Mild: (Grade 0) The value is deviated from the normal ranges at the site, but the value does not satisfy the Grade 1 of DAIDS grading. (Grade 1) A sign or symptom is present, but does not interfere with the subject's daily activities and does not require treatment.

Moderate: (Grade 2) An event that interferes with the subject's daily activities because of discomfort, or affects the clinical condition and requires treatment.

Severe: (Grade 3, Grade 4) An event by which the subject is unable to conduct daily activities or significant clinical effects are observed.

The grade of abnormal value was written in the CRF.

9.5.2.7.3 Evaluation of AEs

If an AE occurred, the principal investigator was to enter the following information in the CRF: the details, onset date/time, severity and seriousness (serious or non-serious) of the AE, other actions, outcome (not resolved, resolved with sequelae, resolved, unknown or; for other cases, their details), and the causal relationship with the study drug. The severity and causal relationship with the study drug were to be assessed using the following criteria as a reference.

• Criteria for severity

Mild: Treatment or action was not necessary for the AE.

Moderate: Treatment or action was required for the AE.

Severe: Therapy or treatment was required for the AE and the study was discontinued.

• Criteria for assessment of the causal relationship with the study drug

Changes over time in symptoms, laboratory values, etc. before/after administration and at follow-up observation were to be fully compared, and while taking account of changes, diurnal variation, measurement errors, etc. in related symptoms or tests, the causal relationship with the study drug was to be evaluated. For events assessed as "Unknown", "Probably not related" or "Not related" with the study drug, the reasons were to be recorded in the CRF.

(1) Related:

There is a clear temporal correlation with study drug administration, and the known response of the study drug is shown, and there are hardly other possible reasons.

(2) Probably related:

There is a clear temporal correlation with study drug administration. The expected response based on pharmacological effect of the study drug is shown. The relationship with medical history of subjects and factors other than study drug are denied, and the relationship with the study drug cannot be denied.

(3) Unknown:

There is a clear temporal correlation with study drug administration. The relationship with medical history of patients and factors other than study drug are supposed, but the relationship with the study drug cannot be denied.

(4) Probably not related:

There is unlikely to be a temporal correlation with study drug administration, or there is some information denying the relationship with the study drug.

(5) Not related:

There is not a temporal correlation with study drug administration, or there is enough information that the event is not related to the study drug.

9.5.2.7.4 Handling at Onset of AE and Follow-up Action

(1) Handling at onset of AE (clinical symptom)

1) In the event of AEs, the principal investigator was to consider medical actions, etc. as necessary for assurance of subjects' safety.
2) When medical actions were required, the principal investigator was to take the best action and, in principle, continue a follow-up until the symptoms resolved after informing such a fact to the subject.
3) When the unknown serious AE was shown, followed the below section (4).
4) The principal investigator was to confirm that the developed AE resolved or became stable.
5) When the continuation of the study was judged to be difficult due to AEs, the principal investigator was to discontinue the study and follow up the subsequent course.

Predictability was defined as follows: Unknown was when the onset trend, such as onset, number of cases, incidence and onset condition, of the case could not be predicted based on information in the package insert of the study drug, and known was when the case could be predicted.

(2) Actions at the onset of abnormal laboratory values

1) When abnormal laboratory values were noted after study drug administration, the principal investigator was to, in principle, perform a follow-up investigation until they returned to reference or baseline levels and as necessary give treatment.
2) When the continuation of the study was judged to be difficult due to AEs, the principal investigator was to discontinue the study and follow up the subsequent course.
3) When the unknown serious AE was shown, follow the below section (4).

(3) Handling at onset of serious AE

1) In the event of serious AEs, the principal investigator was to consider medical actions, etc. as necessary for assurance of subjects' safety.
2) When medical actions were required, the principal investigator was to inform such a fact to the subject.
3) The principal investigator was to confirm that the developed AE resolved or became stable.
4) When the unknown serious AE was shown, follow the below section (4).

(4) Reporting at onset of serious AE

When a serious AE occurred, the principal investigator was immediately to report to the head of the study site, executive investigator, and principal investigators in other study sites (by e-mail or Fax). And the principal investigator was to inform manufacturer, Boehringer Ingelheim and its affiliated companies in Japan, China and the US. Only in Korea, a serous AE was to be reported to KFDA. (by e-mail or Fax in Japan, China, and Korea; by telephone in the US). What was informed by e-mail or Fax is shown in "Protocol 22 Appendix 2".

