Full Novartis CTRD Template

Sponsor

Novartis

Generic Drug Name

LIK066

Therapeutic Area of Trial

Type 2 diabetes mellitus

Approved Indication

Investigational

Protocol Number

CLIK066X2101

Title

A randomized, double-blind, placebo-controlled, 4-part, interwoven single- and multiple-ascending dose study to assess safety, tolerability, pharmacokinetics and pharmacodynamics of LIK066 in healthy subjects and in patients with type 2 diabetes mellitus

Study Phase

Phase I

Study Start/End Dates

30 Jun 2011 to 14 Feb 2013

Study Design/Methodology

This was a randomized, double-blind, placebo-controlled study. The study was comprised of four parts (I-IV) and assessed safety, tolerability, pharmacodynamics (PD, effect on urinary glucose excretion and blood glucose level following an oral glucose challenge) and pharmacokinetics (PK) of single and multiple doses of LIK066.

Parts I and III enrolled healthy subjects to assess single and multiple-ascending doses, respectively.

Part II was a multiple dose study in which LIK066 (15 mg) was administered once daily for 14 days in patients with type 2 diabetes mellitus (T2DM). Part IV enrolled patients with T2DM in 5 sequential single-dose treatment periods separated by at least 14-day washout periods in a double-blinded crossover study design. Each patient was treated with only one of the following treatments during each treatment period in different sequences according to the randomization schedule: placebo, LIK066 2.5 mg in the morning, LIK066 30 mg in the morning, LIK066 300 mg in the morning or LIK066 300 mg in the evening.

Centers

1 center in the United States

Publication

N/A

Test Product (s), Dose(s), and Mode(s) of Administration

LIK066 80 mg powder and Placebo 0 mg powder reconstituted to a solution for oral administration. The following doses were administered in this study:

Single dose: 2.5, 5, 15, 30, 50, 100, 200, 300 and 350 mg.

Multiple doses (once daily for 14 days): 2.5, 15, 30, 100, 150, 200, and 300 mg.

Statistical Methods

Analysis of primary variables:

In Parts I, II and III, safety/tolerability data are listed with no formal inferential statistical analysis performed.

Area under the concentration-time curve for plasma glucose from time zero (pre-dose) to 4h post-dose (AUC0-4h) and incremental AUC0-4h (iAUC0-4h; AUC above the pre-test fasting glucose level) following an oral glucose tolerance test (OGTT) were also primary PD variables in Parts II and IV. The PD parameters were summarized at each time point by descriptive statistics (sample size, arithmetic mean, standard deviation, and coefficient of variation (CV%), minimum, median, maximum, geometric mean and CV% geometric mean as appropriate). Arithmetic mean (+SE) and geometric mean (95% CI) time profiles were provided.

Statistical analysis in Part II: change from baseline glucose AUC0-4h and iAUC0-4h was analyzed using analysis of covariance (ANCOVA) with treatment as the classification factor and baseline AUC as the covariate. Point estimate and the associated 95% confidence interval for the difference between LIK066 and placebo, along with the corresponding p-value, were obtained from the ANCOVA. Log-transformation was performed prior to the analysis. For incremental AUC0-4h, time weighted average change from baseline (log[AUC0-4h/4]-log[baseline]) was analyzed.

Statistical analysis in Part IV: an analysis of variance (ANOVA) with fixed effects for sequence, treatment, and period and random effect for subject nested within sequence was performed on log-transformed glucose AUC0-4h and iAUC0-4h. Each of the 3 morning doses were compared to the placebo treatment. Additionally the evening dose was compared to the comparable morning dose.

All results were back-transformed and reported in the original scale.

Analysis of secondary variables:

The observed values for urinary excretion of glucose at each sample collection interval were summarized by descriptive statistics. The cumulative amount of glucose excreted in urine over the time interval of 0-t hours (t=ending time of each collection interval) was also summarized/analyzed.

The change from time-matched baseline for Part II urinary excretion of glucose was analyzed in the same manner as described for the primary PD variables while an ANOVA was used to analyze the observed values in Parts I, III and IV. The Part IV ANOVA analysis included sequence, treatment, period as fixed effects, and patient nested within sequence as a random effect. Again, data was log-transformed prior to statistical analysis.

For Part II fasting blood glucose measured on day -1 prior to OGTT and day 14 prior to study drug administration as well as days 2, 4, 8, 12, change from baseline was analyzed similarly. Parts III and IV data were also analyzed as appropriate.

The following key PK parameters for LIK066 were determined from each individual concentration time profile using non-compartmental methods:

Parts I and IV: AUC0-24h, AUClast, AUCinf, Cmax, Tmax, T1/2, CL/F, Vz/F.

Parts II and III: day 1 and day 14: AUCtau, Cmax, Tmax. Day 14 only: Racc, CLss/F, Vss/F.

Urine: Ae0-t, CLr and %Fe from the selected dose cohort in Parts I, II, and III (day 14 only).

Study Population: Inclusion/Exclusion Criteria and Demographics

Inclusion Criteria

Parts I and III:

- Healthy male and female subjects age 18 to 55 years of age included, and in good health as determined by past medical history, physical examination, electrocardiogram, and laboratory tests at screening.

Parts II and IV:

- Patients, age 18-65 years, must have been diagnosed with T2DM at least 8 weeks prior to screening with HbA_{1c} 6.5 to 10.0%, inclusive, at screening.
- Fasting plasma glucose ≤250mg/dL at screening and baseline.
- If treated with metformin, patients must be on a stable dose for 12 weeks prior to randomization and maintain the dose until the end of the study.

