SUPPLEMENTARY INFORMATION

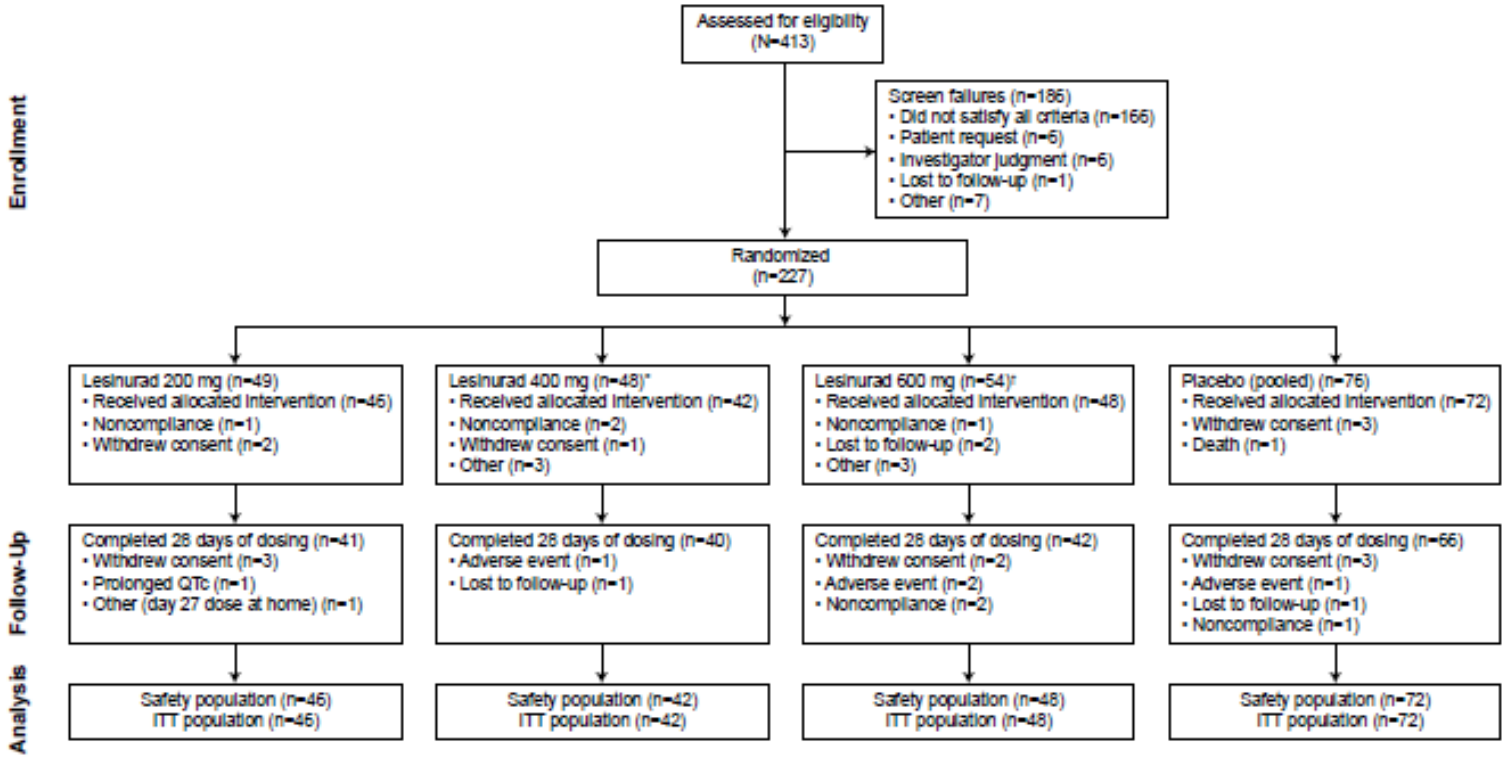
METHODS

Pharmacokinetic analysis and pharmacokinetic substudy

The PK population included all randomized patients who received active drug and had sufficient samples for analysis. Parameters measured included plasma trough (predose) concentrations on days 7, 13, 14, 21, and 28; time of maximum observed plasma concentration; maximum observed plasma concentration (C_{max}); apparent plasma terminal elimination half-life; and area under the plasma concentration-time curve from time zero up to the dosing interval tau of 24 hours ($AUC_{0–24}$). In the PK substudy, these parameters were determined from individual concentration-time profiles using samples collected on day 13; thus, results for lesinurad 400 mg included data from patients in the 600-mg group while receiving 400 mg. C_{max} and $AUC_{0–24}$ were derived by noncompartmental analysis using validated WinNonlin Professional, version 5.2 (Pharsight Corporation, Cary, NC).

