1	Methylprednisolone	12	ONCE	Oral Administration	15.00	Rash maculo-papular	148	159	3
	157	1	Methylprednisolone	8	ONCE	Oral Administration	10.00	Rash maculo-papular	148	159	3
	158	1	Methylprednisolone	4	ONCE	Oral Administration	5.00	Rash maculo-papular	148	159	3
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	64	6	Dexamethasone	5	QD	Oral Administration	33.35	Rash pruritic	8	29	3
Trial Number=3475-001, Site Number=0134, Subject ID=001182, Gender=M, Race=Black Or African American, Age=59 Years, Rel Day of Study Medication Discontinuance‡=292											
001182	181	16	Prednisone	20	QD	Oral Administration	20.00	Erythema multiforme	180	196	3
	209	7	Prednisone	10	ONCE	Oral Administration	10.00	Erythema multiforme	207	222	2
Trial Number=3475-006, Site Number=0002, Subject ID=361797, Gender=F, Race=White, Age=48 Years, Rel Day of Study Medication Discontinuance‡=15											
361797	51	3	Methylprednisolone	1	QD	Intravenous	1.25	Lichen planus	18	.	3

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Listing of Concomitant Systemic Corticosteroid Use for AEOSI -Skin Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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
	28	2	Prednisone	25	QD	Oral	25.00	Lichen planus	18	.	3
	30	3	Prednisone	10	QD	Oral	10.00	Lichen planus	18	.	3
	54	.	Prednisone	50	QD	Oral	50.00	Lichen planus	18	.	3
Trial Number=3475-006, Site Number=0002, Subject ID=362392, Gender=M, Race=White, Age=71 Years, Rel Day of Study Medication Discontinuance‡=253											
362392	273	.	Prednisone	38	QD	Oral	37.50	Pemphigoid	8	.	3

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Listing of Concomitant Systemic Corticosteroid Use for AEOSI -Skin Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=1804, Subject ID=364814, Gender=F, Race=White, Age=84 Years, Rel Day of Study Medication Discontinuance‡=196											
364814	49	21	Prednisone	5	QD	Oral	5.00	Psoriasis	48	.	3
	70	.	Prednisone	10	QD	Oral	10.00	Psoriasis	48	.	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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted].
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Subjects With Adverse Events by Outcome
(Incidence > 0% in One or More Treatment Groups)
AEOSI- Skin
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

		P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	Outcome	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population		682		1,232		1,567		2,799	
With one or more adverse events	Overall	11	(1.6)	18	(1.5)	28	(1.8)	46	(1.6)
	Fatal	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
	Not Resolved	1	(0.1)	4	(0.3)	7	(0.4)	11	(0.4)
	Resolved	9	(1.3)	13	(1.1)	19	(1.2)	32	(1.1)
	Resolving	1	(0.1)	1	(0.1)	2	(0.1)	3	(0.1)
	Unknown	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

Outcome: Resolved = RECOVERED/RESOLVED, Not resolved = NOT RECOVERED/NOT RESOLVED.
Every subject is counted once for the AE outcome, with the order: Fatal>Not Resolved>Resolving>Unknown>Sequelae>Resolved.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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付録 2.7.4- 72　　免疫関連のギラン・バレー症候群の AEOSI 解析

001 試験＋002 試験＋006 試験＋010 試験

MK-3475 を投与された悪性黒色腫及び非小細胞肺癌患者（安全性解析対象集団）

Adverse Event Summary
AEOSI - Guillain-Barre Syndrome
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1,232		1,567		2,799	
with one or more adverse events	0	(0.0)	0	(0.0)	2	(0.1)	2	(0.1)
with no adverse event	682	(100.0)	1,232	(100.0)	1,565	(99.9)	2,797	(99.9)
with drug-related[†] adverse events	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
with Grade 3- 5 adverse events	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
with Grade 3- 5 drug-related adverse events	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
with serious adverse events	0	(0.0)	0	(0.0)	2	(0.1)	2	(0.1)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	1	(0.1)	1	(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)	1	(0.1)	1	(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)	1	(0.1)	1	(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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of AEOSI - Guillain-Barre Syndrome
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1232		1567		2799	
Subjects with Guillain-Barre Syndrome	0		0		2	(0.1)	2	(0.1)
Time to Onset of First Guillain-Barre Syndrome (days)†								
Mean (Std)	0		0		186.0 (223.4)		186.0 (223.4)	
Median	0.0		0.0		186.0		186.0	
Range	0 to 0		0 to 0		28 to 344		28 to 344	
Total episodes of Guillain-Barre Syndrome	0		0		2		2	
Average Episodes per subject	0		0		1.00		1.00	
Episode duration (days)‡								

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Summary of AEOSI - Guillain-Barre Syndrome
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Median	0		0		96.0		96.0	
Range	0 to 0		0 to 0		54+ to 96		54+ to 96	

(%) = Number of subjects with Guillain-Barre Syndrome / Number of subjects in population.

† Time to onset statistics are based on number of subjects with Guillain-Barre Syndrome.

‡ From product-limit (Kaplan-Meier) method for censored data. 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.

+ indicates the AE episode is not recovered/resolved by the time of the cutoff date or date of death.

Std = Standard Deviation.

Grades are based on NCI CTCAE version 4.0.

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

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

(MK-3475 PN002 Database Cutoff Date: [redacted]).

(MK-3475 PN006 Database Cutoff Date: 03MAR2015).

(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Subjects With Adverse Events by Maximum Toxicity Grade
(Incidence >0% in One or More Treatment Groups)
AEOSI- Guillain-Barre Syndrome
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1,232		1,567		2,799	
with one or more adverse events	0	(0.0)	0	(0.0)	2	(0.1)	2	(0.1)
Grade 2	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Grade 4	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
with no adverse events	682	(100.0)	1,232	(100.0)	1,565	(99.9)	2,797	(99.9)
Nervous system disorders	**0**	**(0.0)**	**0**	**(0.0)**	**2**	**(0.1)**	**2**	**(0.1)**
Grade 2	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Grade 4	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Axonal neuropathy	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Grade 2	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Guillain-Barre syndrome	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Grade 4	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)

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 for MEL: [redacted]).

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

(MK-3475 PN002 Database Cutoff Date: [redacted]).

(MK-3475 PN006 Database Cutoff Date: 03MAR2015).

(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of Concomitant Corticosteroid Use for AEOSI - Guillain-Barre Syndrome PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475 (APaT Population)

	P010 (N=682)		NSCLC (N=1232)		PN001 Mel, PN002, PN006 (N=1567)		PN001,PN002, PN006, PN010 (N=2799)	
	n	%	n	%	n	%	n	%
Subjects with one or more Guillain-Barre Syndrome	0		0		2		2	
Treated with systemic corticosteroid	0	0	0	0	1	50.0	1	50.0
High starting dose†	0	0	0	0	1	50.0	1	50.0
Low starting dose‡	0	0	0	0	0	0	0	0
Not treated with systemic corticosteroid	0	0	0	0	1	50.0	1	50.0

The number of Subjects with one or more Guillain-Barre Syndrome is used as the denominator for the percentage calculation.
† 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.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of Concomitant Corticosteroid Use for AEOSI - Guillain-Barre Syndrome Episodes PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475 (APaT Population)

	P010	PN001 Lung, PN010	PN001 Mel, PN002, PN006	PN001,PN002, PN006, PN010
Total Episodes	0	0	2	2
High Starting Dose (%) †	**0 (0.0)**	**0 (0.0)**	**1 (50.0)**	**1 (50.0)**
Starting dose (mg/day)				
Mean (Std)	0 (0)	0 (0)	107 (.)	107 (.)
Median (Range)	0 (0-0)	0 (0-0)	107 (107-107)	107 (107-107)
Duration (days)§				
Mean (Std)	0 (0)	0 (0)	421 (.)	421 (.)
Median (Range)	0 (0-0)	0 (0-0)	421 (421-421)	421 (421-421)
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)**	**1 (50.0)**	**1 (50.0)**

† 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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Listing of Subjects With Adverse Events
AEOSI- Guillain-Barre Syndrome
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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	N/A	Sequelae
MK-3475 10 mg/kg Q2W										
Trial Number=3475-006, Site Number=1502, Subject ID=367365, Gender=M, Race=White, Age=43 Years, Rel Day of Study Medication Discontinuance†=323										
367365	Safety Follow-up	344	Axonal neuropathy	Continuing		2	Y	N	Discontinued	Resolving

†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 for MEL: [redacted]).

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

(MK-3475 PN002 Database Cutoff Date: [redacted]).

(MK-3475 PN006 Database Cutoff Date: 03MAR2015).