Exclusion criteria

- Patients with type 1 diabetes mellitus.
- Patients with history of acute diabetic complications within the 6 months prior to screening.
- Women of child-bearing potential.
- Patients with signs or symptoms of significant diabetic complications.
- Patients treated with certain blood pressure or lipid lowering medications unless patients have been on stable doses for the 12 weeks prior to dosing.
- History of drug or alcohol abuse within the 12 months prior to dosing.
- Any surgical or medical condition, acute or unstable chronic disease which may, based on the investigator's opinion, jeopardize the patient in case of participation in the study.

Other protocol-defined inclusion/exclusion criteria applied.

Participant Flow

Subject disposition - n (%) of subjects - Part I (single-ascending dose in healthy subjects)

	LIK066 5mg N=6 n (%)	LIK066 15mg N=6 n (%)	LIK066 50mg N=6 n (%)	LIK066 100mg N=6 n (%)	LIK066 200mg N=6 n (%)	LIK066 350mg N=6 n (%)	Placebo N=12 n (%)	Total N=48 n (%)
Completed	6 (100.0)	6 (100.0)	6 (100.0)	6 (100.0)	6 (100.0)	6 (100.0)	12 (100.0)	48 (100.0)

Subject disposition - n (%) of subjects - Part II (multiple-dose study in T2DM patients)

	LIK066 15mg N=15 n (%)	Placebo N=15 n (%)	Total N=30 n (%)
Completed	15 (100.0)	15 (100.0)	30 (100.0)

Subject disposition - n (%) of subjects - Part III (multiple-ascending dose in healthy subjects)

	LIK066 2.5mg N=6 n (%)	LIK066 30mg N=6 n (%)	LIK066 100mg N=6 n (%)	LIK066 150mg N=6 n (%)	LIK066 200mg N=6 n (%)	LIK066 300mg N=6 n (%)	Placebo N=12 n (%)	Total N=48 n (%)
Completed	6 (100.0)	6 (100.0)	5 (83.3)	6 (100.0)	6 (100.0)	6 (100.0)	12 (100.0)	47 (97.9)
Discontinued from study	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.1)
Primary reason for discontinuation:								
Subject withdrew consent	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.1)

Subject disposition - n (%) of subjects - Part IV (5-treatment period single dose crossover study in patients with T2DM)

	ABCDE* N=2 n (%)	BDECA* N=3 n (%)	CEBAD* N=3 n (%)	DCAEB* N=2 n (%)	EADBC* N=2 n (%)	Total N=12 n (%)
Completed	2 (100.0)	2 (66.7)	2 (66.7)	2 (100.0)	2 (100.0)	10 (83.3)
Discontinued from study	0 (0.0)	1 (33.3)	1 (33.3)	0 (0.0)	0 (0.0)	2 (16.7)
Primary reason for discontinuation:						
Subject withdrew consent	0 (0.0)	1 (33.3)	1 (33.3)	0 (0.0)	0 (0.0)	2 (16.7)

*Treatment sequence; **A**-Placebo, **B**-LIK066 2.5mg, **C**-LIK066 30mg, **D**-LIK066 300mg (morning), **E**-LIK066 300mg (evening).

Baseline Characteristics

Part I:

		LIK066 5mg N=6	LIK066 15mg N=6	LIK066 50mg N=6	LIK066 100mg N=6	LIK066 200mg N=6	LIK066 350mg N=6	Placebo N=12	Total N=48
Age (years)	**Mean (SD)**	48.3 (9.99)	46.0 (13.46)	42.8 (8.84)	45.5 (5.43)	39.5 (14.58)	46.2 (8.66)	43.0 (11.01)	44.3 (10.35)
Sex - n (%)	**Male**	3 (50.0)	3 (50.0)	4 (66.7)	5 (83.3)	3 (50.0)	6 (100.0)	9 (75.0)	33 (68.8)
	Female	3 (50.0)	3 (50.0)	2 (33.3)	1 (16.7)	3 (50.0)	0 (0.0)	3 (25.0)	15 (31.3)
Race - n (%)	**Caucasian**	6 (100.0)	6 (100.0)	6 (100.0)	5 (83.3)	6 (100.0)	1 (16.7)	11 (91.7)	41 (85.4)
	Black	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	4 (66.7)	1 (8.3)	6 (12.5)
	Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	1 (2.1)
Ethnicity - n (%)	**Hispanic/ Latino**	6 (100.0)	6 (100.0)	6 (100.0)	6 (100.0)	6 (100.0)	5 (83.3)	12 (100.0)	47 (97.9)
	Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	1 (2.1)
Weight (kg)	**Mean (SD)**	69.57 (2.784)	74.47 (6.896)	76.55 (8.298)	81.70 (7.540)	67.37 (10.018)	82.25 (9.967)	76.98 (9.969)	75.73 (9.392)
Height (cm)	**Mean (SD)**	163.67 (7.494)	166.50 (8.216)	169.00 (8.877)	169.52 (4.760)	167.33 (8.220)	179.08 (4.128)	170.94 (7.090)	169.62 (7.942)
BMI (kg/m²)	**Mean (SD)**	26.04 (1.574)	26.92 (2.491)	26.78 (1.879)	28.41 (1.973)	24.06 (3.060)	25.69 (3.403)	26.26 (2.025)	26.30 (2.498)

SD: standard deviation, BMI: body mass index.

