
FRM-7043019 version 2.0

Sponsor

Novartis

Generic Drug Name

LNA043

Trial Indication(s)

Primary osteoarthritis (OA) patients scheduled for total knee replacement (TKR)

Protocol Number

CLNA043X2101

Protocol Title

A randomized, placebo controlled, double-blind first-in-human single ascending dose (SAD) study of LNA043 in primary osteoarthritis (OA) patients scheduled for total knee replacement (TKR).

Clinical Trial Phase

Phase I

Phase of Drug Development

Phase II

Study Start/End Dates

16 Nov 2015 to 06-Mar 2018

Reason for Termination (If applicable)

N/A

Study Design/Methodology

This was a non-confirmatory, double-blind, first-in-human, randomized, placebo controlled study of LNA043 in patients diagnosed with primary OA who were eligible for TKR surgery. The study consisted of an up to 7-day screening period, an up to 7-day baseline period, one single *intra-articular* (i.a.) injection one week (cohort 1 to 4 and 7), 2 hours (cohort 5), and 3 weeks (cohort 6), prior to TKR surgery. Safety follow-up visits or calls were done after dosing and surgery respectively. In case of safety concerns, the patient were asked to return to the hospital for a safety control visit. An End of Study (EoS) visit occurred approximately 28-days after the TKR surgery for all cohorts.

Centers

One study center in the USA.

Objectives:

The primary objective was to evaluate the safety and tolerability of LNA043 after one i.a. injection into the knee of OA patients scheduled for TKR.

Secondary objectives included evaluation of the joint presence and persistence of LNA043 within the cartilage knee tissue, LNA043 pharmacokinetics in serum and concentration in synovial fluid, ANGPTL levels in serum and the synovial fluid, and immunogenicity in serum.

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

One single i.a. injection one week (cohorts 1 to 4 and 7), 2 hours (cohort 5), and 3 weeks (cohort 6), prior to TKR surgery. LNA043 10 mg or placebo powder for solution for injection was reconstituted and further diluted to reach the below doses and administered by ultrasound-guided i.a. injection into the knee joint.

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- Cohort 1: 0.2 mg/knee; 0.3 mL
- Cohort 2: 2 mg/knee; 3 mL
- Cohort 3: 10 mg/knee; 1.5 mL
- Cohort 4-6: 20 mg/knee; 3 mL
- Cohort 7: 40 mg/knee; 4 mL

Statistical Methods

The primary objective was to evaluate the safety and tolerability of LNA043 after one i.a. injection into the knee of OA patients scheduled for TKR. Summary tables with the number, percentage and severity of adverse events (AEs) were provided to assess safety and tolerability by treatment group. The number and percentage of patients with AEs were tabulated by body system and preferred term with a breakdown by treatment group. Separate tables and listings were presented indicating event severity and study drug relationship. Placebo patients were pooled in these summaries

All data for vital signs, ECG evaluations, hematology, blood chemistry, Knee injury and Osteoarthritis Outcome Score (KOOS) and urinalysis were listed for each patient and summarized by descriptive statistics by cohort, treatment group, and visit/time where appropriate. Arithmetic mean and overlaying individual raw values and absolute change from baseline vs time profiles were produced by treatment.

Pharmacokinetics (PK) concentrations data (both serum and synovial fluid) were listed by cohort, treatment, patient, and visit/sampling time point. Descriptive summary statistics of PK parameters was provided by cohort and treatment. Summary statistics included arithmetic mean, SD, CV, median, minimum, maximum.

A summary of H-score from Immunohistochemistry (IHC) staining analysis for individual patient level data was reported by tissue location, tissue type/indication and tissue status for each treatment group. Instead of reporting the H-score, the intensity of individual level ANGPTL and result was reported.

Study Population: Key Inclusion/Exclusion Criteria

Key Inclusion Criteria:

- Male and female patients age 50 to 75 years of age inclusive, and in good health as determined by past medical history, physical examination, vital signs, electrocardiogram, and laboratory tests at screening
- Patients diagnosed with primary osteoarthritis of the knee assessed locally for whom a total knee replacement is planned
- General health status acceptable for total knee replacement surgery in the opinion of the investigator
- Stable medications within 3 months prior to enrollment (such as appropriate pain medication, antibiotics prophylaxis) and standard of care

Key Exclusion Criteria:

- Presence of inflammatory arthropathy (including but not limited to rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, gout), active acute or chronic infection, or systemic cartilage disorder
- Prior cartilage repair surgery, e.g. microfracture, autologous cartilage implantation (ACI) or else, at the same knee
- Any surgical therapy or local treatment i.a. into the knee (viscosupplementation) to the knee within 2 months prior to enrollment
- BMI > 40; presence of uncontrolled diabetes or hyperthyroidism
- Large effusion in the knee to be replaced, more than (>)1 cm fluid in the suprapatellar space at the midline
- Corticosteroid use by any route except topical and nasal in the 3 months prior to enrollment
- History of malignancy of any organ system (other than localized basal cell carcinoma of the skin or in-situ cervical cancer), treated or untreated, within the past 5 years, regardless of whether there is evidence of local recurrence or metastases
- Pregnant or nursing (lactating) women
- Women of child-bearing potential, defined as all women physiologically capable of becoming pregnant

Participant Flow Table

Population	Number (percent) of subjects in the analysis sets (All subjects)								
	Cohort 1 LNA043 0.2mg/Joint N=3 n (%)	Cohort 2 LNA043 2mg/Joint N=3 n (%)	Cohort 3 LNA043 10mg/Joint N=3 n (%)	Cohort 4 LNA043 20mg/Joint N=4 n (%)	Cohort 5 LNA043 20mg/Joint N=3 n (%)	Cohort 6 LNA043 20mg/Joint N=3 n (%)	Cohort 7 LNA043 40mg/Joint N=3 n (%)	Placebo N=8 n (%)	Total N=30 n (%)
Subjects randomized	3 (100.0)	3 (100.0)	3 (100.0)	4 (100.0)	3 (100.0)	3 (100.0)	3 (100.0)	8 (100.0)	30 (100.0)
Safety analysis set	3 (100.0)	3 (100.0)	3 (100.0)	3 (75.0)	3 (100.0)	3 (100.0)	3 (100.0)	7 (87.5)	28 (93.3)
PK analysis set	3 (100.0)	3 (100.0)	3 (100.0)	3 (75.0)	3 (100.0)	3 (100.0)	3 (100.0)	7 (87.5)	28 (93.3)
Biomarker analysis set	3 (100.0)	3 (100.0)	3 (100.0)	3 (75.0)	3 (100.0)	3 (100.0)	3 (100.0)	7 (87.5)	28 (93.3)

Subjects	Subject disposition - n (%) of subjects (Safety analysis set)								
	Cohort 1 LNA043 0.2mg/Joint N=3 n (%)	Cohort 2 LNA043 2mg/Joint N=3 n (%)	Cohort 3 LNA043 10mg/Joint N=3 n (%)	Cohort 4 LNA043 20mg/Joint N=3 n (%)	Cohort 5 LNA043 20mg/Joint N=3 n (%)	Cohort 6 LNA043 20mg/Joint N=3 n (%)	Cohort 7 LNA043 40mg/Joint N=3 n (%)	Placebo N=7 n (%)	Total N=28 n (%)
Completed	3 (100.0)	3 (100.0)	3 (100.0)	3 (100.0)	3 (100.0)	3 (100.0)	3 (100.0)	7 (100.0)	28 (100.0)

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Baseline Characteristics
Demographic summary (Safety analysis set)

		Cohort 1 LNA043 0.2mg/Joint N=3	Cohort 2 LNA043 2mg/Joint N=3	Cohort 3 LNA043 10mg/Joint N=3	Cohort 4 LNA043 20mg/Joint N=3	Cohort 5 LNA043 20mg/Joint N=3	Cohort 6 LNA043 20mg/Joint N=3	Cohort 7 LNA043 40mg/Joint N=3	Placebo N=7	Total N=28
Age (years)	Mean (SD)	57.7 (7.23)	63.3 (3.79)	67.7 (2.08)	68.0 (5.20)	60.7 (8.39)	66.0 (4.00)	61.3 (9.50)	60.6 (7.85)	62.8 (6.77)
	Median	54.0	65.0	67.0	65.0	65.0	66.0	61.0	59.0	65.0
	Range	53 - 66	59 - 66	66 - 70	65 - 74	51 - 66	62 - 70	52 - 71	51 - 73	51 - 74
Gender - n(%)	Female	1 (33%)	1 (33%)	3 (100%)	2 (67%)	2 (67%)	3 (100%)	2 (67%)	5 (71%)	19 (68%)
	Male	2 (67%)	2 (67%)	0	1 (33%)	1 (33%)	0	1 (33%)	2 (29%)	9 (32%)
Predominant race - n(%)	Asian	0	0	0	0	0	0	0	1 (14%)	1 (4%)
	Caucasian	3 (100%)	3 (100%)	3 (100%)	3 (100%)	3 (100%)	3 (100%)	3 (100%)	6 (86%)	27 (96%)
Ethnicity - n(%)	Hispanic/Latino	0	0	0	0	0	0	0	1 (14%)	1 (4%)
	Other	3 (100%)	3 (100%)	3 (100%)	3 (100%)	3 (100%)	3 (100%)	3 (100%)	6 (86%)	27 (96%)
Height (cm)	Mean (SD)	170.6 (10.18)	174.5 (3.21)	159.4 (6.85)	169.3 (12.02)	161.3 (9.56)	170.6 (1.03)	172.3 (8.19)	164.5 (12.25)	167.3 (9.60)
	Median	171.4	174.2	161.3	165.1	160.0	170.9	168.9	165.1	169.2
	Range	160 - 180	171 - 178	152 - 165	160 - 183	152 - 171	170 - 172	166 - 182	146 - 182	146 - 183