(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Listing of Concomitant Systemic Corticosteroid Use for AEOSI - Guillain-Barre Syndrome Episodes Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Subjects With Adverse Events by Outcome
(Incidence > 0% in One or More Treatment Groups)
AEOSI- Guillain-Barre Syndrome
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

		P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	Outcome	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population		682		1,232		1,567		2,799	
With one or more adverse events	Overall	0	(0.0)	0	(0.0)	2	(0.1)	2	(0.1)
	Fatal	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
	Not Resolved	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
	Resolved	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
	Resolving	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
	Sequelae	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
	Unknown	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

Outcome: Resolved = RECOVERED/RESOLVED, Not resolved = NOT RECOVERED/NOT RESOLVED.
Every subject is counted once for the AE outcome, with the order: Fatal>Not Resolved>Resolving>Unknown>Sequelae>Resolved.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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付録 2.7.4- 73　　Infusion Reaction の AEOSI 解析

001 試験＋002 試験＋006 試験＋010 試験

MK-3475 を投与された悪性黒色腫及び非小細胞肺癌患者（安全性解析対象集団）

Adverse Event Summary
AEOSI - Infusion Reactions
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1,232		1,567		2,799	
with one or more adverse events	12	(1.8)	31	(2.5)	39	(2.5)	70	(2.5)
with no adverse event	670	(98.2)	1,201	(97.5)	1,528	(97.5)	2,729	(97.5)
with drug-related† adverse events	8	(1.2)	23	(1.9)	23	(1.5)	46	(1.6)
with Grade 3- 5 adverse events	2	(0.3)	3	(0.2)	3	(0.2)	6	(0.2)
with Grade 3- 5 drug-related adverse events	0	(0.0)	1	(0.1)	2	(0.1)	3	(0.1)
with serious adverse events	1	(0.1)	1	(0.1)	4	(0.3)	5	(0.2)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	2	(0.1)	2	(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)	1	(0.1)	2	(0.1)
discontinued due to a drug-related adverse event	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)
discontinued due to a serious adverse event	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	0	(0.0)	1	(0.1)	1	(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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of AEOSI - Infusion Reactions
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1232		1567		2799	
Subjects with Infusion Reactions	12	(1.8)	31	(2.5)	39	(2.5)	70	(2.5)
Time to Onset of First Infusion Reactions (days)†								
Mean (Std)	81.1 (105.9)		74.6 (98.1)		121.3 (133.9)		100.6 (120.8)	
Median	24.0		22.0		58.0		42.5	
Range	19 to 320		1 to 342		1 to 521		1 to 521	
Total episodes of Infusion Reactions	15		40		45		85	
Average Episodes per subject	1.25		1.29		1.15		1.21	
Episode duration (days)‡								

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Summary of AEOSI - Infusion Reactions
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Median	1.0		1.0		1.0		1.0	
Range	1 to 293+		1 to 293+		1 to 444+		1 to 444+	

(%) = Number of subjects with Infusion Reactions / Number of subjects in population.
† Time to onset statistics are based on number of subjects with Infusion Reactions.
‡ From product-limit (Kaplan-Meier) method for censored data. 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.
+ indicates the AE episode is not recovered/resolved by the time of the cutoff date or date of death.
Std = Standard Deviation.
Grades are based on NCI CTCAE version 4.0.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted].
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted].
(MK-3475 PN002 Database Cutoff Date: [redacted].
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Subjects With Adverse Events by Maximum Toxicity Grade
(Incidence >0% in One or More Treatment Groups)
AEOSI- Infusion Reactions
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1,232		1,567		2,799	
with one or more adverse events	12	(1.8)	31	(2.5)	39	(2.5)	70	(2.5)
Grade 1	4	(0.6)	11	(0.9)	21	(1.3)	32	(1.1)
Grade 2	6	(0.9)	17	(1.4)	15	(1.0)	32	(1.1)
Grade 3	2	(0.3)	3	(0.2)	2	(0.1)	5	(0.2)
Grade 4	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
with no adverse events	670	(98.2)	1,201	(97.5)	1,528	(97.5)	2,729	(97.5)
Immune system disorders	**7**	**(1.0)**	**16**	**(1.3)**	**25**	**(1.6)**	**41**	**(1.5)**
Grade 1	2	(0.3)	6	(0.5)	16	(1.0)	22	(0.8)
Grade 2	3	(0.4)	7	(0.6)	6	(0.4)	13	(0.5)
Grade 3	2	(0.3)	3	(0.2)	2	(0.1)	5	(0.2)
Grade 4	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Anaphylactic reaction	2	(0.3)	2	(0.2)	1	(0.1)	3	(0.1)
Grade 2	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
Grade 3	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
Grade 4	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Cytokine release syndrome	0	(0.0)	0	(0.0)	2	(0.1)	2	(0.1)
Grade 1	0	(0.0)	0	(0.0)	2	(0.1)	2	(0.1)
Drug hypersensitivity	4	(0.6)	5	(0.4)	8	(0.5)	13	(0.5)
Grade 1	1	(0.1)	1	(0.1)	5	(0.3)	6	(0.2)
Grade 2	2	(0.3)	3	(0.2)	2	(0.1)	5	(0.2)
Grade 3	1	(0.1)	1	(0.1)	1	(0.1)	2	(0.1)
Hypersensitivity	1	(0.1)	8	(0.6)	14	(0.9)	22	(0.8)

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Subjects With Adverse Events by Maximum Toxicity Grade
(Incidence >0% in One or More Treatment Groups)
AEOSI- Infusion Reactions
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Hypersensitivity	1	(0.1)	8	(0.6)	14	(0.9)	22	(0.8)
Grade 1	1	(0.1)	5	(0.4)	9	(0.6)	14	(0.5)
Grade 2	0	(0.0)	3	(0.2)	4	(0.3)	7	(0.3)
Grade 3	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Serum sickness	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
Grade 3	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
Injury, poisoning and procedural complications	**5**	**(0.7)**	**15**	**(1.2)**	**14**	**(0.9)**	**29**	**(1.0)**
Grade 1	2	(0.3)	5	(0.4)	5	(0.3)	10	(0.4)
Grade 2	3	(0.4)	10	(0.8)	9	(0.6)	19	(0.7)
Infusion related reaction	5	(0.7)	15	(1.2)	14	(0.9)	29	(1.0)
Grade 1	2	(0.3)	5	(0.4)	5	(0.3)	10	(0.4)
Grade 2	3	(0.4)	10	(0.8)	9	(0.6)	19	(0.7)

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 for MEL: [redacted]).

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

(MK-3475 PN002 Database Cutoff Date: [redacted]).

(MK-3475 PN006 Database Cutoff Date: 03MAR2015).

(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of Concomitant Corticosteroid Use for AEOSI - Infusion Reactions PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475 (APaT Population)

	P010 (N=682)		PN001 Lung, PN010 (N=1232)		PN001 Mel, PN002, PN006 (N=1567)		PN001,PN002, PN006, PN010 (N=2799)	
	n	%	n	%	n	%	n	%
Subjects with one or more Infusion Reactions	12		31		39		70	
Treated with systemic corticosteroid	4	33.3	9	29.0	11	28.2	20	28.6
High starting dose†	3	25.0	5	16.1	3	7.7	8	11.4
Low starting dose‡	1	8.3	4	12.9	8	20.5	12	17.1
Not treated with systemic corticosteroid	8	66.7	22	71.0	28	71.8	50	71.4

The number of Subjects with one or more Infusion Reactions is used as the denominator for the percentage calculation.
† 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.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of Concomitant Corticosteroid Use for AEOSI - Infusion Reactions Episodes PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475 (APaT Population)

	P010	PN001 Lung, PN010	PN001 Mel, PN002, PN006	PN001,PN002, PN006, PN010
Total Episodes	15	40	45	85
High Starting Dose (%) †	**3 (20.0)**	**5 (12.5)**	**4 (8.9)**	**9 (10.6)**
Starting dose (mg/day)				
Mean (Std)	100 (25)	101 (24)	129 (21)	114 (26)
Median (Range)	100 (75-125)	100 (75-125)	133 (100-150)	125 (75-150)
Duration (days)§				
Mean (Std)	1 (0)	7 (13)	1 (1)	4 (9)
Median (Range)	1 (1-1)	1 (1-29)	1 (1-2)	1 (1-29)
Low Starting Dose (%) ‡	**1 (6.7)**	**4 (10.0)**	**8 (17.8)**	**12 (14.1)**
Starting dose (mg/day)				
Mean (Std)	25 (.)	18 (8)	24 (5)	22 (6)
Median (Range)	25 (25-25)	19 (10-25)	25 (13-27)	25 (10-27)
Duration (days)§				
Mean (Std)	1 (.)	2 (3)	3 (3)	3 (3)
Median (Range)	1 (1-1)	1 (1-6)	1 (1-9)	1 (1-9)
Not Treated with Systemic Corticosteroid (%)	**11 (73.3)**	**31 (77.5)**	**33 (73.3)**	**64 (75.3)**

† 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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Listing of Subjects With Adverse Events
AEOSI- Infusion Reactions
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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†=526										
100049	Treatment Cycle 10	207	Hypersensitivity	1.02 Months		2	N	N	None	Resolved
Trial Number=3475-010, Site Number=0014, Subject ID=301535, Gender=F, Race=White, Age=74 Years, Rel Day of Study Medication Discontinuance†=232										
301535	Treatment Cycle 2	36	Drug hypersensitivity	1.14 Weeks		2	N	N	None	Resolved
Trial Number=3475-010, Site Number=0128, Subject ID=306051, Gender=M, Race=White, Age=46 Years, Rel Day of Study Medication Discontinuance†=1										