Part II:

		LIK066 15mg N=15	Placebo N=15	Total N=30
Age (years)	**Mean (SD)**	54.5 (7.74)	56.6 (5.22)	55.5 (6.58)
Sex - n (%)	**Male**	7 (46.7)	6 (40.0)	13 (43.3)
	Female	8 (53.3)	9 (60.0)	17 (56.7)
Race - n (%)	**Caucasian**	15 (100.0)	13 (86.7)	28 (93.3)
	Black	0 (0.0)	2 (13.3)	2 (6.7)
Ethnicity - n (%)	**Hispanic/Latino**	15 (100.0)	15 (100.0)	30 (100.0)
Weight (kg)	**Mean (SD)**	86.07 (17.656)	82.99 (15.709)	84.53 (16.495)
Height (cm)	**Mean (SD)**	166.45 (9.266)	166.15 (9.960)	166.30 (9.453)
BMI (kg/m²)	**Mean (SD)**	30.75 (3.305)	29.84 (3.488)	30.30 (3.371)

Part III:

		LIK066 2.5mg N=6	LIK066 30mg N=6	LIK066 100mg N=6	LIK066 150mg N=6	LIK066 200mg N=6	LIK066 300mg N=6	Placebo N=12	Total N=48
Age (years)	**Mean (SD)**	46.8 (5.19)	47.0 (4.56)	49.2 (3.13)	39.7 (8.78)	39.2 (12.61)	38.7 (4.50)	45.8 (6.78)	44.0 (7.72)
Sex - n (%)	**Male**	5 (83.3)	4 (66.7)	4 (66.7)	5 (83.3)	3 (50.0)	5 (83.3)	10 (83.3)	36 (75.0)
	Female	1 (16.7)	2 (33.3)	2 (33.3)	1 (16.7)	3 (50.0)	1 (16.7)	2 (16.7)	12 (25.0)
Race - n (%)	**Caucasian**	6 (100.0)	4 (66.7)	6 (100.0)	5 (83.3)	6 (100.0)	6 (100.0)	9 (75.0)	42 (87.5)
	Black	0 (0.0)	2 (33.3)	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	2 (16.7)	5 (10.4)
	Other	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (8.3)	1 (2.1)
Ethnicity - n (%)	**Hispanic/ Latino**	5 (83.3)	6 (100.0)	6 (100.0)	5 (83.3)	6 (100.0)	6 (100.0)	12 (100.0)	46 (95.8)
	Other	1 (16.7)	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)	2 (4.2)
Weight (kg)	**Mean (SD)**	81.55 (14.159)	83.15 (14.596)	68.07 (2.616)	75.33 (8.565)	72.43 (6.574)	75.77 (12.660)	81.27 (10.489)	77.35 (11.194)
Height (cm)	**Mean (SD)**	172.83 (14.257)	174.17 (10.847)	164.67 (5.456)	173.92 (7.710)	169.83 (7.494)	169.90 (7.074)	172.50 (9.190)	171.29 (9.134)
BMI (kg/m²)	**Mean (SD)**	27.19 (1.802)	27.18 (2.112)	25.13 (1.060)	24.95 (2.797)	25.25 (3.305)	26.08 (2.375)	27.31 (2.893)	26.30 (2.552)

Part IV:

		ABCDE* N=2	BDECA* N=3	CEBAD* N=3	DCAEB* N=2	EADBC* N=2	Total N=12
Age (years)	**Mean (SD)**	50.5 (2.12)	59.0 (0.00)	53.0 (11.36)	53.0 (7.07)	49.0 (12.73)	53.4 (7.54)
Sex - n (%)	**Male**	1 (50.0)	1 (33.3)	2 (66.7)	1 (50.0)	1 (50.0)	6 (50.0)
	Female	1 (50.0)	2 (66.7)	1 (33.3)	1 (50.0)	1 (50.0)	6 (50.0)
Race - n (%)	**Caucasian**	2 (100.0)	3 (100.0)	3 (100.0)	1 (50.0)	2 (100.0)	11 (91.7)
	Black	0 (0.0)	0 (0.0)	0 (0.0)	1 (50.0)	0 (0.0)	1 (8.3)
Ethnicity - n (%)	**Hispanic/Latino**	2 (100.0)	3 (100.0)	3 (100.0)	2 (100.0)	2 (100.0)	12 (100.0)
Weight (kg)	**Mean (SD)**	83.15 (10.677)	81.90 (25.737)	76.77 (1.041)	101.3 (20.648)	86.65 (14.354)	84.85 (16.093)
Height (cm)	**Mean (SD)**	166.80 (6.788)	163.00 (9.165)	169.33 (7.506)	170.00 (8.485)	168.25 (12.374	167.26 (7.607)
BMI (kg/m²)	**Mean (SD)**	30.12 (6.284)	30.31 (6.274)	26.88 (2.505)	34.83 (3.663)	30.48 (0.585)	30.20 (4.478)

*Treatment sequence; **A**-Placebo, **B**-LIK066 2.5mg, **C**-LIK066 30mg, **D**-LIK066 300mg (morning), **E**-LIK066 300mg (evening).

Outcome Measures

Primary Outcome Result(s)

Safety and tolerability were the primary outcome measured from Parts I, II and III of the study. **Please see Safety Section for Safety results**

Baseline and day 14 (end of treatment) glucose following OGTT in Part II

PD Assessment	PD parameter	Treatment	Baseline mean (SD)	Day 14 mean (SD)
Glucose (mg/dL-hr)	AUC0-4h	Placebo	1128.12 (249.828)	1154.63 (305.952)
		LIK066 15mg	1141.76 (143.072)	822.34 (153.757)
Glucose (mg/dL-hr)	Incr. AUC0-4h	Placebo	429.18 (137.567)	490.63 (129.860)
		LIK066 15mg	453.49 (102.634)	258.08 (87.907)

Glucose assessment following OGTT in Part IV

PD Assessment	PD parameter	Treatment	Mean (SD)
Glucose (mg/dL-hr)	AUC0-4h	Placebo	1207.25 (220.012)
		LIK066 2.5mg	997.77 (154.242)
		LIK066 30mg	819.07 (174.061)
		LIK066 300mg (morning)	623.95 (128.910)
		LIK066 300mg (evening)	941.70 (104.217)
Glucose (mg/dL-hr)	Incr. AUC0-4h	Placebo	500.85 (118.711)
		LIK066 2.5mg	323.95 (80.388)
		LIK066 30mg	116.16 (82.221)
		LIK066 300mg (morning)	-11.25 (69.139)
		LIK066 300mg (evening)	381.30 (67.784)