【Contact address for serious AEs 】

- Executive investigator

  Professor Shinichi Kawai

  Division of Rheumatology, Department of Internal Medicine (Omori), Toho University School of Medicine

  e-mail : skawai@med.toho-u.ac.jp

  Fax : +81-3-5753-8513

- Manufacturer

<Japan>

Nippon Boehringer Ingelheim Co., Ltd.
Medical Development Division, Safety Management dept. Risk Evaluation and Management Group 1
Noriyuki Sebata, Mai Kitashiro
e-mail: ADR@kaw.boehringer-ingelheim.com
Fax : +81-3-5435-2911

<China>

Boehringer Ingelheim Shanghai Pharmaceuticals Co., Ltd.
Associate Drug Safety Director, Medical Department
Rui Liu
Fax : +86-21-5882-2656
e-mail : Rui.liu@boehringer-ingelheim.com

<Korea>

Korean Food and Drug Administration (KFDA)
Pharmaceutical safety Bureau, Pharmaceutical Management Division

<US>

Boehringer Ingelheim Pharmaceuticals, Inc.
Drug Information Unit
Tel : +1-800-542-6257

9.5.2.8 Appropriateness of Measurements

All clinical and laboratory procedures that were used in this study were standard and generally accepted. Details of all methodology and reference ranges are provided in Appendix 7.

9.6 Data Quality Assurance

Throughout the study, close interaction was maintained between the principal investigator, the researchers, the executive investigator and the study monitors. Periodic visits were made to the study site to carry out trial monitoring and source document review.

The Quality Assurance Department, Quality Management Division, CMIC Co., Ltd. conducted a procedural audit at Pharmacokinetics and Bioanalysis Center, Shin Nippon Biomedical Laboratories, Ltd in Japan and Seoul National University Hospital in Korea which included review of the trial master file and the obtaining of informed consent. The audit certificate is included in Appendix 6.

A quality control check of the database against the source data was performed. Further quality control checks were performed on the data listings and summary tables presented in this report.

9.7 Statistical Methods Planned in the Protocol and Determination of Sample Size

9.7.1 Handling of Data in Analyses

After study completion, the executive investigator was to fix the CRFs and decide the handling of incomplete subjects falling into the following items, as necessary, based on the specialist's advice:

1) Ineligible: Those who did not fulfill the inclusion criteria or met the exclusion criteria
2) Discontinuation: Those who satisfied the discontinuation criteria for subjects
3) Action violation: Those who deviated from the protocol in terms of administration, observation method, implementation timing, etc.
4) Other deviations

Of the above Items 1) to 4), "1) Ineligible," "3) Action violation" and "4) Other deviations" were considered to be deviations.

The following time allowance of blood sampling and laboratory tests was not to be regarded as deviations.

(1) Acceptable range of blood collection time (plasma concentration)

- 1 to 8 hours after administration: ± 5 minutes
- 12 and 24 hours after administration: ± 10 minutes
- 36 to 72 hours after administration: ± 30 minutes

(2) Acceptable range of laboratory testing time

- 72 hours after administration: ± 1 hour

(3) Acceptable range of vital sign measuring time

- 24 hours after administration: ± 30 minutes
- 48 and 72 hours after administration: ± 1 hour

How to deal with missing and outlying (abnormal) values:

When the subject discontinued the study at early stage, the data were to be treated as missed and not compensated. Missing data due to the leakage of specimens by the breakage of the container, back-up samples were to be measured and used to compensate the data as references. The outlying (abnormal) value was not to be disregarded and handling of these data was to be written in the study report, if necessary.

9.7.2 Statistical and Analytical Plan for Clinical Safety Data

9.7.2.1 Criteria for Evaluation

Individual and summary blood pressure, pulse rate, body temperature, clinical laboratory tests (hematology, blood biochemistry and urinalysis), and AEs were to be included in the evaluation of safety.

9.7.2.2 Analytical Plan

All subjects who received the study drug, including those who did not complete the study, were to be included in the safety data analysis.

The list of baseline backgrounds of the safety analysis set (at screening) was prepared and frequency tabulation or basic statistics (mean, median, minimum and maximum) was calculated.

Individual and summary blood pressures, pulse rate, body temperature, body weight and clinical laboratory data, were to be presented in tabular form with mean, median, standard deviation (SD) and range (minimum and maximum) as appropriate.

For the laboratory safety data out of range values were to be flagged in the data listings and a list of clinically significant abnormal values was to be presented.

AEs were to be tabulated and summarised according to MedDRA (Ver. 13.0 or more), and classified by preferred term and system organ class.

9.7.3 Determination of Sample Size

The number of subjects required for the study examining PK differences between the ethnic groups was calculated. The number of subjects of each ethnic group required for detecting 20% differences of $AUC_{0-\infty}$ between the ethnic groups at 5% of significance level and 80% or more of detective power was calculated. For multiplicity of the test, the significant level of each test can be set to be 5%, assuming that the equivalence of 4 countries can be indicated only if the equivalence between Japanese/Koreans, Japanese/Chinese, and Japanese/Caucasians is statistically verified. In addition, calculation is made with 0.928... ($\sqrt[3]{0.8}$) of detective power of each study so that the detective power of the whole study may be 80% or more. The number of subjects of each ethnic group was estimated, using the existing Japanese data as basic mean and variance, to be 29, but considering discontinued cases and withdrawals, the target number of subjects of this study was defined to be 30.