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Listing of Subjects With Adverse Events
AEOSI- Infusion Reactions
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=3475-010, Site Number=0128, Subject ID=306051, Gender=M, Race=White, Age=46 Years, Rel Day of Study Medication Discontinuance†=1										
306051	Safety Follow-up	19	Anaphylactic reaction	Unknown		3	N	N	N/A	Unknown
Trial Number=3475-010, Site Number=0182, Subject ID=301330, Gender=F, Race=White, Age=63 Years, Rel Day of Study Medication Discontinuance†=125										
301330	Treatment Cycle 2	20	Infusion related reaction	5 Minutes		1	N	Y	Interrupted	Resolved
Trial Number=3475-010, Site Number=0284, Subject ID=309628, Gender=F, Race=White, Age=58 Years, Rel Day of Study Medication Discontinuance†=40										
309628	Treatment Cycle 2	26	Hypersensitivity	4.14 Weeks		1	N	Y	None	Resolved
Trial Number=3475-010, Site Number=1245, Subject ID=301979, Gender=M, Race=Asian, Age=71 Years, Rel Day of Study Medication Discontinuance†=										
301979	Treatment Cycle 15	320	Drug hypersensitivity	Continuing		3	Y	N	None	Not Resolved
MK-3475 10 mg/kg Q3W										
Trial Number=3475-001, Site Number=0003, Subject ID=001526, Gender=F, Race=White, Age=72 Years, Rel Day of Study Medication Discontinuance†=156										
001526	Treatment Cycle 6	123	Drug hypersensitivity	1 Days	Moderate	2		N	N/A	Resolved
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
Trial Number=3475-001, Site Number=0011, Subject ID=000822, Gender=M, Race=White, Age=51 Years, Rel Day of Study Medication Discontinuance†=170										
000822	Treatment Cycle 1	1	Infusion related reaction	2 Days	Mild	1		Y	N/A	Resolved

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Listing of Subjects With Adverse Events
AEOSI- Infusion Reactions
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=0015, Subject ID=001085, Gender=F, Race=White, Age=61 Years, Rel Day of Study Medication Discontinuance†=296										
001085	Treatment Cycle 13	257	Hypersensitivity	Continuing	Mild	1		N	N/A	Not Resolved
Trial Number=3475-001, Site Number=0015, Subject ID=001537, Gender=F, Race=White, Age=78 Years, Rel Day of Study Medication Discontinuance†=										
001537	Treatment Cycle 3	61	Hypersensitivity	1.14 Weeks	Moderate	2		N		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=0020, Subject ID=000911, Gender=M, Race=Asian, Age=70 Years, Rel Day of Study Medication Discontinuance†=324										

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Listing of Subjects With Adverse Events
AEOSI- Infusion Reactions
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=000911, Gender=M, Race=Asian, Age=70 Years, Rel Day of Study Medication Discontinuance†=324										
000911	Safety Follow-up	342	Serum sickness	1.51 Months	Severe	3		Y	Discontinued	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=3475-001, Site Number=0033, Subject ID=001037, Gender=F, Race=Asian, Age=54 Years, Rel Day of Study Medication Discontinuance†=										
001037	Treatment Cycle 1	1	Hypersensitivity	1 Days	Mild	1		Y		Resolved
	Treatment Cycle 3	44	Hypersensitivity	1 Days	Mild	1		Y		Resolved
Trial Number=3475-001, Site Number=0092, Subject ID=001180, Gender=M, Race=White, Age=57 Years, Rel Day of Study Medication Discontinuance†=										
001180	Treatment Cycle 1	1	Infusion related reaction	1 Days	Moderate	2		Y		Resolved
	Treatment Cycle 4	66	Infusion related reaction	2 Days	Mild	1		Y	N/A	Resolved
Trial Number=3475-001, Site Number=0120, Subject ID=001076, Gender=M, Race=White, Age=63 Years, Rel Day of Study Medication Discontinuance†=106										
001076	Treatment Cycle 2	38	Hypersensitivity	9 Months	Mild	1		N	N/A	Resolved
Trial Number=3475-001, Site Number=0120, Subject ID=001087, Gender=F, Race=White, Age=69 Years, Rel Day of Study Medication Discontinuance†=296										
001087	Treatment Cycle 2	18	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

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Listing of Subjects With Adverse Events
AEOSI- Infusion Reactions
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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	None	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=0033, Subject ID=100663, Gender=F, Race=White, Age=33 Years, Rel Day of Study Medication Discontinuance†=64										
100663	Treatment Cycle 3	43	Infusion related reaction	2 Days		1	N	N	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	Interrupted	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 1	1	Hypersensitivity	31 Minutes		1	N	Y	Interrupted	Resolved
	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

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Listing of Subjects With Adverse Events
AEOSI- Infusion Reactions
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=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										
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
Trial Number=3475-010, Site Number=0003, Subject ID=300217, Gender=M, Race=White, Age=67 Years, Rel Day of Study Medication Discontinuance†=99										
300217	Treatment Cycle 1	20	Drug hypersensitivity	23 Hours		1	N	N	None	Resolved
Trial Number=3475-010, Site Number=0006, Subject ID=300114, Gender=F, Race=White, Age=75 Years, Rel Day of Study Medication Discontinuance†=66										

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Listing of Subjects With Adverse Events
AEOSI- Infusion Reactions
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=3475-010, Site Number=0006, Subject ID=300114, Gender=F, Race=White, Age=75 Years, Rel Day of Study Medication Discontinuance†=66										
300114	Treatment Cycle 4	66	Anaphylactic reaction	1.5 Hours		2	N	Y	Interrupted	Resolved
Trial Number=3475-010, Site Number=0007, Subject ID=307774, Gender=F, Race=White, Age=78 Years, Rel Day of Study Medication Discontinuance†=43										
307774	Treatment Cycle 2	22	Infusion related reaction	26 Minutes		1	N	Y	None	Resolved
	Treatment Cycle 3	43	Infusion related reaction	1.25 Hours		2	N	Y	Interrupted	Resolved
Trial Number=3475-010, Site Number=0083, Subject ID=302776, Gender=F, Race=, Age=70 Years, Rel Day of Study Medication Discontinuance†=106										
302776	Treatment Cycle 2	22	Infusion related reaction	1.58 Hours		2	N	Y	Interrupted	Resolved
	Treatment Cycle 3	42	Infusion related reaction	23 Hours		2	N	Y	Interrupted	Resolved
Trial Number=3475-010, Site Number=0211, Subject ID=313160, Gender=M, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance†=147										
313160	Treatment Cycle 7	126	Infusion related reaction	23.02 Hours		2	N	Y	Interrupted	Resolved
	Treatment Cycle 8	147	Infusion related reaction	23.02 Hours		2	N	Y	Interrupted	Resolved
Trial Number=3475-010, Site Number=0561, Subject ID=313427, Gender=M, Race=White, Age=59 Years, Rel Day of Study Medication Discontinuance†=365										
313427	Treatment Cycle 14	274	Infusion related reaction	4 Hours		1	N	Y	None	Resolved
Trial Number=3475-010, Site Number=0563, Subject ID=303662, Gender=M, Race=White, Age=54 Years, Rel Day of Study Medication Discontinuance†=85										
303662	Treatment Cycle 2	22	Drug hypersensitivity	10 Minutes		2	N	Y	Interrupted	Resolved
MK-3475 10 mg/kg Q2W										

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Listing of Subjects With Adverse Events
AEOSI- Infusion Reactions
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q2W										
Trial Number=3475-001, Site Number=0010, Subject ID=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
Trial Number=3475-001, Site Number=0011, Subject ID=000949, Gender=F, Race=, Age=53 Years, Rel Day of Study Medication Discontinuance†=57										
000949	Treatment Cycle 2	15	Infusion related reaction	1 Days	Moderate	2		Y	Interrupted	Resolved
Trial Number=3475-001, Site Number=0011, Subject ID=001084, Gender=F, Race=White, Age=54 Years, Rel Day of Study Medication Discontinuance†=										
001084	Treatment Cycle 1	1	Infusion related reaction	2.14 Weeks	Mild	1		Y	N/A	Resolved
Trial Number=3475-001, Site Number=0011, Subject ID=001129, Gender=F, Race=White, Age=64 Years, Rel Day of Study Medication Discontinuance†=15										
001129	Treatment Cycle 2	15	Hypersensitivity	2 Days	Moderate	2		Y	Interrupted	Resolved
Trial Number=3475-001, Site Number=0012, Subject ID=001714, Gender=F, Race=White, Age=60 Years, Rel Day of Study Medication Discontinuance†=183										
001714	Treatment Cycle 13	170	Infusion related reaction	1 Days	Moderate	2		Y	N/A	Resolved
Trial Number=3475-001, Site Number=0013, Subject ID=001154, Gender=M, Race=White, Age=54 Years, Rel Day of Study Medication Discontinuance†=43										
001154	Treatment Cycle 1	1	Infusion related reaction	1 Days	Moderate	2		Y	Interrupted	Resolved
Trial Number=3475-001, Site Number=0015, Subject ID=000912, Gender=M, Race=White, Age=59 Years, Rel Day of Study Medication Discontinuance†=										