Fasting blood glucose during the 14-day treatment period in Part II

Parameter	Treatment	Mean (SD)
Day 4 Fasting glucose (mmol/L)	**Placebo**	9.803 (2.8508)
	15 mg	8.489 (1.0525)
Day 8 Fasting glucose (mmol/L)	**Placebo**	10.140 (3.2297)
	15 mg	8.660 (1.4685)
Day 12 Fasting glucose (mmol/L)	**Placebo**	9.551 (3.0869)
	15 mg	8.460 (1.5319)
Day 15 Fasting glucose (mmol/L)	**Placebo**	9.681 (3.1385)
	15 mg	8.545 (1.5994)

Fasting blood glucose (mmol/L) after a single dose of LIK066 in Part IV

Treatment	Mean (SD)
Placebo	9.259 (2.3230)
LIK066 2.5mg	8.453 (1.3490)
LIK066 30mg	8.205 (1.6284)
LIK066 300mg (morning)	7.449 (1.1376)
LIK066 300mg (evening)	7.583 (1.2758)

Secondary Outcome Results:

Urinary glucose excretion (g) over 24 h after a single dose of LIK066 in Part I

Treatment	Mean (SD)
Placebo	1.59 (4.948)
LIK066 5 mg	35.20 (12.838)
LIK066 15 mg	63.07 (13.413)
LIK066 50 mg	66.37 (16.048)
LIK066 100 mg	77.00 (14.696)
LIK066 200 mg	75.98 (29.612)
LIK066 350 mg	82.39 (15.101)

Urinary glucose excretion (g) over 24 h after 14 days treatment with LIK066 in Part II

Treatment	Mean (SD)
Placebo	19.62 (25.252)
LIK066 15 mg	109.35 (33.404)

Urinary glucose excretion (g) over 24 h after 14 days treatment with LIK066 in Part III

Treatment	Mean (SD)
Placebo	0.17 (0.248)
LIK066 2.5 mg	24.64 (8.569)
LIK066 30 mg	45.33 (18.399)
LIK066 100 mg	67.32 (20.585)
LIK066 150 mg	78.33 (8.808)
LIK066 200 mg	70.63 (17.125)
LIK066 300 mg	72.69 (14.179)

Urinary glucose excretion (g) over 24 h after a single dose of LIK066 in Part IV

Treatment	Mean (SD)
Placebo	29.09 (35.870)
LIK066 2.5 mg	65.81 (22.752)
LIK066 30 mg	115.64 (52.479)
LIK066 300 mg (morning)	112.25 (28.088)
LIK066 300 mg (evening)	120.88 (36.136)

Summary of plasma pharmacokinetic parameters following single dose administration of LIK066 in Part I

		5 mg	15 mg	50 mg	100 mg	200 mg	350 mg
Tmax	N	6	6	6	6	6	6
(hr)	Median	0.5	0.5	0.5	0.5	0.5	0.5
Cmax	N	6	6	6	6	6	6
(ng/mL)	Mean (SD)	109.3 (42.39)	343.5 (111.23)	666.8 (146.30)	1323.7 (319.75)	3866.7 (886.02)	5798.3 (1580.02)
Cmax/D	N	6	6	6	6	6	6
(ng/mL/mg)	Mean (SD)	21.9 (8.48)	22.9 (7.42)	13.3 (2.93)	13.2 (3.20)	19.3 (4.43)	16.6 (4.51)
AUCinf	N	6	6	6	6	6	6
(hr*ng/mL)	Mean (SD)	373.2 (57.10)	1259.0 (88.02)	3732.4 (796.63)	5424.0 (675.07)	13582.3 (4683.32)	22276.4 (2865.31)
AUCinf/D	N	6	6	6	6	6	6
(hr*ng/mL/	Mean (SD)	74.6	83.9 (5.87)	74.6	54.2 (6.75)	67.9	63.6 (8.19)

		5 mg	15 mg	50 mg	100 mg	200 mg	350 mg
mg)		(11.42)		(15.93)		(23.42)	
AUClast	N	6	6	6	6	6	6
(hr*ng/mL)	Mean (SD)	365.7 (58.64)	1239.2 (69.02)	3711.2 (785.63)	5393.8 (692.32)	13567.7 (4687.74)	22227.7 (2836.96)
AUC0-24h	N	6	6	6	6	6	6
(hr*ng/mL)	Mean (SD)	342.0 (63.77)	1126.4 (64.88)	3342.8 (635.26)	4948.7 (617.53)	12607.7 (3858.34)	20476.0 (2319.19)
T1/2	N	6	6	6	6	6	6
(hr)	Mean (SD)	12.8 (7.10)	16.3 (9.62)	9.9 (2.73)	11.0 (1.72)	10.5 (1.92)	13.3 (5.44)
CL/F	N	6	6	6	6	6	6
(L/hr)	Mean (SD)	13.6 (1.92)	12.0 (0.82)	14.0 (3.32)	18.7 (2.73)	15.9 (4.41)	15.9 (2.17)
Vz/F	N	6	6	6	6	6	6
(L)	Mean (SD)	260.7 (167.31)	275.4 (139.28)	193.8 (46.12)	301.3 (89.89)	236.9 (59.63)	300.6 (109.94)

Summary of urine pharmacokinetic parameters following single dose administration of LIK066 to healthy subjects