9.8 Changes to the Conduct of the Study and Planned Analyses

<Japan, China, Korea and the US>
Two protocol amendments were issued for this study.
Amendment 1 (Version 1.1) was issued on 28 September 2010, and called for the following change:

- Two drug-concentration-measuring sites in Japan became integrated according to SNBL's convenience.

Amendment 2 (Version 1.2) was issued on 4 October 2010, and called for the following change:

- Since the space for seal or signature is not set for CRF of this study, the last sentence of item 1 in Chapter 14 was deleted.

<Korea>
One more protocol amendment was issued in Korea.

Amendment of the protocol attachment (Version 1.3K) was issued on 7 January 2011, and called for the following change:

- The monitor has been changed.

The same version number, 1.3K, has assigned to both main part and attachment according to the IRB's request although there was no change in main part.

The pre and post amendment points are included in Appendix 1.

10. STUDY SUBJECTS

10.1 Disposition of Subjects

The disposition of the subjects is shown in Figure 10- 1.

The study was conducted from 16 November 2010 to 21 December 2010 (Table 10-2).

Total 121 subjects (30 in Japan, 30 in China, 30 in Korea and 31 in the US) were enrolled into the study after confirmation of the eligibility, and 119 subjects (30 in Japan, 30 in China, 29 in Korea and 30 in the US) except 2 (1 in Korea and 1 in the US) were completed the study. The incomplete 2 subjects were withdrawn from the study because 1 Korean subject did not fulfill inclusion or exclusion criteria and 1 Caucasian subject withdrew his consent before administration of the study drug. Information about the 2 subjects with withdrawal and the 10 subjects with ineligible/action violation/other deviations is shown in Appendix 8.3 and Appendix 8.4, respectively. The 119 subjects were regarded as the safety population (Table 10-1).

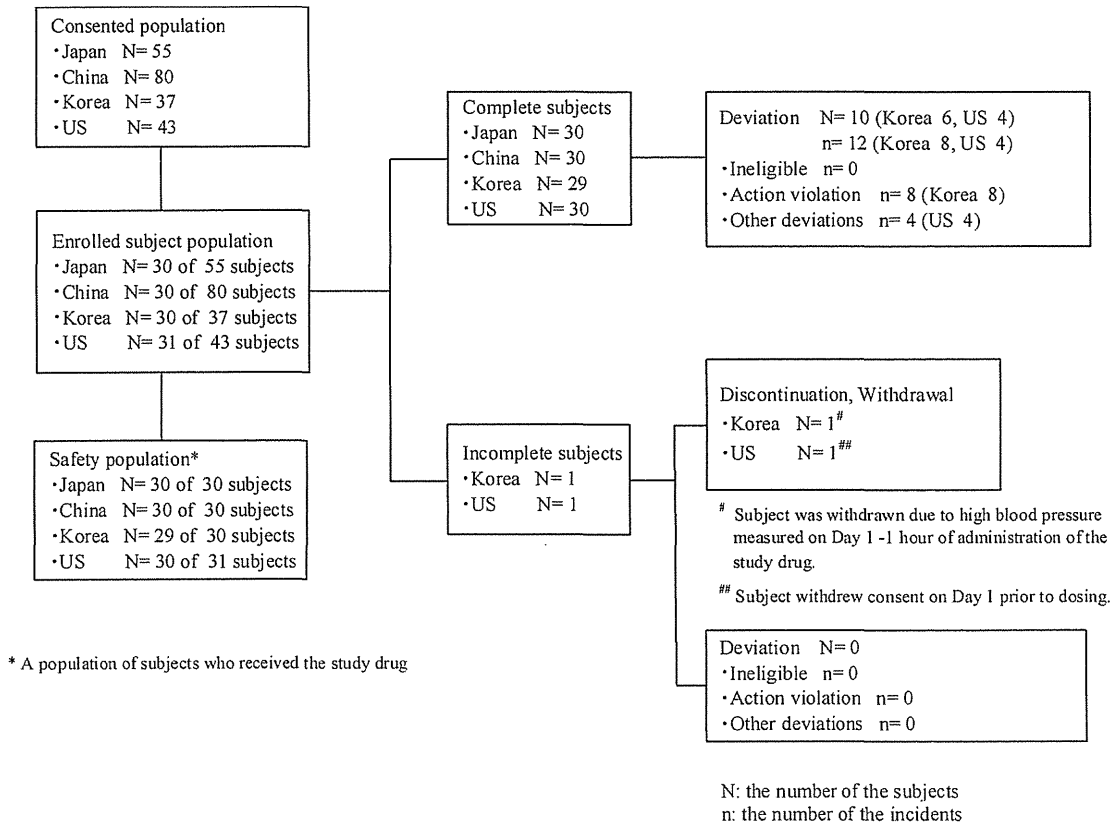

Figure 10- 1 Disposition of Subjects

Table 10-1 Analysis Population

Population	Japanese (Japan)	Chinese (China)	Korean (Korea)	Caucasian (US)	Total
Consented population	55	80	37	43	215
Enrolled subject population	30	30	30	31	121
Safety population	30	30	29*	30**	119

* After enrolling the subject into the study, it was confirmed that this subject deviated from the study protocol. The subject dropped out before study drug administration.