Supplemental Figure 1. Patient disposition. ITT=intent-to-treat. *Initial dose of 200 mg for 7 days, followed by 400 mg for 21 days.

†Initial dose of 200 mg for 7 days, followed by 400 mg for 7 days, followed by 600 mg for 14 days.



Supplementary Table 1 Median trough lesinurad plasma concentrations at 4 weeks

	Lesinurad 200 mg + allopurinol			**Lesinurad 400 mg + allopurinol**			**Lesinurad 600 mg + allopurinol**		
	CrCl ≥90 mL/min (normal renal function)	**CrCl 60–89 mL/min (mild renal impairment)**	**CrCl 30–59 mL/min (moderate renal impairment)**	**CrCl ≥90 mL/min (normal renal function)**	**CrCl 60–89 mL/min (mild renal impairment)**	**CrCl 30–59 mL/min (moderate renal impairment)**	**CrCl ≥90 mL/min (normal renal function)**	**CrCl 60–89 mL/min (mild renal impairment)**	**CrCl 30–59 mL/min (moderate renal impairment)**
n	21	16	2	17	17	2	24	13	2
Median trough lesinurad plasma concentration (ng/mL)	69	96	585	77	177	727	237	161	548

CrCl=creatinine clearance; PK=pharmacokinetics.

Supplementary Table 2 Median plasma PK of lesinurad according to dose and CrCl* (PK population)

	Lesinurad 200 mg + allopurinol			Lesinurad 400 mg + allopurinol†	
Median (range)	**CrCl ≥90 mL/min (normal renal function)**	**CrCl 60–89 mL/min (mild renal impairment)**	**CrCl 30–59 mL/min (moderate renal impairment)**	**CrCl ≥90 mL/min (normal renal function)**	**CrCl 60–89 mL/min (mild renal impairment)**
t_{max}, h	n=4	n=4	n=1	n=17	n=6
	4.0 (2.5–6.0)	3.5 (3.0–6.0)	3.0	2.5 (0.0–4.0)	2.0 (1.0–6.0)
C_{max}, µg/mL	n=4	n=4	n=1	n=17	n=6
	3.6 (2.6–8.7)	5.3 (2.9–7.2)	7.7	8.9 (0.1–20.2)	16.3 (8.2–25.6)
$AUC_{0–24}$, µg·h/mL	n=4	n=3	n=1	n=17	n=6
	21.2 (18.9–40.4)	37.6 (21.9–42.9)	55.3	54.4 (0.4–72.9)	78.7 (40.9–212.0)
$t_{1/2}$, h	n=4	n=3	n=1	n=17	n=5
	3.9 (3.2–4.1)	3.4 (3.4–3.9)	4.4	3.7 (3.1–25.2)	3.4 (2.6–4.0)

$AUC_{0–24}$=area under the plasma concentration-time curve from time zero up to the dosing interval tau (24 h); C_{max}=maximum observed plasma concentration; CrCl=creatinine clearance; PK=pharmacokinetics; $t_{1/2}$=apparent plasma terminal elimination half-life; t_{max}=time of maximum observed plasma concentration.

*****Based on Cockcroft-Gault formula using ideal body weight.

†No patients with moderate renal function impairment.

Supplementary Table 3 Serum creatinine and estimated creatinine clearance at baseline and 4 weeks and change from baseline at 4 weeks.

	Lesinurad 200 mg + allopurinol (n=46)	**Lesinurad 400 mg + allopurinol (n=42)**	**Lesinurad 600 mg + allopurinol (n=48)**	**Placebo + allopurinol (n=72)**
Serum Creatinine (mg/dL)				
Baseline	0.953 (0.1718)	0.971 (0.1932)	1.013 (0.1758)	0.991 (0.1709)
4 weeks	0.973 (0.1837)	1.076 (0.2878)	1.098 (0.2403)	0.998 (0.1702)
Change from baseline	0.031 (0.0717)	0.101 (0.2057)	0.072 (0.1574)	-0.003 (0.1036)
eCrCl (mL/min)				
Baseline	135.1 (45.35)	134.6 (46.79)	134.4 (34.04)	127.0 (35.90)
4 weeks	133.9 (45.31)	132.7 (67.04)	132.2 (39.69)	124.1 (34.84)
Change from baseline	-5.0 (12.41)	-0.7 (36.15)	-2.6 (22.97)	0.7 (19.12)

Data are mean (SD). eCrCl, estimated creatinine clearance.