		5 mg	15 mg	50 mg	100 mg	200 mg	350 mg
Ae0-72hr	N	6	6	6	6	6	6
(mg)	Mean (SD)	0.2 (0.04)	0.7 (0.14)	2.1 (0.87)	3.9 (0.58)	8.0 (2.40)	9.7 (2.77)
CLr	N	6	6	6	6	6	6
(L/hr)	Mean (SD)	0.6 (0.17)	0.5 (0.11)	0.6 (0.16)	0.7 (0.10)	0.6 (0.25)	0.4 (0.10)
%Fe	N	6	6	6	6	6	6
	Mean (SD)	4.0 (0.72)	4.5 (0.96)	4.2 (1.74)	3.9 (0.58)	4.0 (1.20)	2.8 (0.79)

Summary of plasma pharmacokinetic parameters following multiple dose administration of LIK066 in Part II

		15 mg Day 1	15 mg Day 14
Tmax	N	15	15
(hr)	Median	0.5	0.5
Cmax	N	15	15
(ng/mL)	Mean (SD)	330.4 (81.25)	306.7 (112.96)
Cmax/Dose	N	15	15
(ng/mL/mg)	Mean (SD)	22.0 (5.42)	20.4 (7.53)
AUCtau	N	15	15
(hr*ng/mL)	Mean (SD)	865.7 (196.40)	1065.6 (248.52)
AUCtau/Dose	N	15	15
(hr*ng/mL/mg)	Mean (SD)	57.7 (13.09)	71.0 (16.57)
Racc	N		15
	Mean (SD)		1.2 (0.14)

Summary of urine pharmacokinetic parameters following multiple dose administration of LIK066 to patients with T2DM

		15 mg- Day 14
Ae0-72h	N	15
(mg)	Mean (SD)	0.6 (0.20)
CLr	N	15
(L/hr)	Mean (SD)	0.6 (0.19)
%Fe	N	15

		15 mg- Day 14
	Mean (SD)	4.3 (1.37)

Summary of plasma pharmacokinetic parameters following multiple ascending dose administration of LIK066 in Part III

		Cmax (ng/mL)	Cmax/D (ng/mL/mg)	AUCtau (hr*ng/mL)	AUCtau/D (hr*ng/ml/mg)	Racc
2.5 mg	N	6	6	6	6	
Day 1	Mean (SD)	36.6 (21.34)	14.6 (8.53)	161.0 (40.69)	64.4 (16.28)	
2.5 mg	N	6	6	6	6	6
Day 14	Mean (SD)	62.6 (12.11)	25.0 (4.85)	200.7 (39.69)	80.3 (15.88)	1.3 (0.15)
30 mg	N	6	6	6	6	
Day 1	Mean (SD)	726.0 (317.17)	24.2 (10.57)	2279.7 (889.06)	76.0 (29.64)	
30 mg	N	6	6	6	6	6
Day 14	Mean (SD)	479.2 (284.24)	16.0 (9.47)	2647.1 (927.49)	88.2 (30.92)	1.2 (0.10)
100 mg	N	6	6	6	6	
Day 1	Mean (SD)	2268.3 (486.02)	22.7 (4.86)	7620.6 (1179.37)	76.2 (11.79)	
100 mg	N	5	5	5	5	5
Day 14	Mean (SD)	2664.0 (453.68)	26.6 (4.54)	8138.7 (1746.06)	81.4 (17.46)	1.1 (0.09)
150 mg	N	6	6	6	6	
Day 1	Mean (SD)	2765.0 (612.43)	18.4 (4.08)	10380.8 (1517.67)	69.2 (10.12)	
150 mg	N	6	6	6	6	6
Day 14	Mean (SD)	2853.3 (957.28)	19.0 (6.38)	11206.5 (1575.26)	74.7 (10.50)	1.1 (0.09)
200 mg	N	6	6	6	6	
Day 1	Mean (SD)	3325.0 (879.97)	16.6 (4.40)	12802.8 (2025.49)	64.0 (10.13)	
200 mg	N	6	6	6	6	6
Day 14	Mean (SD)	4270.0 (142.13)	21.4 (0.71)	13993.6 (2737.43)	70.0 (13.69)	1.1 (0.10)
300 mg	N	6	6	6	6	
Day 1	Mean (SD)	4173.3 (1116.13)	13.9 (3.72)	21900.1 (4345.41)	73.0 (14.48)	
300 mg	N	6	6	6	6	6
Day 14	Mean (SD)	3985.0 (1021.58)	13.3 (3.41)	20404.7 (4101.52)	68.0 (13.67)	0.9 (0.06)

Summary of urine pharmacokinetic parameters following multiple dose administration to healthy subjects

		30 mg Day 14
Ae0-24h	N	6
(mg)	Mean (SD)	1.4 (0.38)
CLr	N	6
(L/hr)	Mean (SD)	0.5 (0.14)
%Fe	N	6
	Mean (SD)	4.6 (1.25)

Summary of plasma pharmacokinetic parameters following single dose administration of LIK066 in Part IV

		2.5 mg	30 mg	300 mg	300 mg (evening)
Tmax	N	11	10	9	10
(hr)	Median	2	2.5	2	11.9
Cmax	N	11	10	9	10
(ng/mL)	Mean (SD)	37.3 (7.36)	388.5 (140.16)	3427.8 (1233.78)	740.5 (334.29)