** The subject withdrew the consent on Day 1 prior to dosing.

Table 10-2 Study period in each ethnic group

Group No.	Japanese (Japan)	Chinese (China)	Korean (Korea)	Caucasian (US)
Group 1	16-20 Nov 2010 (15)	18-22 Nov 2010 (19)	24-28 Nov 2010 (6)	13-17 Dec 2010 (11)
Group 2	30 Nov-4 Dec 2010 (15)	25-29 Nov 2010 (11)	1-5 Dec 2010 (7)	17-21 Dec 2010 (19)
Group 3			6-10 Dec 2010 (7)	
Group 4			8-12 Dec 2010 (3)	
Group 5			13-17 Dec 2010 (6)	

The dates of the admission and follow-up of each group were described.
The figures in parentheses are the number of subjects who received the study drug.

10.2 Protocol Deviations

The subjects with ineligible, action violation or other deviation are listed in Appendix 8.4. There were no major protocol deviations. A number of minor deviations were noted for various study assessments, and a small number of assessments were not performed in error. These were not considered to have a significant effect on the validity of the study.

No subjects were excluded from the safety population due to the protocol deviation.

<Japanese (Japan)>

No deviation.

<Chinese (China)>

No deviation.

<Korean (Korea)>

The PK sampling at 6 hours was conducted 8 minutes later than the scheduled time in 1 subject (Subject No. 000030001). It was deviated 3 minutes from time allowance (acceptable range: ± 5 minutes).

Four subjects* drank water from water purifier instead of soft mineral water.

* Subject Nos. 000030007, 000030011, 000030013, 000030014

The assessments of 3 incidents (body temperature, blood pressure and pulse rate) at 24 hours after administration of the study drug were conducted 34 minutes earlier than the scheduled time in 1 subject (Subject No. 000030024). These were deviated 4 minutes from the time allowance (acceptable range: ± 30 minutes).

<Caucasian (US)>

Four subjects* checked into the study site after the scheduled time (16:30) on the day before study drug administration.

* Subject Nos. 000040003, 000040009, 000040032, 000040039

10.3 Demographic and Other Baseline Characteristics

Table 10-3 shows summary statistics of demographic and other baseline characteristic data for the safety population. All subjects who received the study drug in each study site were healthy male volunteers who fulfilled all of the inclusion criteria and none of the exclusion criteria.