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Listing of Subjects With Adverse Events
AEOSI- Infusion Reactions
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=000912, Gender=M, Race=White, Age=59 Years, Rel Day of Study Medication Discontinuance†=										
000912	Treatment Cycle 6	71	Hypersensitivity	1 Days	Moderate	2		Y		Resolved
	Treatment Cycle 7	85	Hypersensitivity	1 Days	Moderate	2		N	Interrupted	Resolved
	Treatment Cycle 8	99	Hypersensitivity	1 Days	Moderate	2		Y		Resolved
Trial Number=3475-001, Site Number=0020, Subject ID=001701, Gender=F, Race=White, Age=59 Years, Rel Day of Study Medication Discontinuance†=										
001701	Treatment Cycle 10	127	Infusion related reaction	1 Days	Mild	1		Y	N/A	Resolved
	Treatment Cycle 24	343	Infusion related reaction	4 Days	Mild	1		Y	N/A	Resolved
Trial Number=3475-001, Site Number=0023, Subject ID=001306, Gender=F, Race=White, Age=52 Years, Rel Day of Study Medication Discontinuance†=210										
001306	Treatment Cycle 2	14	Infusion related reaction	1 Days	Moderate	2		Y	Interrupted	Resolved
Trial Number=3475-001, Site Number=0090, Subject ID=001051, Gender=M, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance†=										
001051	Treatment Cycle 2	15	Hypersensitivity	1 Days	Mild	1		Y		Resolved
		29	Hypersensitivity	1 Days	Mild	1		Y	N/A	Resolved
Trial Number=3475-001, Site Number=0120, Subject ID=001580, Gender=F, Race=White, Age=46 Years, Rel Day of Study Medication Discontinuance†=267										
001580	Treatment Cycle 2	15	Infusion related reaction	1 Days	Moderate	2		Y	Interrupted	Resolved
Trial Number=3475-001, Site Number=0134, Subject ID=001572, Gender=M, Race=White, Age=57 Years, Rel Day of Study Medication Discontinuance†=										
001572	Treatment Cycle 6	69	Infusion related reaction	1 Days	Moderate	2		Y		Resolved

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Listing of Subjects With Adverse Events
AEOSI- Infusion Reactions
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=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	15 Minutes		1	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=0102, Subject ID=362687, Gender=M, Race=White, Age=52 Years, Rel Day of Study Medication Discontinuance†=										
362687	Treatment Cycle 24	331	Drug hypersensitivity	3 Days		1	N	N	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†=323										
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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Listing of Subjects With Adverse Events
AEOSI- Infusion Reactions
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=1809, Subject ID=365737, Gender=M, Race=White, Age=73 Years, Rel Day of Study Medication Discontinuance†=										
365737	Treatment Cycle 19	253	Hypersensitivity	2.14 Weeks		1	N	N	None	Resolved
	Treatment Cycle 21	289	Hypersensitivity	3 Weeks		1	N	N	None	Resolved
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
Trial Number=3475-006, Site Number=1902, Subject ID=365024, Gender=F, Race=White, Age=61 Years, Rel Day of Study Medication Discontinuance†=197										
365024	Safety Follow-up	222	Hypersensitivity	Continuing		3	Y	N	N/A	Resolving

†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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Listing of Concomitant Systemic Corticosteroid Use for AEOSI - Infusion Reactions Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=0061, Subject ID=100049, Gender=M, Race=White, Age=57 Years, Rel Day of Study Medication Discontinuance‡=526											
100049	207	7	Methylprednisolone	20	OTHER	Oral	25.00	Hypersensitivity	207	237	2
Trial Number=3475-010, Site Number=0128, Subject ID=306051, Gender=M, Race=White, Age=46 Years, Rel Day of Study Medication Discontinuance‡=1											
306051	19	1	Prednisolone Sodium Succinate	100	ONCE	Intravenous	100.00	Anaphylactic reaction	19	.	3
MK-3475 10 mg/kg Q3W											
Trial Number=3475-001, Site Number=0020, Subject ID=000911, Gender=M, Race=Asian, Age=70 Years, Rel Day of Study Medication Discontinuance‡=324											
000911	344	6	Prednisone	10	BID	Oral Administration	10.00	Serum sickness	342	387	3
	358	28	Prednisone	20	BID	Oral Administration	20.00	Serum sickness	342	387	3
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											

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Listing of Concomitant Systemic Corticosteroid Use for AEOSI - Infusion Reactions Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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
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
Trial Number=3475-010, Site Number=0006, Subject ID=300114, Gender=F, Race=White, Age=75 Years, Rel Day of Study Medication Discontinuance‡=66											
300114	66	.	Dexamethasone	4	QD	Oral	26.68	Anaphylactic reaction	66	.	2
	66	1	Methylprednisolone	100	ONCE	Intravenous	125.00	Anaphylactic reaction	66	.	2
Trial Number=3475-010, Site Number=0083, Subject ID=302776, Gender=F, Race=, Age=70 Years, Rel Day of Study Medication Discontinuance‡=106											
302776	42	1	Methylprednisolone	60	ONCE	Intravenous	75.00	Infusion related reaction	42	.	2
Trial Number=3475-010, Site Number=0211, Subject ID=313160, Gender=M, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance‡=147											
313160	147	1	Hydrocortisone	100	QD	Intravenous	25.00	Infusion related reaction	147	.	2
MK-3475 10 mg/kg Q2W											
Trial Number=3475-001, Site Number=0011, Subject ID=000949, Gender=F, Race=, Age=53 Years, Rel Day of Study Medication Discontinuance‡=57											
000949	15	1	Dexamethasone	12	ONCE	Intravenous Administration	80.04	Infusion related reaction	15	15	2

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Listing of Concomitant Systemic Corticosteroid Use for AEOSI - Infusion Reactions Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=0090, Subject ID=001051, Gender=M, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance‡=											
001051	15	1	Hydrocortisone Sodium Phosphate	100	QD	Intravenous Bolus	25.00	Hypersensitivity	15	15	1
Trial Number=3475-001, Site Number=0120, Subject ID=001580, Gender=F, Race=White, Age=46 Years, Rel Day of Study Medication Discontinuance‡=267											
001580	15	1	Hydrocortisone Sodium Succinate	250	ONCE	Intravenous Administration	62.50	Infusion related reaction	15	15	2
	15	29	Methylprednisolone Sodium Succinate	100	ONCE	Intravenous Administration	125.00	Infusion related reaction	15	15	2

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Listing of Concomitant Systemic Corticosteroid Use for AEOSI - Infusion Reactions Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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
	99	1	Methylprednisolone Sodium Succinate	100	ONCE	Intravenous Administration	125.00	Infusion related reaction	15	15	2
Trial Number=3475-001, Site Number=0134, Subject ID=001572, Gender=M, Race=White, Age=57 Years, Rel Day of Study Medication Discontinuance‡=											
001572	69	1	Hydrocortisone	50	ONCE	Intravenous Administration	12.50	Infusion related reaction	69	69	2
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

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Listing of Concomitant Systemic Corticosteroid Use for AEOSI - Infusion Reactions Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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
	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

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Listing of Concomitant Systemic Corticosteroid Use for AEOSI - Infusion Reactions Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=365737, Gender=M, Race=White, Age=73 Years, Rel Day of Study Medication Discontinuance[‡]=											
365737	281	2	Prednisone	150	TID	Oral	150.00	Hypersensitivity	253	267	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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Subjects With Adverse Events by Outcome
(Incidence > 0% in One or More Treatment Groups)
AEOSI- Infusion Reactions
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

		P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	Outcome	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population		682		1,232		1,567		2,799	
With one or more adverse events	Overall	12	(1.8)	31	(2.5)	39	(2.5)	70	(2.5)
	Fatal	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
	Not Resolved	1	(0.1)	2	(0.2)	5	(0.3)	7	(0.3)
	Resolved	10	(1.5)	28	(2.3)	32	(2.0)	60	(2.1)
	Resolving	0	(0.0)	0	(0.0)	2	(0.1)	2	(0.1)
	Unknown	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)

Outcome: Resolved = RECOVERED/RESOLVED, Not resolved = NOT RECOVERED/NOT RESOLVED.
Every subject is counted once for the AE outcome, with the order: Fatal>Not Resolved>Resolving>Unknown>Sequelae>Resolved.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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付録 2.7.4- 74　　特に注目すべき有害事象（重要な潜在的リスク）

（いずれかの投与群で発現割合 0%超）

001 試験＋002 試験＋006 試験＋010 試験

MK-3475 を投与された悪性黒色腫及び非小細胞肺癌患者（安全性解析対象集団）

Subjects With Potential Adverse Events of Special Interest
(Incidence > 0% in One or More Treatment Groups)
Include All Subjects Receiving MK-3475 Treatment
from PN001, PN002, PN006 and PN010
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1,232		1,567		2,799	
with one or more adverse events	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)
with no adverse events	682	(100.0)	1,231	(99.9)	1,566	(99.9)	2,797	(99.9)
Myasthenic Syndrome	**0**	**(0.0)**	**1**	**(0.1)**	**1**	**(0.1)**	**2**	**(0.1)**
Myasthenic syndrome	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)

Every subject is counted a single time for each applicable row and column.

An AEOSI category or specific adverse event appears on this report only if its incidence in one or more of the columns meets the incidence criterion in the report title, after rounding.

MedDRA version used is 18.0

Include all treated subjects in PN001 Part B1, B2, B3, D, C, F1, F2, F3 and all subjects in PN002 treated with Pembrolizumab in the original phase , and all subjects in PN006 and PN010 treated with Pembrolizumab.

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

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

(MK-3475 PN002 Database Cutoff Date: [redacted]).

(MK-3475 PN006 Database Cutoff Date: 03MAR2015).

