

NATHAN 1 Trial: Participating centers

US/Canada: Jackie R. See, Arthur Charles, Tustin, CA; Jerry Nadler, Duarte, CA; Mark H. Tuszynski, San Diego, CA; Roy Freeman, Boston, MA; Miriam Freimer, Columbus, OH; Jeremy Gleeson, Albuquerque, NM; Michael Giuliani, Pittsburgh, PA; Douglas A. Greene, Ann Arbor, MI; Greg Gruener, Maywood, IL; Yadollah Harati, Houston, TX; Steven Horowitz, Columbia, MO; Peter Lodewick, Birmingham, AL; Adi Mehta, Cleveland, OH; Richard Olney, San Francisco, CA; Winfried Raabe, Minneapolis, MN; M. Perley, Long Beach, CA; Michael A. Pfeifer, Greenville, NC; Philip Raskin, Dallas, TX; Marc Rendell, Omaha, NE; Julio Rosenstock, Dallas, TX; Michael Rubin, New York, NY; Sherwyn Schwartz, San Antonio, TX; J. Clarke Stevens, Scottsdale, AZ; Aaron I. Vinik, Norfolk, VA; Bruce Zimmermann, Rochester, MN.

Europe: Andrew J.M. Boulton, Manchester, UK; Jean-Raymond Attali, Bondy, France; Domenico Fedele, Padova, Italy; Dario Giugliano, Napoli, Italy; Carlo Coscelli, Parma, Italy; Miroslav Reljanovic, Ante Bilic, Zagreb, Croatia; P. Sytze van Dam, Utrecht, The Netherlands; Göran Sundkvist, Malmö, Sweden; Jannik Hilsted, Hvidovre, Denmark; José Cabezas-Cerrato, Santiago de Compostela, Spain; José M. Espadaler, R. Gomis, H. Odriozola, Barcelona, Spain.

Steering committee: Peter J. Dyck (coordinator), Rochester, MN; Andrew J.M. Boulton, Manchester, UK; Douglas A. Greene, Ann Arbor, MI; William J. Litchy, Rochester, MN; Philip A. Low, Rochester, MN; Peter O'Brien, Rochester, MN; Michael A. Pfeifer, Greenville, NC; Dan Ziegler, Düsseldorf, Germany.

Statistical analysis and reporting: Barbara Eilers-Lenz, Marcel Machiewicz, SIRO Clinpharm (formerly Omega Mediation), Offenbach, Germany; Ullrich Munzel, Hanna Michalke, Joachim Maus, Michael Necker, MEDA, Bad Homburg, Germany.

Supervisory committee: F. Arnold Gries, Düsseldorf, Germany; John Lachin, Rockville, MD; John D. Ward, Sheffield, UK.

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SUPPLEMENTARY DATA

Supplementary Table 1. Safety analysis: incidences by body system class

Body system class	α-Lipoic acid (n/%) n=231	Placebo (n/%) n=225	P value
Heart rate and rhythm disorders	16 (6.9)	6 (2.7)	0.047
Urinary system disorders	51 (22.1)	34 (15.1)	0.071
Myo-, endo-, pericardial and valve disorders	29 (12.6)	17 (7.6)	0.088
Respiratory system disorders	107 (46.3)	90 (40.0)	0.186
Body as a whole	110 (47.6)	93 (41.3)	0.188
Cardiovascular disorders, general	81 (35.1)	69 (30.7)	0.321
Musculo-skeletal system disorders	90 (39.0)	77 (34.2)	0.331
Secondary terms	108 (46.8)	95 (42.2)	0.347
Autonomic nervous system disorders	12 (5.2)	7 (3.1)	0.350
Application site disorders	23 (10.0)	18 (8.0)	0.515
Gastro-intestinal disorders	80 (34.6)	74 (32.9)	0.766
Metabolic and nutritional disorders	84 (36.4)	80 (35.6)	0.922
Neoplasm	14 (6.1)	12 (5.3)	0.841
Psychiatric disorders	26 (11.3)	25 (11.1)	1.000
Platelet, bleeding and clotting disorders	13 (5.6)	13 (5.8)	1.000
Central and peripheral nervous system disorders	64 (27.7)	66 (29.3)	0.756
Vascular (extracardiac) disorders	26 (11.3)	30 (13.3)	0.569
Resistance mechanism disorders	43 (18.6)	48 (21.3)	0.484
Skin and appendages disorders	81 (35.1)	90 (40.0)	0.289
Vision disorders	30 (13.0)	41 (18.2)	0.155

SUPPLEMENTARY DATA

Supplementary Table 2: Safety analysis: individual cardiovascular disorders.

	α-Lipoic acid (n/%) n=231	Placebo (n/%) n=225	P value
Heart rate and rhythm disorders			
Tachycardia	7 (3.0)	2 (0.9)	0.176
Arrhythmia	4 (1.7)	0	0.123
Palpitation	2 (0.9)	1 (0.4)	1.000
AV block	1 (0.4)	0	1.000
Bradycardia	1 (0.4)	0	1.000
Cardiac arrest	1 (0.4)	0	1.000
Tachycardia ventricular	1 (0.4)	0	1.000
Bundle branch block	0	1 (0.4)	1.000
Extrasystoles	0	1 (0.4)	1.000
Myocardial, endocardial, or pericardial and valve disorders			
Coronary artery disorder	13 (5.6)	6 (2.7)	0.159
Angina pectoris	6 (2.6)	3 (1.3)	0.504
Myocardial infarction	9 (3.9)	6 (2.7)	0.602
Coronary thrombosis	1 (0.4)	0	1.000
Myocardial ischemia	3 (1.3)	5 (2.2)	0.499

Supplementary Table 3: Global assessment of treatment tolerability.

		Very good/good n (%)	Satisfactory n (%)	Insufficient n (%)
End of year 2	Investigators	ALA 132 (57.1)	65 (28.1)	5 (2.2)
	Placebo	123 (54.7)	63 (28.0)	7 (3.1)
	Patients	ALA 131 (56.7)	59 (26.2)	6 (2.6)
	Placebo	118 (52.4)	47 (26.7)	9 (4.0)
End of year 4	Investigators	ALA 108 (70.1)	41 (26.6)	5 (3.3)
	Placebo	102 (66.2)	45 (29.2)	7 (4.6)
	Patients	ALA 109 (71.2)	39 (25.5)	5 (3.3)
	Placebo	98 (63.6)	47 (30.5)	9 (5.8)