Table 10-3 Summary of demographic and other baseline characteristics

Parameter		Japanese	Chinese	Korean	Caucasian
Number of subjects		30	30	29	30
Sex	Male	30 (100.0)	30 (100.0)	29 (100.0)	30 (100.0)
	Female	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Race	Chinese	0 (0.0)	30 (100.0)	0 (0.0)	0 (0.0)
	Japanese	30 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Korean	0 (0.0)	0 (0.0)	29 (100.0)	0 (0.0)
	White	0 (0.0)	0 (0.0)	0 (0.0)	30 (100.0)
	Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Age [years]	Mean	24.6	31.3	24.2	26.5
	SD	2.99	2.52	2.05	4.08
	Minimum	21.0	23.0	21.0	21.0
	Median	24.00	31.00	24.00	25.50
	Maximum	30.0	34.0	29.0	35.0
Height [cm]	Mean	171.2	168.7	176.7	176.5
	SD	4.85	5.17	5.21	7.88
	Minimum	160.5	160.0	168.1	162.0
	Median	172.00	168.00	176.50	176.75
	Maximum	179.6	180.0	186.3	195.0
Body Weight [kg]	Mean	64.7	67.0	69.7	77.8
	SD	9.59	9.25	7.56	12.96
	Minimum	52.1	51.0	56.3	55.9
	Median	63.50	67.00	69.10	74.45
	Maximum	84.5	91.0	84.4	100.0
BMI [kg/m^2]	Mean	22.1	23.5	22.3	24.9
	SD	3.01	2.57	1.93	3.10
	Minimum	18.6	19.2	19.2	19.9
	Median	21.65	23.45	22.60	24.55
	Maximum	29.1	29.0	26.3	29.8
Medical History	No	15 (50.0)	30 (100.0)	23 (79.3)	16 (53.3)
	Yes	15 (50.0)	0 (0.0)	6 (20.7)	14 (46.7)
Smoking History	No	21 (70.0)	29 (96.7)	27 (93.1)	24 (80.0)
	Yes	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Previously	9 (30.0)	1 (3.3)	2 (6.9)	6 (20.0)
Alcohol History	No	5 (16.7)	30 (100.0)	17 (58.6)	9 (30.0)
	Yes	10 (33.3)	0 (0.0)	12 (41.4)	21 (70.0)
	Previously	15 (50.0)	0 (0.0)	0 (0.0)	0 (0.0)
SBP [mmHg]	Mean	109.7	118.0	119.1	121.3
	SD	11.59	10.60	9.83	11.38
	Minimum	93.0	90.0	98.0	100.0
	Median	109.00	120.00	120.00	120.00
	Maximum	136.0	136.0	137.0	152.0
DBP [mmHg]	Mean	64.5	76.5	71.0	67.2
	SD	9.36	6.21	10.81	7.55
	Minimum	50.0	64.0	46.0	54.0
	Median	64.00	80.00	72.00	66.00
	Maximum	86.0	90.0	89.0	84.0
Pulse Rate [bpm]	Mean	66.4	65.3	71.2	64.2
	SD	9.59	6.65	9.68	11.50
	Minimum	46.0	58.0	50.0	50.0
	Median	66.50	63.00	70.00	61.50
	Maximum	89.0	90.0	90.0	90.0
Body Temperature [°C]	Mean	36.3	36.2	36.4	36.1
	SD	0.38	0.28	0.42	0.32
	Minimum	35.6	35.8	35.7	35.5
	Median	36.40	36.20	36.40	36.10
	Maximum	36.9	36.8	37.2	36.7
12 Lead ECG	Normal	25 (83.3)	27 (90.0)	12 (41.4)	14 (46.7)
	Abnormal-NCS[1)]	5 (16.7)	3 (10.0)	17 (58.6)	16 (53.3)
	Abnormal-CS[2)]	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

1) Abnormal - not clinically significant

2) Abnormal - clinically significant

Allergy to drugs, food, etc.

None of the subjects allergic to drugs, food, etc. were enrolled in any study site.

Medical History

Of 119 subjects, 35 subjects (15 in Japan; 6 in Korea; 14 in the US) had medical history at screening. None of these were significant for inclusion of the subjects into the study. All subjects were well at the screening visit.

Smoking History

None of the patients smoked just before the study. Although 18 patients (9 in Japan; 1 in China; 2 in Korea; 6 in the US) smoked previously, they refrained from smoking more than 6 months before the study.

Alcohol History

About 40 percent or more subjects in each study site except China drank alcohol less than 50 g per day just before the study or previously, did not comply with the exclusion criteria. In China, none of subjects drank alcohol.

Vital Signs and 12-Lead ECG

All values of vital sign measurements (SBP, DBP, pulse rate and body temperature) were judged as normal. Several abnormalities were observed in ECG measurements, but were not clinically significant.

10.4 Measurement of Treatment Compliance

A hand-and-mouth check was performed following study drug administration, and all drug administration times were recorded in the appropriate CRF.

10.5 Concomitant Medication or Intervention

No concomitant medications or intervention was necessary in any country during the course of this study.

11. PHARMACOKINETIC EVALUATION

PK evaluation of meloxicam and gene polymorphism test of the CYP2C9 were conducted in healthy adult male subjects in each ethnic group. See the report written by Dr. Masahiro Tohkin.

12. SAFETY EVALUATIONS

12.1 Extent of Exposure

Every subject received 7.5 mg of meloxicam in these 4 ethnic groups.

12.2 Adverse Events

An AE referred to any unfavourable and unintended sign, symptom or disease newly occurred after administration of the study drug, regardless of the causal relationship with the study drug.

12.2.1 Brief Summary of Adverse Events

Totally, 23 AEs were reported by 18 subjects. The most frequent AEs were blood triglyceride increased and pruritus (2 events each). Eight AEs were judged as "probably related" (each 1 event of blood uric acid increased, white blood cell count decreased, haemoglobin decreased, rash maculo-papular, rash generalised and rash pruritic, and 2 events of pruritus. and the other AEs were judged to be "unknown", "probably not related" or "not related". Four events were judged moderate in severity (each 1 event of hyperbilirubinaemia, elevated C-reactive protein, elevated total cholesterol and elevated LDL cholesterol). AEs other than 3 AEs* (each 1 event of elevated C-reactive protein, elevated total cholesterol and elevated LDL cholesterol) were short lasting and resolved without concomitant medication or other intervention. No serious AE were observed in these 4 ethnic groups. There were no deaths or other serious AEs.