(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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付録 2.7.4- 75　　筋無力症候群の AEOSI 解析

001 試験＋002 試験＋006 試験＋010 試験

MK-3475 を投与された悪性黒色腫及び非小細胞肺癌患者（安全性解析対象集団）

Adverse Event Summary
AEOSI - Myasthenic Syndrome
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1,232		1,567		2,799	
with one or more adverse events	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)
with no adverse event	682	(100.0)	1,231	(99.9)	1,566	(99.9)	2,797	(99.9)
with drug-related† adverse events	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)
with Grade 3- 5 adverse events	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
with Grade 3- 5 drug-related adverse events	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
with serious adverse events	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	1	(0.1)	1	(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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of AEOSI - Myasthenic Syndrome
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1232		1567		2799	
Subjects with Myasthenic Syndrome	0		1	(0.1)	1	(0.1)	2	(0.1)
Time to Onset of First Myasthenic Syndrome (days)†								
Mean (Std)	0		41.0		74.0		57.5 (23.3)	
Median	0.0		41.0		74.0		57.5	
Range	0 to 0		41 to 41		74 to 74		41 to 74	
Total episodes of Myasthenic Syndrome	0		1		1		2	
Average Episodes per subject	0		1.00		1.00		1.00	
Episode duration (days)‡								

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Summary of AEOSI - Myasthenic Syndrome
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Median	0		330.0		Not reached		330.0	
Range	0 to 0		330 to 330		255+ to 255+		255+ to 330	

(%) = Number of subjects with Myasthenic Syndrome / Number of subjects in population.
† Time to onset statistics are based on number of subjects with Myasthenic Syndrome.
‡ From product-limit (Kaplan-Meier) method for censored data. 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.
+ indicates the AE episode is not recovered/resolved by the time of the cutoff date or date of death.
Std = Standard Deviation.
Grades are based on NCI CTCAE version 4.0.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted].
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted].
(MK-3475 PN002 Database Cutoff Date: [redacted].
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Subjects With Adverse Events by Maximum Toxicity Grade
(Incidence >0% in One or More Treatment Groups)
AEOSI- Myasthenic Syndrome
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1,232		1,567		2,799	
with one or more adverse events	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)
Grade 2	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
Grade 3	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
with no adverse events	682	(100.0)	1,231	(99.9)	1,566	(99.9)	2,797	(99.9)
Nervous system disorders	**0**	**(0.0)**	**1**	**(0.1)**	**1**	**(0.1)**	**2**	**(0.1)**
Grade 2	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
Grade 3	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Myasthenic syndrome	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)
Grade 2	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
Grade 3	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)

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 for MEL: [redacted]).

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

(MK-3475 PN002 Database Cutoff Date: [redacted]).

(MK-3475 PN006 Database Cutoff Date: 03MAR2015).

(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of Concomitant Corticosteroid Use for AEOSI - Myasthenic Syndrome PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475 (APaT Population)

	P010 (N=682)		PN001 Lung, PN010 (N=1232)		PN001 Mel, PN002, PN006 (N=1567)		PN001,PN002, PN006, PN010 (N=2799)	
	n	%	n	%	n	%	n	%
Subjects with one or more Myasthenic Syndrome	0		1		1		2	
Treated with systemic corticosteroid	0	0	0	0	1	100.0	1	50.0
High starting dose†	0	0	0	0	1	100.0	1	50.0
Low starting dose‡	0	0	0	0	0	0	0	0
Not treated with systemic corticosteroid	0	0	1	100.0	0	0	1	50.0

The number of Subjects with one or more Myasthenic Syndrome is used as the denominator for the percentage calculation.
† 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.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of Concomitant Corticosteroid Use for AEOSI - Myasthenic Syndrome Episodes PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475 (APaT Population)

	P010	PN001 Lung, PN010	PN001 Mel, PN002, PN006	PN001,PN002, PN006, PN010
Total Episodes	0	1	1	2
High Starting Dose (%) †	**0 (0.0)**	**0 (0.0)**	**1 (100.0)**	**1 (50.0)**
Starting dose (mg/day)				
Mean (Std)	0 (0)	0 (0)	1250 (.)	1250 (.)
Median (Range)	0 (0-0)	0 (0-0)	1250 (1250-1250)	1250 (1250-1250)
Duration (days)§				
Mean (Std)	0 (0)	0 (0)	3 (.)	3 (.)
Median (Range)	0 (0-0)	0 (0-0)	3 (3-3)	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)**	**1 (100.0)**	**0 (0.0)**	**1 (50.0)**

†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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Listing of Subjects With Adverse Events
AEOSI- Myasthenic Syndrome
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q3W										
Trial Number=3475-001, Site Number=0023, Subject ID=001503, Gender=M, Race=White, Age=83 Years, Rel Day of Study Medication Discontinuance†=										
001503	Treatment Cycle 2	41	Myasthenic syndrome	1.68 Months	Moderate	2		Y	Interrupted	Resolved
	Treatment Cycle 4	92	Myasthenic syndrome	9.17 Months	Mild	1		Y		Resolved
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	Continuing		3	Y	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 for MEL: [redacted]).

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

(MK-3475 PN002 Database Cutoff Date: [redacted].

(MK-3475 PN006 Database Cutoff Date: 03MAR2015).

(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Listing of Concomitant Systemic Corticosteroid Use for AEOSI - Myasthenic Syndrome Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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	.	3
	120	16	Cortisone	30	QD	Oral	6.00	Myasthenic syndrome	74	.	3
	87	3	Methylprednisolone	1000	QD	Intravenous	1250.00	Myasthenic syndrome	74	.	3

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Listing of Concomitant Systemic Corticosteroid Use for AEOSI - Myasthenic Syndrome Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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
	104	6	Prednisolone	60	QD	Oral	60.00	Myasthenic syndrome	74	.	3
	135	31	Prednisolone	5	QD	Oral	5.00	Myasthenic syndrome	74	.	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 for MEL: [redacted].
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted].
(MK-3475 PN002 Database Cutoff Date: [redacted].
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Subjects With Adverse Events by Outcome
(Incidence > 0% in One or More Treatment Groups)
AEOSI- Myasthenic Syndrome
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

		P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	Outcome	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population		682		1,232		1,567		2,799	
With one or more adverse events	Overall	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)
	Fatal	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
	Not Resolved	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
	Resolved	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
	Unknown	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

Outcome: Resolved = RECOVERED/RESOLVED, Not resolved = NOT RECOVERED/NOT RESOLVED.
Every subject is counted once for the AE outcome, with the order: Fatal>Not Resolved>Resolving>Unknown>Sequelae>Resolved.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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付録 2.7.4- 76　　溶血性貧血の AEOSI 解析

001 試験＋002 試験＋006 試験＋010 試験

MK-3475 を投与された悪性黒色腫及び非小細胞肺癌患者（安全性解析対象集団）

Adverse Event Summary
AEOSI - Hematologic
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1,232		1,567		2,799	
with one or more adverse events	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
with no adverse event	682	(100.0)	1,231	(99.9)	1,567	(100.0)	2,798	(100.0)
with drug-related† adverse events	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
with Grade 3- 5 adverse events	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
with Grade 3- 5 drug-related adverse events	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
with serious adverse events	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
with serious drug-related adverse events	0	(0.0)	1	(0.1)	0	(0.0)	1	(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)	1	(0.1)	0	(0.0)	1	(0.0)
discontinued due to a drug-related adverse event	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
discontinued due to a serious adverse event	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
discontinued due to a serious drug-related adverse event	0	(0.0)	1	(0.1)	0	(0.0)	1	(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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted].
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of AEOSI - Hematologic
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1232		1567		2799	
Subjects with Hematologic	0		1	(0.1)	0		1	(0.0)
Time to Onset of First Hematologic (days)†								
Mean (Std)	0		286.0		0		286.0	
Median	0.0		286.0		0.0		286.0	
Range	0 to 0		286 to 286		0 to 0		286 to 286	
Total episodes of Hematologic	0		1		0		1	
Average Episodes per subject	0		1.00		0		1.00	
Episode duration (days)‡								

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Summary of AEOSI - Hematologic
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Median	0		Not reached		0		Not reached	
Range	0 to 0		214+ to 214+		0 to 0		214+ to 214+	

(%) = Number of subjects with Hematologic / Number of subjects in population.
† Time to onset statistics are based on number of subjects with Hematologic.
‡ From product-limit (Kaplan-Meier) method for censored data. 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.
+ indicates the AE episode is not recovered/resolved by the time of the cutoff date or date of death.
Std = Standard Deviation.
Grades are based on NCI CTCAE version 4.0.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted].
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted].
(MK-3475 PN002 Database Cutoff Date: [redacted].
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Subjects With Adverse Events by Maximum Toxicity Grade
(Incidence >0% in One or More Treatment Groups)
AEOSI- Hematologic
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1,232		1,567		2,799	
with one or more adverse events	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
Grade 3	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
with no adverse events	682	(100.0)	1,231	(99.9)	1,567	(100.0)	2,798	(100.0)
Blood and lymphatic system disorders	**0**	**(0.0)**	**1**	**(0.1)**	**0**	**(0.0)**	**1**	**(0.0)**
Grade 3	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
Autoimmune haemolytic anaemia	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
Grade 3	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)

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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of Concomitant Corticosteroid Use for AEOSI - Hematologic PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475 (APaT Population)

	P010 (N=682)		PN001 Lung, PN010 (N=1232)		Melanoma (N=1567)		PN001,PN002, PN006, PN010 (N=2799)	
	n	%	n	%	n	%	n	%
Subjects with one or more Hematologic	0		1		0		1	
Treated with systemic corticosteroid	0	0	1	100.0	0	0	1	100.0
High starting dose†	0	0	1	100.0	0	0	1	100.0
Low starting dose‡	0	0	0	0	0	0	0	0
Not treated with systemic corticosteroid	0	0	0	0	0	0	0	0

The number of Subjects with one or more Hematologic is used as the denominator for the percentage calculation.
† 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.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of Concomitant Corticosteroid Use for AEOSI - Hematologic Episodes PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475 (APaT Population)

	P010	PN001 Lung, PN010	PN001 Mel, PN002, PN006	PN001,PN002, PN006, PN010
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)	70 (.)	0 (0)	70 (.)
Median (Range)	0 (0-0)	70 (70-70)	0 (0-0)	70 (70-70)
Duration (days)§				
Mean (Std)	0 (0)	1 (.)	0 (0)	1 (.)
Median (Range)	0 (0-0)	1 (1-1)	0 (0-0)	1 (1-1)
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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Listing of Subjects With Adverse Events
AEOSI- Hematologic
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=0020, Subject ID=000987, Gender=M, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance[†]=272										
000987	Safety Follow-up	286	Autoimmune haemolytic anaemia	Continuing	Severe	3	Y	Y	Discontinued	Not Resolved

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

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

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

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

Grades are based on NCI CTCAE version 4.0.