		2.5 mg	30 mg	300 mg	300 mg (evening)
Cmax/D	N	11	10	9	
(ng/mL/mg)	Mean (SD)	14.9 (2.95)	13.0 (4.67)	11.4 (4.11)	
AUCinf	N	11	10	9	
(hr*ng/mL)	Mean (SD)	230.1 (56.70)	2601.2 (951.22)	22967.0 (7167.73)	
AUCinf/D	N	11	10	9	
(hr*ng/mL/mg)	Mean (SD)	92.0 (22.68)	86.7 (31.71)	76.6 (23.89)	
AUClast	N	11	10	9	10
(hr*ng/mL)	Mean (SD)	220.0 (58.94)	2586.5 (952.18)	22861.0 (7145.31)	11160.4 (4440.86)
AUC0-24hr	N	11	10	9	
(hr*ng/mL)	Mean (SD)	205.4 (48.37)	2139.5 (893.52)	19891.4 (5841.44)	
T1/2	N	11	10	9	
(hr)	Mean (SD)	10.6 (5.60)	12.9 (3.85)	14.6 (5.98)	
CL/F	N	11	10	9	
(L/hr)	Mean (SD)	11.5 (2.76)	13.7 (7.62)	14.1 (3.93)	
Vz/F	N	11	10	9	
(L)	Mean (SD)	171.3 (85.94)	261.9 (216.81)	286.3 (99.94)	

Safety Results

Incidence of AEs by preferred term- n (%) of subjects (Part I)

	LIK066 5mg N=6 n (%)	LIK066 15mg N=6 n (%)	LIK066 50mg N=6 n (%)	LIK066 100mg N=6 n (%)	LIK066 200mg N=6 n (%)	LIK066 350mg N=6 n (%)	Placebo N=12 n (%)	Total N=48 n (%)
Subjects with AE(s)	2 (33.3)	0 (0.0)	4 (66.7)	5 (83.3)	5 (83.3)	4 (66.7)	1 (8.3)	21 (43.8)
Preferred term								
Diarrhea	2 (33.3)	0 (0.0)	1 (16.7)	4 (66.7)	4 (66.7)	4 (66.7)	1 (8.3)	16 (33.3)
Flatulence	0 (0.0)	0 (0.0)	2 (33.3)	3 (50.0)	0 (0.0)	1 (16.7)	1 (8.3)	7 (14.6)
Abdominal pain	2 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	1 (8.3)	4 (8.3)
Abdominal distension	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	2 (4.2)
Headache	0 (0.0)	0 (0.0)	2 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (4.2)
Abdominal discomfort	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.1)
Abdominal tenderness	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	1 (2.1)
Balanitis	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.1)
Dyspepsia	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	1 (2.1)
Nausea	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.1)
Upper respiratory tract infection	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	1 (2.1)
Vomiting	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.1)

Incidence of AEs by primary system organ class - n (%) of subjects (Part I)

	LIK066 5mg N=6 n (%)	LIK066 15mg N=6 n (%)	LIK066 50mg N=6 n (%)	LIK066 100mg N=6 n (%)	LIK066 200mg N=6 n (%)	LIK066 350mg N=6 n (%)	Placebo N=12 n (%)	Total N=48 n (%)
Subjects with AE(s)	2 (33.3)	0 (0.0)	4 (66.7)	5 (83.3)	5 (83.3)	4 (66.7)	1 (8.3)	21 (43.8)
System organ class								

	LIK066 5mg N=6 n (%)	LIK066 15mg N=6 n (%)	LIK066 50mg N=6 n (%)	LIK066 100mg N=6 n (%)	LIK066 200mg N=6 n (%)	LIK066 350mg N=6 n (%)	Placebo N=12 n (%)	Total N=48 n (%)
Gastrointestinal disorders	2 (33.3)	0 (0.0)	3 (50.0)	5 (83.3)	5 (83.3)	4 (66.7)	1 (8.3)	20 (41.7)
Nervous system disorders	0 (0.0)	0 (0.0)	2 (33.3)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (4.2)
Infections and infestations	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	1 (2.1)
Reproductive system and breast disorders	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.1)

Incidence of AEs by preferred term- n (%) of subjects (Part II)

	LIK066 15mg N=15 n (%)	Placebo N=15 n (%)	Total N=30 n (%)
Subjects with AE(s)	10 (66.7)	11 (73.3)	21 (70.0)
Preferred term			
Diarrhea	3 (20.0)	2 (13.3)	5 (16.7)
Abdominal pain	1 (6.7)	2 (13.3)	3 (10.0)
Back pain	0 (0.0)	3 (20.0)	3 (10.0)
Dyspepsia	2 (13.3)	1 (6.7)	3 (10.0)
Headache	2 (13.3)	1 (6.7)	3 (10.0)
Oropharyngeal pain	2 (13.3)	1 (6.7)	3 (10.0)
Abdominal distension	1 (6.7)	1 (6.7)	2 (6.7)
Constipation	1 (6.7)	1 (6.7)	2 (6.7)
Dizziness	1 (6.7)	1 (6.7)	2 (6.7)
Pain in extremity	2 (13.3)	0 (0.0)	2 (6.7)
Viral infection	1 (6.7)	1 (6.7)	2 (6.7)
Vomiting	1 (6.7)	1 (6.7)	2 (6.7)
Arthritis	1 (6.7)	0 (0.0)	1 (3.3)
Asthenia	1 (6.7)	0 (0.0)	1 (3.3)
Dermatitis contact	1 (6.7)	0 (0.0)	1 (3.3)
Device breakage	0 (0.0)	1 (6.7)	1 (3.3)
Dry mouth	1 (6.7)	0 (0.0)	1 (3.3)
Dry skin	1 (6.7)	0 (0.0)	1 (3.3)
Dysphonia	1 (6.7)	0 (0.0)	1 (3.3)
Dyspnoea	1 (6.7)	0 (0.0)	1 (3.3)
Foreign body	1 (6.7)	0 (0.0)	1 (3.3)
Gastrooesophageal reflux disease	1 (6.7)	0 (0.0)	1 (3.3)
Implant site haemorrhage	0 (0.0)	1 (6.7)	1 (3.3)
Implant site pain	0 (0.0)	1 (6.7)	1 (3.3)
Muscular weakness	1 (6.7)	0 (0.0)	1 (3.3)
Musculoskeletal pain	1 (6.7)	0 (0.0)	1 (3.3)
Nausea	1 (6.7)	0 (0.0)	1 (3.3)
Neck pain	1 (6.7)	0 (0.0)	1 (3.3)
Pain	1 (6.7)	0 (0.0)	1 (3.3)
Palpitations	1 (6.7)	0 (0.0)	1 (3.3)
Pruritus	1 (6.7)	0 (0.0)	1 (3.3)
Rash pruritic	1 (6.7)	0 (0.0)	1 (3.3)