* The outcome of 3 AEs in 2 Caucasian subjects was not confirmed since the subjects did not accept a follow-up test.

12.2.2 Display of Adverse Events

Complete listings of all AEs by subject reported during the course of the study are presented in Table 12-1. The reported term (original), MedDRA preferred term and system organ class, severity, seriousness, date and time administered, onset and outcome, relationship to study drug and treatment required taken are listed.

Table 12- 2 summarizes the severity of AEs including the number of subjects, the number of events and incidence of reporting each AE after administration of the study drug.

<Japanese (Japan)>

Three subjects reported 3 AEs. All 3 AEs (each 1 events of rash, white blood cells urine positive and somnolence) occurred were mild in severity and estimated to be "unknown". These AEs except rash were resolved without concomitant medication or other intervention.

<Chinese (China)>

Four subjects reported 5 EAs. All 5 AEs occurred were mild in severity. Of them, 3 AEs (each 1 event of blood uric acid increased, white blood cell count decreased and haemoglobin decreased) were estimated to be "probably related" to the study drug, and 2 AEs (2 events of blood triglycerides increased) were estimated to be "probably not related". The 5 AEs were resolved without concomitant medication or other intervention.

<Korean (Korea)>

Eight subjects reported 11 AEs. One (hyperbilirubinaemia) of 11 AEs occurred was moderate in severity and estimated to be "unknown".

All the other 10 AEs were mild in severity. Of them, 5 AEs (2 events of pruritus, each 1 event of rash maculo-papular, rash generalised and rash pruritus) were estimated to be "probably related" to the study drug, and the others were estimated to be "probably not related", "not related" or "unknown".

These AEs except each 1 event of pruritus and feeling hot were resolved without concomitant medication or other intervention.

<Caucasian (US)>

Three subjects reported 4 AEs. Three of 4 AEs occurred were moderate in severity and estimated to be "not related" to the study drug. The other AE (cold symptoms) was mild in severity and estimated to be "not related". All 4 AEs were resolved without concomitant medication or other intervention.

Table 12-1 Listing of Adverse Events by Subject

<Japanese>

Subject Identifier	Age (years)	Adverse Event			Severity	Seriousness	Administered		Onset		Outcome			Relationship to Study Drug	Treatment Required
		SOC	PT	Original			Date	Time	Date	Time	Assessment	End Date	End Time		
000010007	30	Skin and subcutaneous tissue disorders	Rash	Skin rash (right elbow)	Mild	No	17/Nov/2010	09:12	24/Nov/2010	03:00	Resolved / Recovered without sequelae	08/Dec/2010	11:00	Unknown	Drug treatment
000010009	23	Investigations	White blood cells urine positive	Urine sediment WBC	Mild	No	17/Nov/2010	09:16	20/Nov/2010	08:20	Resolved / Recovered without sequelae	11/Dec/2010	09:00	Unknown	None
000010016	24	Nervous system disorders	Somnolence	Sleepiness	Mild	No	01/Dec/2010	09:00	01/Dec/2010	20:30	Resolved / Recovered without sequelae	01/Dec/2010	21:00	Unknown	None

<Chinese>

Subject Identifier	Age (years)	Adverse Event			Severity	Seriousness	Administered		Onset		Outcome			Relationship to Study Drug	Treatment Required
		SOC	PT	Original			Date	Time	Date	Time	Assessment	End Date	End Time		
000020008	31	Investigations	Blood triglycerides increased	Triglyceride increased	Mild	No	19/Nov/2010	08:08	22/Nov/2010	08:08	Resolved / Recovered without sequelae	29/Nov/2010	07:54	Probably not related	None
000020009	26	Investigations	Blood triglycerides increased	Triglyceride increased	Mild	No	19/Nov/2010	08:10	22/Nov/2010	08:10	Resolved / Recovered without sequelae	16/Dec/2010	08:02	Probably not related	None
000020018	29	Investigations	Blood uric acid increased	Uric acid increased	Mild	No	19/Nov/2010	08:18	22/Nov/2010	08:19	Resolved / Recovered without sequelae	29/Nov/2010	07:52	Probably related	None
000020025	32	Investigations	White blood cell count decreased	White blood cell count decreased	Mild	No	26/Nov/2010	08:01	29/Nov/2010	08:01	Resolved / Recovered without sequelae	06/Dec/2010	08:02	Probably related	None
000020025	32	Investigations	Haemoglobin decreased	Hemoglobin decreased	Mild	No	26/Nov/2010	08:01	06/Dec/2010	08:02	Resolved / Recovered without sequelae	16/Dec/2010	08:20	Probably related	None

SOC: Sysyem Organ Class
PT: Preferred Term

Table 12-1 Listing of Adverse Events by Subject (continued)