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

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

(MK-3475 PN002 Database Cutoff Date: [redacted].

(MK-3475 PN006 Database Cutoff Date: 03MAR2015).

(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

Confidential

Listing of Concomitant Systemic Corticosteroid Use for AEOSI - Hematologic Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=3475-001, Site Number=0020, Subject ID=000987, Gender=M, Race=White, Age=66 Years, Rel Day of Study Medication Discontinuance‡=272											
000987	295	4	Dexamethasone	40	QD	Oral Administration	266.80	Autoimmune haemolytic anaemia	286	.	3
	286	1	Hydrocortisone Sodium Succinate	50	ONCE	Intravenous Administration	12.50	Autoimmune haemolytic anaemia	286	.	3
	292	1	Methylprednisolone Sodium Succinate	60	ONCE	Intravenous Administration	75.00	Autoimmune haemolytic anaemia	286	.	3

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Listing of Concomitant Systemic Corticosteroid Use for AEOSI - Hematologic Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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
	286	1	Prednisone	70	ONCE	Oral Administration	70.00	Autoimmune haemolytic anaemia	286	.	3
	288	1	Prednisone	140	QD	Oral Administration	140.00	Autoimmune haemolytic anaemia	286	.	3
	289	3	Prednisone	70	QD	Oral Administration	70.00	Autoimmune haemolytic anaemia	286	.	3
	299	.	Prednisone	105	QD	Oral Administration	105.00	Autoimmune haemolytic anaemia	286	.	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 for MEL: [redacted].
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted].
(MK-3475 PN002 Database Cutoff Date: [redacted].
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Subjects With Adverse Events by Outcome
(Incidence > 0% in One or More Treatment Groups)
AEOSI- Hematologic
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

		P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	Outcome	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population		682		1,232		1,567		2,799	
With one or more adverse events	Overall	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
	Fatal	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
	Not Resolved	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
	Resolved	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
	Unknown	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

Outcome: Resolved = RECOVERED/RESOLVED, Not resolved = NOT RECOVERED/NOT RESOLVED.
Every subject is counted once for the AE outcome, with the order: Fatal>Not Resolved>Resolving>Unknown>Sequelae>Resolved.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted].
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted].
(MK-3475 PN002 Database Cutoff Date: [redacted].
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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付録 2.7.4- 77　　心膜炎の AEOSI 解析

001 試験＋002 試験＋006 試験＋010 試験

MK-3475 を投与された悪性黒色腫及び非小細胞肺癌患者（安全性解析対象集団）

Adverse Event Summary
AEOSI - Pericarditis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1,232		1,567		2,799	
with one or more adverse events	1	(0.1)	1	(0.1)	1	(0.1)	2	(0.1)
with no adverse event	681	(99.9)	1,231	(99.9)	1,566	(99.9)	2,797	(99.9)
with drug-related† adverse events	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
with Grade 3- 5 adverse events	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
with Grade 3- 5 drug-related adverse events	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
with serious adverse events	1	(0.1)	1	(0.1)	1	(0.1)	2	(0.1)
with serious drug-related adverse events	0	(0.0)	0	(0.0)	1	(0.1)	1	(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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of AEOSI - Pericarditis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1232		1567		2799	
Subjects with Pericarditis	1	(0.1)	1	(0.1)	1	(0.1)	2	(0.1)
Time to Onset of First Pericarditis (days)†								
Mean (Std)	37.0		37.0		3.0		20.0 (24.0)	
Median	37.0		37.0		3.0		20.0	
Range	37 to 37		37 to 37		3 to 3		3 to 37	
Total episodes of Pericarditis	1		1		1		2	
Average Episodes per subject	1.00		1.00		1.00		1.00	
Episode duration (days)‡								

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Summary of AEOSI - Pericarditis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Median	Not reached		Not reached		11.0		Not reached	
Range	24+ to 24+		24+ to 24+		11 to 11		11 to 24+	

(%) = Number of subjects with Pericarditis / Number of subjects in population.
† Time to onset statistics are based on number of subjects with Pericarditis.
‡ From product-limit (Kaplan-Meier) method for censored data. 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.
+ indicates the AE episode is not recovered/resolved by the time of the cutoff date or date of death.
Std = Standard Deviation.
Grades are based on NCI CTCAE version 4.0.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Subjects With Adverse Events by Maximum Toxicity Grade
(Incidence >0% in One or More Treatment Groups)
AEOSI- Pericarditis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1,232		1,567		2,799	
with one or more adverse events	1	(0.1)	1	(0.1)	1	(0.1)	2	(0.1)
Grade 1	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
Grade 3	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
with no adverse events	681	(99.9)	1,231	(99.9)	1,566	(99.9)	2,797	(99.9)
Cardiac disorders	**1**	**(0.1)**	**1**	**(0.1)**	**1**	**(0.1)**	**2**	**(0.1)**
Grade 1	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
Grade 3	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Pericarditis	1	(0.1)	1	(0.1)	1	(0.1)	2	(0.1)
Grade 1	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
Grade 3	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)

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 for MEL: [redacted]).

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

(MK-3475 PN002 Database Cutoff Date: [redacted]).

(MK-3475 PN006 Database Cutoff Date: 03MAR2015).

(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of Concomitant Corticosteroid Use for AEOSI - Pericarditis PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475 (APaT Population)

	P010 (N=682)		PN001 Lung, PN010 (N=1232)		PN001 Mel, PN002, PN006 (N=1567)		PN001,PN002, PN006, PN010 (N=2799)	
	n	%	n	%	n	%	n	%
Subjects with one or more Pericarditis	1		1		1		2	
Treated with systemic corticosteroid	1	100.0	1	100.0	0	0	1	50.0
High starting dose†	0	0	0	0	0	0	0	0
Low starting dose‡	1	100.0	1	100.0	0	0	1	50.0
Not treated with systemic corticosteroid	0	0	0	0	1	100.0	1	50.0

The number of Subjects with one or more Pericarditis is used as the denominator for the percentage calculation.
† 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.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of Concomitant Corticosteroid Use for AEOSI - Pericarditis Episodes PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475 (APaT Population)

	P010	PN001 Lung, PN010	PN001 Mel, PN002, PN006	PN001,PN002, PN006, PN010
Total Episodes	1	1	1	2
High Starting Dose (%) †	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**
Low Starting Dose (%) ‡	**1 (100.0)**	**1 (100.0)**	**0 (0.0)**	**1 (50.0)**
Starting dose (mg/day)				
Mean (Std)	20 (.)	20 (.)	0 (0)	20 (.)
Median (Range)	20 (20-20)	20 (20-20)	0 (0-0)	20 (20-20)
Duration (days)§				
Mean (Std)	8 (.)	8 (.)	0 (0)	8 (.)
Median (Range)	8 (8-8)	8 (8-8)	0 (0-0)	8 (8-8)
Not Treated with Systemic Corticosteroid (%)	**0 (0.0)**	**0 (0.0)**	**1 (100.0)**	**1 (50.0)**

† 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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Listing of Subjects With Adverse Events
AEOSI- Pericarditis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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
Trial Number=3475-010, Site Number=0004, Subject ID=309510, Gender=F, Race=White, Age=61 Years, Rel Day of Study Medication Discontinuance[†]=22										
309510	Safety Follow-up	37	Pericarditis	Continuing		1	Y	N	None	Resolving

[†]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 for MEL: [redacted]).

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

(MK-3475 PN002 Database Cutoff Date: [redacted]).

(MK-3475 PN006 Database Cutoff Date: 03MAR2015).