	LIK066 15mg N=15 n (%)	Placebo N=15 n (%)	Total N=30 n (%)
Sinus tachycardia	0 (0.0)	1 (6.7)	1 (3.3)
Temporomandibular joint syndrome	1 (6.7)	0 (0.0)	1 (3.3)
Upper respiratory tract infection	0 (0.0)	1 (6.7)	1 (3.3)
Vessel puncture site pain	0 (0.0)	1 (6.7)	1 (3.3)
Vulvovaginal candidiasis	1 (6.7)	0 (0.0)	1 (3.3)
Weight decreased	0 (0.0)	1 (6.7)	1 (3.3)

Incidence of AEs by primary system organ class - n (%) of subjects (Part II)

	LIK066 15mg N=15 n (%)	Placebo N=15 n (%)	Total N=30 n (%)
Subjects with AE(s)	10 (66.7)	11 (73.3)	21 (70.0)
System organ class			
Gastrointestinal disorders	7 (46.7)	6 (40.0)	13 (43.3)
Musculoskeletal and connective tissue disorders	5 (33.3)	3 (20.0)	8 (26.7)
General disorders and administration site conditions	2 (13.3)	3 (20.0)	5 (16.7)
Infections and infestations	2 (13.3)	2 (13.3)	4 (13.3)
Nervous system disorders	2 (13.3)	2 (13.3)	4 (13.3)
Respiratory, thoracic and mediastinal disorders	3 (20.0)	1 (6.7)	4 (13.3)
Skin and subcutaneous tissue disorders	4 (26.7)	0 (0.0)	4 (13.3)
Cardiac disorders	1 (6.7)	1 (6.7)	2 (6.7)
Injury, poisoning and procedural complications	1 (6.7)	0 (0.0)	1 (3.3)
Investigations	0 (0.0)	1 (6.7)	1 (3.3)

Incidence of AEs by preferred term- n (%) of subjects (Part III)

	LIK066 2.5mg N=6 n (%)	LIK066 30mg N=6 n (%)	LIK066 100mg N=6 n (%)	LIK066 150mg N=6 n (%)	LIK066 200mg N=6 n (%)	LIK066 300mg N=6 n (%)	Placebo N=12 n (%)	Total N=48 n (%)
Subjects with AE(s)	2 (33.3)	5 (83.3)	4 (66.7)	6 (100.0)	6 (100.0)	6 (100.0)	6 (50.0)	35 (72.9)
Preferred term								
Diarrhea	0 (0.0)	5 (83.3)	3 (50.0)	5 (83.3)	6 (100.0)	6 (100.0)	1 (8.3)	26 (54.2)
Flatulence	0 (0.0)	2 (33.3)	1 (16.7)	6 (100.0)	0 (0.0)	2 (33.3)	2 (16.7)	13 (27.1)
Gastrointestinal sounds abnormal	0 (0.0)	1 (16.7)	0 (0.0)	3 (50.0)	0 (0.0)	4 (66.7)	2 (16.7)	10 (20.8)
Abdominal distension	0 (0.0)	2 (33.3)	1 (16.7)	4 (66.7)	0 (0.0)	2 (33.3)	0 (0.0)	9 (18.8)
Abdominal pain	0 (0.0)	0 (0.0)	2 (33.3)	1 (16.7)	3 (50.0)	3 (50.0)	0 (0.0)	9 (18.8)
Headache	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (50.0)	1 (16.7)	0 (0.0)	4 (8.3)
Eructation	0 (0.0)	0 (0.0)	0 (0.0)	2 (33.3)	0 (0.0)	0 (0.0)	1 (8.3)	3 (6.3)
Alopecia effluvium	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (33.3)	0 (0.0)	0 (0.0)	2 (4.2)
Asthenia	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (33.3)	0 (0.0)	0 (0.0)	2 (4.2)
Chapped lips	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	1 (8.3)	2 (4.2)
Constipation	1 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (8.3)	2 (4.2)
Dyspepsia	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	1 (8.3)	2 (4.2)
Nausea	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	1 (16.7)	0 (0.0)	2 (4.2)
Abdominal pain lower	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (8.3)	1 (2.1)
Abdominal pain upper	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.1)

	LIK066 2.5mg N=6 n (%)	LIK066 30mg N=6 n (%)	LIK066 100mg N=6 n (%)	LIK066 150mg N=6 n (%)	LIK066 200mg N=6 n (%)	LIK066 300mg N=6 n (%)	Placebo N=12 n (%)	Total N=48 n (%)
Back pain	1 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.1)
Conjunctivitis	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.1)
Dermatitis contact	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.1)
Dizziness	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (8.3)	1 (2.1)
Dry mouth	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	1 (2.1)
Myalgia	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	1 (2.1)
Penis disorder	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	1 (2.1)
Presyncope	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	1 (2.1)
Proctalgia	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	1 (2.1)
Tremor	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (8.3)	1 (2.1)
Upper respiratory tract infection	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	1 (2.1)
Vomiting	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	1 (2.1)
Vulvovaginal mycotic infection	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	1 (2.1)
Weight decreased	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	1 (2.1)