<Korean>

Subject Identifier	Age (years)	Adverse Event			Severity	Seriousness	Administered		Onset		Outcome			Relationship to Study Drug	Treatment Required
		SOC	PT	Original			Date	Time	Date	Time	Assessment	End Date	End Time		
000030004	25	Musculoskeletal and connective tissue disorders	Pain in extremity	Pain in extremity	Mild	No	25/Nov/2010	09:50	26/Nov/2010	20:00	Resolved / Recovered without sequelae	26/Nov/2010	22:30	Probably not related	None
000030006	28	Skin and subcutaneous tissue disorders	Pruritus	Pruritus	Mild	No	25/Nov/2010	09:54	25/Nov/2010	13:52	Resolved / Recovered without sequelae	25/Nov/2010	14:54	Probably related	None
000030006	28	Skin and subcutaneous tissue disorders	Rash maculo-papular	Rash maculo-papular	Mild	No	25/Nov/2010	09:54	25/Nov/2010	15:54	Resolved / Recovered without sequelae	26/Nov/2010	19:53	Probably related	None
000030007	25	Skin and subcutaneous tissue disorders	Rash generalised	Rash generalised	Mild	No	02/Dec/2010	09:36	02/Dec/2010	15:30	Resolved / Recovered without sequelae	03/Dec/2010	08:00	Probably related	None
000030012	23	Injury, poisoning and procedural complications	Nail injury	Nail injury	Mild	No	02/Dec/2010	09:46	02/Dec/2010	19:40	Resolved / Recovered without sequelae	03/Dec/2010	09:28	Not related	None
000030020	29	Skin and subcutaneous tissue disorders	Pruritus	Pruritus	Mild	No	07/Dec/2010	09:48	09/Dec/2010	14:00	Resolved / Recovered without sequelae	13/Dec/2010	12:00	Probably related	Drug treatment
000030020	29	Skin and subcutaneous tissue disorders	Rash pruritic	Rash pruritic	Mild	No	07/Dec/2010	09:48	09/Dec/2010	14:00	Resolved / Recovered without sequelae	19/Dec/2010	20:00	Probably related	None
000030027	22	Injury, poisoning and procedural complications	Skin laceration	Skin laceration	Mild	No	14/Dec/2010	09:54	15/Dec/2010	14:41	Resolved / Recovered without sequelae	15/Dec/2010	19:13	Not related	None
000030028	24	Hepatobiliary disorders	Hyper-bilirubinaemia	Hyper-bilirubinaemia	Moderate	No	14/Dec/2010	09:56	17/Dec/2010	12:05	Resolved / Recovered without sequelae	20/Dec/2010	14:15	Unknown	None
000030029	25	Respiratory, thoracic and mediastinal disorders	Cough	Cough	Mild	No	14/Dec/2010	09:58	15/Dec/2010	10:00	Resolved / Recovered without sequelae	17/Dec/2010	08:00	Unknown	None
000030029	25	General disorders and administration site conditions	Feeling hot	Feeling hot	Mild	No	14/Dec/2010	09:58	16/Dec/2010	10:00	Resolved / Recovered without sequelae	17/Dec/2010	08:00	Unknown	Drug treatment

SOC: Sysyem Organ Class
PT: Preferred Term

Table 12-1 Listing of Adverse Events by Subject (continued)

<Caucasian>

Subject Identifier	Age (years)	Adverse Event			Severity	Seriousness	Administered		Onset		Outcome			Relationship to Study Drug	Treatment Required
		SOC	PT	Original			Date	Time	Date	Time	Assessment	End Date	End Time		
000040011*	31	Other (Laboratory)	Elevated C-Reactive Protein		Moderate	No	18/Dec/2010	09:09	18/Dec/2010	08:59	Not Resolved / Not Recovered			Not Related	None
000040037**	24	Other (Laboratory)	Elevated Total Cholesterol		Moderate	No	18/Dec/2010	09:48	21/Dec/2010	09:48	Not Resolved / Not Recovered			Not Related	None
000040037**	24	Other (Laboratory)	Elevated LDL Cholesterol		Moderate	No	18/Dec/2010	09:48	21/Dec/2010	09:48	Not Resolved / Not Recovered			Not Related	None
000040038	21	Respiratory System	Cold Symptoms		Mild	No	18/Dec/2010	09:51	18/Dec/2010	09:00	Resolved / Recovered without sequelae	23/Dec/2010	10:00	Not Related	None

SOC: Sysyem Organ Class
PT: Preferred Term

*: Subject 000040011 did not respond to call / letter request to repeat labs.

**: Subject 000040037 Elevated Total Cholesterol and Elevated LDL Cholesterol were considered Not Clinically Significant for the study.