(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Listing of Concomitant Systemic Corticosteroid Use for AEOSI - Pericarditis Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=3475-010, Site Number=0004, Subject ID=309510, Gender=F, Race=White, Age=61 Years, Rel Day of Study Medication Discontinuance[‡]=22											
309510	37	8	Prednisone	20	QD	Oral	20.00	Pericarditis	37	.	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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Subjects With Adverse Events by Outcome
(Incidence > 0% in One or More Treatment Groups)
AEOSI- Pericarditis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

		P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	Outcome	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population		682		1,232		1,567		2,799	
With one or more adverse events	Overall	1	(0.1)	1	(0.1)	1	(0.1)	2	(0.1)
	Fatal	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
	Not Resolved	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
	Resolved	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
	Resolving	1	(0.1)	1	(0.1)	0	(0.0)	1	(0.0)
	Unknown	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

Outcome: Resolved = RECOVERED/RESOLVED, Not resolved = NOT RECOVERED/NOT RESOLVED.
Every subject is counted once for the AE outcome, with the order: Fatal>Not Resolved>Resolving>Unknown>Sequelae>Resolved.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

Confidential

付録 2.7.4- 78　　血管炎の AEOSI 解析

001 試験＋002 試験＋006 試験＋010 試験

MK-3475 を投与された悪性黒色腫及び非小細胞肺癌患者（安全性解析対象集団）

Adverse Event Summary
AEOSI - Vasculitis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1,232		1,567		2,799	
with one or more adverse events	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)
with no adverse event	682	(100.0)	1,231	(99.9)	1,566	(99.9)	2,797	(99.9)
with drug-related† adverse events	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)
with Grade 3- 5 adverse events	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
with Grade 3- 5 drug-related adverse events	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
with serious adverse events	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
with serious drug-related adverse events	0	(0.0)	1	(0.1)	0	(0.0)	1	(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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of AEOSI - Vasculitis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1232		1567		2799	
Subjects with Vasculitis	0		1	(0.1)	1	(0.1)	2	(0.1)
Time to Onset of First Vasculitis (days)†								
Mean (Std)	0		113.0		45.0		79.0 (48.1)	
Median	0.0		113.0		45.0		79.0	
Range	0 to 0		113 to 113		45 to 45		45 to 113	
Total episodes of Vasculitis	0		1		1		2	
Average Episodes per subject	0		1.00		1.00		1.00	
Episode duration (days)‡								

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Summary of AEOSI - Vasculitis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001,PN002, PN006, PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Median	0		9.0		145.0		77.0	
Range	0 to 0		9 to 9		145 to 145		9 to 145	

(%) = Number of subjects with Vasculitis / Number of subjects in population.
† Time to onset statistics are based on number of subjects with Vasculitis.
‡ From product-limit (Kaplan-Meier) method for censored data. 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.
+ indicates the AE episode is not recovered/resolved by the time of the cutoff date or date of death.
Std = Standard Deviation.
Grades are based on NCI CTCAE version 4.0.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted].
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted].
(MK-3475 PN002 Database Cutoff Date: [redacted].
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Subjects With Adverse Events by Maximum Toxicity Grade
(Incidence >0% in One or More Treatment Groups)
AEOSI- Vasculitis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

	P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population	682		1,232		1,567		2,799	
with one or more adverse events	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)
Grade 1	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Grade 3	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
with no adverse events	682	(100.0)	1,231	(99.9)	1,566	(99.9)	2,797	(99.9)
Vascular disorders	**0**	**(0.0)**	**1**	**(0.1)**	**1**	**(0.1)**	**2**	**(0.1)**
Grade 1	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Grade 3	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)
Vasculitis	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)
Grade 1	0	(0.0)	0	(0.0)	1	(0.1)	1	(0.0)
Grade 3	0	(0.0)	1	(0.1)	0	(0.0)	1	(0.0)

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 for MEL: [redacted]).

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

(MK-3475 PN002 Database Cutoff Date: [redacted]).

(MK-3475 PN006 Database Cutoff Date: 03MAR2015).

(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of Concomitant Corticosteroid Use for AEOSI - Vasculitis PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475 (APaT Population)

	P010 (N=682)		PN001 Lung, PN010 (N=1232)		PN001 Mel, PN002, PN006 (N=1567)		PN001,PN002, PN006, PN010 (N=2799)	
	n	%	n	%	n	%	n	%
Subjects with one or more Vasculitis	0		1		1		2	
Treated with systemic corticosteroid	0	0	1	100.0	0	0	1	50.0
High starting dose†	0	0	1	100.0	0	0	1	50.0
Low starting dose‡	0	0	0	0	0	0	0	0
Not treated with systemic corticosteroid	0	0	0	0	1	100.0	1	50.0

The number of Subjects with one or more Vasculitis is used as the denominator for the percentage calculation.
† 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.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Summary of Concomitant Corticosteroid Use for AEOSI - Vasculitis Episodes PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475 (APaT Population)

	P010	PN001 Lung, PN010	PN001 Mel, PN002, PN006	PN001,PN002, PN006, PN010
Total Episodes	0	1	1	2
High Starting Dose (%) †	**0 (0.0)**	**1 (100.0)**	**0 (0.0)**	**1 (50.0)**
Starting dose (mg/day)				
Mean (Std)	0 (0)	75 (.)	0 (0)	75 (.)
Median (Range)	0 (0-0)	75 (75-75)	0 (0-0)	75 (75-75)
Duration (days)§				
Mean (Std)	0 (0)	29 (.)	0 (0)	29 (.)
Median (Range)	0 (0-0)	29 (29-29)	0 (0-0)	29 (29-29)
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)**	**1 (100.0)**	**1 (50.0)**

† 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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Listing of Subjects With Adverse Events
AEOSI- Vasculitis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

Subject ID	Epoch	Rel Day of Onset	Adverse Event	Duration	Intensity	Toxicity Grade	Ser-ious	Related	Action Taken	Outcome
MK-3475 10 mg/kg Q3W										
Trial Number=3475-001, Site Number=0023, Subject ID=001589, Gender=M, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance†=169										
001589	Treatment Cycle 4	113	Vasculitis	1.29 Weeks	Severe	3	Y	Y		Resolved
Trial Number=3475-002, Site Number=0070, Subject ID=100691, Gender=M, Race=White, Age=44 Years, Rel Day of Study Medication Discontinuance†=										
100691	Treatment Cycle 3	45	Vasculitis	4.76 Months		1	N	Y	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 for MEL: [redacted]).

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

(MK-3475 PN002 Database Cutoff Date: [redacted]).

(MK-3475 PN006 Database Cutoff Date: 03MAR2015).

(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Listing of Concomitant Systemic Corticosteroid Use for AEOSI - Vasculitis Adverse Events
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

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=0023, Subject ID=001589, Gender=M, Race=White, Age=70 Years, Rel Day of Study Medication Discontinuance[‡]=169											
001589	113	29	Prednisolone	75	QD	Oral Administration	75.00	Vasculitis	113	121	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 for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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Subjects With Adverse Events by Outcome
(Incidence > 0% in One or More Treatment Groups)
AEOSI- Vasculitis
PN001, PN002, PN006 and PN010 Subjects Treated with MK-3475
(APaT Population)

		P010		PN001 Lung, PN010		PN001 Mel, PN002, PN006		PN001 PN002 PN006 PN010	
	Outcome	n	(%)	n	(%)	n	(%)	n	(%)
Subjects in population		682		1,232		1,567		2,799	
With one or more adverse events	Overall	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)
	Fatal	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
	Not Resolved	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)
	Resolved	0	(0.0)	1	(0.1)	1	(0.1)	2	(0.1)
	Unknown	0	(0.0)	0	(0.0)	0	(0.0)	0	(0.0)

Outcome: Resolved = RECOVERED/RESOLVED, Not resolved = NOT RECOVERED/NOT RESOLVED.
Every subject is counted once for the AE outcome, with the order: Fatal>Not Resolved>Resolving>Unknown>Sequelae>Resolved.
(MK-3475 PN001 Database Cutoff Date for MEL: [redacted]).
(MK-3475 PN001 Database Cutoff Date for Lung: [redacted]).
(MK-3475 PN002 Database Cutoff Date: [redacted]).
(MK-3475 PN006 Database Cutoff Date: 03MAR2015).
(MK-3475 PN010 Database Cutoff Date: 30SEP2015).

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付録 2.7.4- 79　　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 C 及び F）（安全性解析対象集団）

Summary of Worsening in Laboratory CTCAE Grades from Baseline to Worst Value Post-baseline
All Subjects with NSCLC by Dose
(All Subjects as Treated)

Laboratory Test	MK-3475 2 mg/kg Q3W (N=61)	MK-3475 10 mg/kg Q3W (N=287)	MK-3475 10 mg/kg Q2W (N=202)	Total (N=550)
APTT Increased				
Improved from baseline	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Worsened from baseline	5 (8.2)	7 (2.4)	13 (6.4)	25 (4.5)
Clinically meaningful[†] worsened from baseline	1 (1.6)	0 (0.0)	2 (1.0)	3 (0.5)
Alanine Aminotransferase Increased				
Improved from baseline	0 (0.0)	1 (0.3)	1 (0.5)	2 (0.4)
Worsened from baseline	11 (18.0)	49 (17.1)	42 (20.8)	102 (18.5)
Clinically meaningful[†] worsened from baseline	1 (1.6)	7 (2.4)	6 (3.0)	14 (2.5)
Albumin Decreased				
Improved from baseline	1 (1.6)	1 (0.3)	2 (1.0)	4 (0.7)
Worsened from baseline	21 (34.4)	90 (31.4)	77 (38.1)	188 (34.2)
Clinically meaningful[†] worsened from baseline	5 (8.2)	13 (4.5)	12 (5.9)	30 (5.5)

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Summary of Worsening in Laboratory CTCAE Grades from Baseline to Worst Value Post-baseline
All Subjects with NSCLC by Dose
(All Subjects as Treated)