Incidence of AEs by primary system organ class - n (%) of subjects (Part III)

	LIK066 2.5mg N=6 n (%)	LIK066 30mg N=6 n (%)	LIK066 100mg N=6 n (%)	LIK066 150mg N=6 n (%)	LIK066 200mg N=6 n (%)	LIK066 300mg N=6 n (%)	Placebo N=12 n (%)	Total N=48 n (%)
Subjects with AE(s)	2 (33.3)	5 (83.3)	4 (66.7)	6 (100.0)	6 (100.0)	6 (100.0)	6 (50.0)	35 (72.9)
System organ class								
Gastrointestinal disorders	1 (16.7)	5 (83.3)	4 (66.7)	6 (100.0)	6 (100.0)	6 (100.0)	6 (50.0)	34 (70.8)
Nervous system disorders	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	3 (50.0)	2 (33.3)	1 (8.3)	6 (12.5)
Skin and subcutaneous tissue disorders	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	2 (33.3)	0 (0.0)	0 (0.0)	3 (6.3)
General disorders and administration site conditions	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (33.3)	0 (0.0)	0 (0.0)	2 (4.2)
Musculoskeletal and connective tissue disorders	1 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	2 (4.2)
Eye disorders	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	0 (0.0)	1 (2.1)
Infections and infestations	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	1 (2.1)
Investigations	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	1 (2.1)
Reproductive system and breast disorders	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (16.7)	0 (0.0)	0 (0.0)	1 (2.1)

Incidence of AEs by preferred term- n (%) of subjects (Part IV)

	LIK066 2.5mg N=11 n (%)	LIK066 30mg N=11 n (%)	LIK066 300mg (morning) N=10 n (%)	LIK066 300mg (evening) N=11 n (%)	Placebo N=10 n (%)	Total N=12 n (%)
Subjects with AE(s)	3 (27.3)	7 (63.6)	9 (90.0)	6 (54.5)	3 (30.0)	11 (91.7)

	LIK066 2.5mg N=11 n (%)	LIK066 30mg N=11 n (%)	LIK066 300mg (morning) N=10 n (%)	LIK066 300mg (evening) N=11 n (%)	Placebo N=10 n (%)	Total N=12 n (%)
Preferred term						
Diarrhea	0 (0.0)	6 (54.5)	9 (90.0)	5 (45.5)	2 (20.0)	10 (83.3)
Abdominal pain	0 (0.0)	1 (9.1)	1 (10.0)	0 (0.0)	1 (10.0)	2 (16.7)
Vomiting	0 (0.0)	1 (9.1)	1 (10.0)	0 (0.0)	0 (0.0)	2 (16.7)
Blood pressure increased	0 (0.0)	1 (9.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (8.3)
Conjunctivitis	0 (0.0)	1 (9.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (8.3)
Dermatitis contact	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (10.0)	1 (8.3)
Ear canal injury	1 (9.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (8.3)
Excoriation	0 (0.0)	1 (9.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (8.3)
Hypertriglyceridemia	0 (0.0)	1 (9.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (8.3)
Implant site pain	0 (0.0)	0 (0.0)	0 (0.0)	1 (9.1)	0 (0.0)	1 (8.3)
Leukocytosis	1 (9.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (8.3)
Nausea	0 (0.0)	0 (0.0)	1 (10.0)	0 (0.0)	0 (0.0)	1 (8.3)
Presyncope	0 (0.0)	0 (0.0)	1 (10.0)	0 (0.0)	0 (0.0)	1 (8.3)
Regurgitation	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (10.0)	1 (8.3)
Toothache	0 (0.0)	0 (0.0)	0 (0.0)	1 (9.1)	0 (0.0)	1 (8.3)
Upper respiratory tract infection	1 (9.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (8.3)
Urinary tract infection	1 (9.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (8.3)

Incidence of AEs by primary system organ class - n (%) of subjects (Part IV)

	LIK066 2.5mg N=11 n (%)	LIK066 30mg N=11 n (%)	LIK066 300mg (morning) N=10 n (%)	LIK066 300mg (evening) N=11 n (%)	Placebo N=10 n (%)	Total N=12 n (%)
Subjects with AE(s)	3 (27.3)	7 (63.6)	9 (90.0)	6 (54.5)	3 (30.0)	11 (91.7)
System organ class						
Gastrointestinal disorders	0 (0.0)	6 (54.5)	9 (90.0)	6 (54.5)	3 (30.0)	10 (83.3)
Infections and infestations	2 (18.2)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	2 (16.7)
Injury, poisoning and procedural complications	1 (9.1)	1 (9.1)	0 (0.0)	0 (0.0)	0 (0.0)	2 (16.7)
Blood and lymphatic system disorders	1 (9.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (8.3)
Eye disorders	0 (0.0)	1 (9.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (8.3)
General disorders and administration site conditions	0 (0.0)	0 (0.0)	0 (0.0)	1 (9.1)	0 (0.0)	1 (8.3)
Investigations	0 (0.0)	1 (9.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (8.3)
Metabolism and nutrition disorders	0 (0.0)	1 (9.1)	0 (0.0)	0 (0.0)	0 (0.0)	1 (8.3)
Nervous system disorders	0 (0.0)	0 (0.0)	1 (10.0)	0 (0.0)	0 (0.0)	1 (8.3)
Skin and subcutaneous tissue disorders	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (10.0)	1 (8.3)

There were no deaths or SAEs reported in this study.

Other Relevant Findings

N/A

Date of Clinical Trial Report

20-Dec-2013

Date Inclusion on Novartis Clinical Trial Results Database

10-Feb-2014

Date of Latest Update:

14-Jan- 2014