Table 12- 2 Incidence of AEs – Evaluation for severity

<Japanese>

N=30

Severity	Mild		Moderate		Severe		Total	
Adverse Event SOC PT	Number of subjects (events)	Incidence (%)	Number of subjects (events)	Incidence (%)	Number of subjects (events)	Incidence (%)	Number of subjects (events)	Incidence (%)
	3 (3)	10.0	0 (0)	0.0	0 (0)	0.0	3 (3)	10.0
Skin and subcutaneous tissue disorders	1 (1)	3.3	0 (0)	0.0	0 (0)	0.0	1 (1)	3.3
Rash	1 (1)	3.3	0 (0)	0.0	0 (0)	0.0	1 (1)	3.3
Investigations	1 (1)	3.3	0 (0)	0.0	0 (0)	0.0	1 (1)	3.3
White blood cells urine positive	1 (1)	3.3	0 (0)	0.0	0 (0)	0.0	1 (1)	3.3
Nervous system disorders	1 (1)	3.3	0 (0)	0.0	0 (0)	0.0	1 (1)	3.3
Somnolence	1 (1)	3.3	0 (0)	0.0	0 (0)	0.0	1 (1)	3.3

<Chinese>

N=30

Severity	Mild		Moderate		Severe		Total	
Adverse Event SOC PT	Number of subjects (events)	Incidence (%)	Number of subjects (events)	Incidence (%)	Number of subjects (events)	Incidence (%)	Number of subjects (events)	Incidence (%)
	4 (5)	13.3	0 (0)	0.0	0 (0)	0.0	4 (5)	13.3
Investigations	4 (5)	13.3	0 (0)	0.0	0 (0)	0.0	4 (5)	13.3
Blood triglycerides increased	2 (2)	6.7	0 (0)	0.0	0 (0)	0.0	2 (2)	6.7
Blood uric acid increased	1 (1)	3.3	0 (0)	0.0	0 (0)	0.0	1 (1)	3.3
White blood cell count decreased	1 (1)	3.3	0 (0)	0.0	0 (0)	0.0	1 (1)	3.3
Haemoglobin decreased	1 (1)	3.3	0 (0)	0.0	0 (0)	0.0	1 (1)	3.3

Incidence = the percentage of subjects
SOC: System Organ Class
PT: Preferred Term

Source: Table 12.1
* Coded using MedDRA (Ver. 13.0)

Table 12-2 Incidence of AEs – Evaluation for severity (continued)

<Korean>

N=29

Severity	Mild		Moderate		Severe		Total	
Adverse Event SOC PT	Number of subjects (events)	Incidence (%)	Number of subjects (events)	Incidence (%)	Number of subjects (events)	Incidence (%)	Number of subjects (events)	Incidence (%)
	7 (10)	24.1	1 (1)	3.4	0 (0)	0.0	8 (11)	27.6
Skin and subcutaneous tissue disorders	3 (5)	10.3	0 (0)	0.0	0 (0)	0.0	3 (5)	10.3
Pruritus	2 (2)	6.9	0 (0)	0.0	0 (0)	0.0	2 (2)	6.9
Rash maculo-papular	1 (1)	3.4	0 (0)	0.0	0 (0)	0.0	1 (1)	3.4
Rash generalised	1 (1)	3.4	0 (0)	0.0	0 (0)	0.0	1 (1)	3.4
Rash pruritic	1 (1)	3.4	0 (0)	0.0	0 (0)	0.0	1 (1)	3.4
Injury, poisoning and procedural complications	2 (2)	6.9	0 (0)	0.0	0 (0)	0.0	2 (2)	6.9
Nail injury	1 (1)	3.4	0 (0)	0.0	0 (0)	0.0	1 (1)	3.4
Skin laceration	1 (1)	3.4	0 (0)	0.0	0 (0)	0.0	1 (1)	3.4
Hepatobiliary disorders	0 (0)	0.0	1 (1)	3.4	0 (0)	0.0	1 (1)	3.4
Hyperbilirubinaemia	0 (0)	0.0	1 (1)	3.4	0 (0)	0.0	1 (1)	3.4
Musculoskeletal and connective tissue disorders	1 (1)	3.4	0 (0)	0.0	0 (0)	0.0	1 (1)	3.4
Pain in extremity	1 (1)	3.4	0 (0)	0.0	0 (0)	0.0	1 (1)	3.4
Respiratory, thoracic and mediastinal disorders	1 (1)	3.4	0 (0)	0.0	0 (0)	0.0	1 (1)	3.4
Cough	1 (1)	3.4	0 (0)	0.0	0 (0)	0.0	1 (1)	3.4
General disorders and administration site conditions	1 (1)	3.4	0 (0)	0.0	0 (0)	0.0	1 (1)	3.4
Feeling hot	1 (1)	3.4	0 (0)	0.0	0 (0)	0.0	1 (1)	3.4

Incidence = the percentage of subjects

SOC: System Organ Class

PT: Preferred Term

Source: Table 12.1

* Coded using MedDRA (Ver. 13.0)