Laboratory Test	MK-3475 2 mg/kg Q3W (N=61)	MK-3475 10 mg/kg Q3W (N=287)	MK-3475 10 mg/kg Q2W (N=202)	Total (N=550)
Alkaline Phosphatase Increased				
Improved from baseline	0 (0.0)	1 (0.3)	0 (0.0)	1 (0.2)
Worsened from baseline	15 (24.6)	68 (23.7)	64 (31.7)	147 (26.7)
Clinically meaningful[†] worsened from baseline	3 (4.9)	6 (2.1)	5 (2.5)	14 (2.5)
Aspartate Aminotransferase Increased				
Improved from baseline	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Worsened from baseline	8 (13.1)	58 (20.2)	49 (24.3)	115 (20.9)
Clinically meaningful[†] worsened from baseline	2 (3.3)	10 (3.5)	5 (2.5)	17 (3.1)
Bilirubinn Increased				
Improved from baseline	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Worsened from baseline	2 (3.3)	18 (6.3)	17 (8.4)	37 (6.7)
Clinically meaningful[†] worsened from baseline	0 (0.0)	10 (3.5)	7 (3.5)	17 (3.1)

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Summary of Worsening in Laboratory CTCAE Grades from Baseline to Worst Value Post-baseline
All Subjects with NSCLC by Dose
(All Subjects as Treated)

Laboratory Test	MK-3475 2 mg/kg Q3W (N=61)	MK-3475 10 mg/kg Q3W (N=287)	MK-3475 10 mg/kg Q2W (N=202)	Total (N=550)
Calcium Decreased				
Improved from baseline	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Worsened from baseline	14 (23.0)	60 (20.9)	42 (20.8)	116 (21.1)
Clinically meaningful[†] worsened from baseline	4 (6.6)	9 (3.1)	8 (4.0)	21 (3.8)
Calcium Increased				
Improved from baseline	0 (0.0)	1 (0.3)	0 (0.0)	1 (0.2)
Worsened from baseline	3 (4.9)	13 (4.5)	12 (5.9)	28 (5.1)
Clinically meaningful[†] worsened from baseline	0 (0.0)	1 (0.3)	2 (1.0)	3 (0.5)
Cholesterol				
Improved from baseline	0 (0.0)	2 (0.7)	0 (0.0)	2 (0.4)
Worsened from baseline	8 (13.1)	62 (21.6)	50 (24.8)	120 (21.8)
Clinically meaningful[†] worsened from baseline	1 (1.6)	6 (2.1)	8 (4.0)	15 (2.7)

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Summary of Worsening in Laboratory CTCAE Grades from Baseline to Worst Value Post-baseline
All Subjects with NSCLC by Dose
(All Subjects as Treated)

Laboratory Test	MK-3475 2 mg/kg Q3W (N=61)	MK-3475 10 mg/kg Q3W (N=287)	MK-3475 10 mg/kg Q2W (N=202)	Total (N=550)
Creatinine Increased				
Improved from baseline	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Worsened from baseline	10 (16.4)	38 (13.2)	18 (8.9)	66 (12.0)
Clinically meaningful[†] worsened from baseline	0 (0.0)	4 (1.4)	0 (0.0)	4 (0.7)
Glucose Decreased				
Improved from baseline	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Worsened from baseline	3 (4.9)	11 (3.8)	11 (5.4)	25 (4.5)
Clinically meaningful[†] worsened from baseline	0 (0.0)	1 (0.3)	2 (1.0)	3 (0.5)
Glucose Increased				
Improved from baseline	0 (0.0)	4 (1.4)	2 (1.0)	6 (1.1)
Worsened from baseline	24 (39.3)	155 (54.0)	98 (48.5)	277 (50.4)
Clinically meaningful[†] worsened from baseline	5 (8.2)	35 (12.2)	18 (8.9)	58 (10.5)

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Summary of Worsening in Laboratory CTCAE Grades from Baseline to Worst Value Post-baseline
All Subjects with NSCLC by Dose
(All Subjects as Treated)

Laboratory Test	MK-3475 2 mg/kg Q3W (N=61)	MK-3475 10 mg/kg Q3W (N=287)	MK-3475 10 mg/kg Q2W (N=202)	Total (N=550)
Hemoglobin Decreased				
Improved from baseline	2 (3.3)	4 (1.4)	3 (1.5)	9 (1.6)
Worsened from baseline	21 (34.4)	107 (37.3)	74 (36.6)	202 (36.7)
Clinically meaningful[†] worsened from baseline	2 (3.3)	12 (4.2)	11 (5.4)	25 (4.5)
Leukocytes Decreased				
Improved from baseline	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Worsened from baseline	2 (3.3)	24 (8.4)	25 (12.4)	51 (9.3)
Clinically meaningful[†] worsened from baseline	0 (0.0)	5 (1.7)	9 (4.5)	14 (2.5)
Lymphocytes Decreased				
Improved from baseline	0 (0.0)	2 (0.7)	2 (1.0)	4 (0.7)
Worsened from baseline	11 (18.0)	55 (19.2)	38 (18.8)	104 (18.9)
Clinically meaningful[†] worsened from baseline	5 (8.2)	26 (9.1)	19 (9.4)	50 (9.1)

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Summary of Worsening in Laboratory CTCAE Grades from Baseline to Worst Value Post-baseline
All Subjects with NSCLC by Dose
(All Subjects as Treated)

Laboratory Test	MK-3475 2 mg/kg Q3W (N=61)	MK-3475 10 mg/kg Q3W (N=287)	MK-3475 10 mg/kg Q2W (N=202)	Total (N=550)
Magnesium Decreased				
Improved from baseline	0 (0.0)	0 (0.0)	1 (0.5)	1 (0.2)
Worsened from baseline	6 (9.8)	38 (13.2)	37 (18.3)	81 (14.7)
Clinically meaningful[†] worsened from baseline	0 (0.0)	0 (0.0)	3 (1.5)	3 (0.5)
Magnesium Increased				
Improved from baseline	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Worsened from baseline	4 (6.6)	23 (8.0)	10 (5.0)	37 (6.7)
Clinically meaningful[†] worsened from baseline	0 (0.0)	0 (0.0)	2 (1.0)	2 (0.4)
Neutrophils Decreased				
Improved from baseline	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Worsened from baseline	0 (0.0)	4 (1.4)	7 (3.5)	11 (2.0)
Clinically meaningful[†] worsened from baseline	0 (0.0)	3 (1.0)	2 (1.0)	5 (0.9)

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Summary of Worsening in Laboratory CTCAE Grades from Baseline to Worst Value Post-baseline
All Subjects with NSCLC by Dose
(All Subjects as Treated)

Laboratory Test	MK-3475 2 mg/kg Q3W (N=61)	MK-3475 10 mg/kg Q3W (N=287)	MK-3475 10 mg/kg Q2W (N=202)	Total (N=550)
Phosphate Decreased				
Improved from baseline	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Worsened from baseline	7 (11.5)	54 (18.8)	41 (20.3)	102 (18.5)
Clinically meaningful[†] worsened from baseline	5 (8.2)	43 (15.0)	36 (17.8)	84 (15.3)
Platelet Decreased				
Improved from baseline	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Worsened from baseline	4 (6.6)	31 (10.8)	18 (8.9)	53 (9.6)
Clinically meaningful[†] worsened from baseline	1 (1.6)	4 (1.4)	5 (2.5)	10 (1.8)
Potassium Decreased				
Improved from baseline	0 (0.0)	2 (0.7)	0 (0.0)	2 (0.4)
Worsened from baseline	2 (3.3)	32 (11.1)	25 (12.4)	59 (10.7)
Clinically meaningful[†] worsened from baseline	0 (0.0)	4 (1.4)	5 (2.5)	9 (1.6)

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Summary of Worsening in Laboratory CTCAE Grades from Baseline to Worst Value Post-baseline
All Subjects with NSCLC by Dose
(All Subjects as Treated)

Laboratory Test	MK-3475 2 mg/kg Q3W (N=61)	MK-3475 10 mg/kg Q3W (N=287)	MK-3475 10 mg/kg Q2W (N=202)	Total (N=550)
Potassium Increased				
Improved from baseline	0 (0.0)	1 (0.3)	0 (0.0)	1 (0.2)
Worsened from baseline	5 (8.2)	34 (11.8)	25 (12.4)	64 (11.6)
Clinically meaningful[†] worsened from baseline	1 (1.6)	6 (2.1)	5 (2.5)	12 (2.2)
Prothrombin Intl. Normalized Ratio In				
Improved from baseline	0 (0.0)	1 (0.3)	0 (0.0)	1 (0.2)
Worsened from baseline	3 (4.9)	10 (3.5)	9 (4.5)	22 (4.0)
Clinically meaningful[†] worsened from baseline	0 (0.0)	2 (0.7)	2 (1.0)	4 (0.7)
Sodium Decreased				
Improved from baseline	0 (0.0)	1 (0.3)	0 (0.0)	1 (0.2)
Worsened from baseline	19 (31.1)	108 (37.6)	86 (42.6)	213 (38.7)
Clinically meaningful[†] worsened from baseline	3 (4.9)	17 (5.9)	14 (6.9)	34 (6.2)

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Summary of Worsening in Laboratory CTCAE Grades from Baseline to Worst Value Post-baseline
All Subjects with NSCLC by Dose
(All Subjects as Treated)

Laboratory Test	MK-3475 2 mg/kg Q3W (N=61)	MK-3475 10 mg/kg Q3W (N=287)	MK-3475 10 mg/kg Q2W (N=202)	Total (N=550)
Triglycerides				
Improved from baseline	0 (0.0)	1 (0.3)	1 (0.5)	2 (0.4)
Worsened from baseline	17 (27.9)	66 (23.0)	53 (26.2)	136 (24.7)
Clinically meaningful† worsened from baseline	1 (1.6)	3 (1.0)	2 (1.0)	6 (1.1)

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])

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