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		Cohort 1 LNA043 0.2mg/Joint N=3	Cohort 2 LNA043 2mg/Joint N=3	Cohort 3 LNA043 10mg/Joint N=3	Cohort 4 LNA043 20mg/Joint N=3	Cohort 5 LNA043 20mg/Joint N=3	Cohort 6 LNA043 20mg/Joint N=3	Cohort 7 LNA043 40mg/Joint N=3	Placebo N=7	Total N=28
Weight (kg)	Mean (SD)	92.4 (25.14)	82.2 (1.60)	70.1 (18.52)	110.0 (21.21)	72.0 (2.46)	86.3 (25.47)	96.1 (14.46)	93.6 (11.20)	88.7 (18.34)
	Median	100.3	82.1	65.3	106.6	71.2	76.6	99.2	93.9	87.5
	Range	64 - 113	81 - 84	54 - 91	91 - 133	70 - 75	67 - 115	80 - 109	78 - 113	54 - 133
BMI (kg/m ²)	Mean (SD)	31.9 (8.97)	27.0 (0.80)	27.3 (5.16)	38.1 (2.30)	28.0 (4.18)	29.6 (8.49)	32.5 (5.96)	34.7 (4.04)	31.7 (5.90)
	Median	34.7	26.6	25.1	39.1	27.8	26.7	30.1	34.5	31.8
	Range	22 - 39	27 - 28	24 - 33	35 - 40	24 - 32	23 - 39	28 - 39	29 - 40	22 - 40
Pain and discomfort score at baseline	Mean (SD)	2.44 (0.401)	1.93 (0.231)	2.19 (1.224)	2.01 (0.236)	2.30 (0.231)	1.63 (0.357)	2.00 (0.588)	2.55 (1.024)	2.19 (0.703)
	Median	2.56	2.00	2.11	2.00	2.22	1.78	2.22	2.89	2.11
	Range	2.0 - 2.8	1.7 - 2.1	1.0 - 3.4	1.8 - 2.3	2.1 - 2.6	1.2 - 1.9	1.3 - 2.4	0.8 - 3.6	0.8 - 3.6

Summary of Efficacy
Primary Outcome Results
Incidence of AEs by primary system organ class - n (%) of subjects (Safety analysis set)

	Cohort 1 LNA043 0.2mg/Joint N=3 n (%)	Cohort 2 LNA043 2mg/Joint N=3 n (%)	Cohort 3 LNA043 10mg/Joint N=3 n (%)	Cohort 4 LNA043 20mg/Joint N=3 n (%)	Cohort 5 LNA043 20mg/Joint N=3 n (%)	Cohort 6 LNA043 20mg/Joint N=3 n (%)	Cohort 7 LNA043 40mg/Joint N=3 n (%)	Placebo N=7 n (%)	Total N=28 n (%)
Patients with at least one AE	1 (33.3)	3 (100.0)	3 (100.0)	2 (66.7)	2 (66.7)	0	3 (100.0)	5 (71.4)	19 (67.9)
Gastrointestinal disorders	0	2 (66.7)	1 (33.3)	2 (66.7)	1 (33.3)	0	1 (33.3)	3 (42.9)	10 (35.7)
Injury, poisoning and procedural complications	0	2 (66.7)	1 (33.3)	0	1 (33.3)	0	2 (66.7)	1 (14.3)	7 (25.0)
Nervous system disorders	1 (33.3)	1 (33.3)	1 (33.3)	0	2 (66.7)	0	2 (66.7)	0	7 (25.0)
Metabolism and nutrition disorders	0	1 (33.3)	0	0	2 (66.7)	0	1 (33.3)	1 (14.3)	5 (17.9)
Psychiatric disorders	0	2 (66.7)	1 (33.3)	0	0	0	1 (33.3)	1 (14.3)	5 (17.9)
Respiratory, thoracic and mediastinal disorders	0	1 (33.3)	1 (33.3)	0	0	0	1 (33.3)	2 (28.6)	5 (17.9)
Blood and lymphatic system disorders	0	2 (66.7)	1 (33.3)	0	0	0	1 (33.3)	0	4 (14.3)
Infections and infestations	0	0	2 (66.7)	0	0	0	2 (66.7)	0	4 (14.3)
Musculoskeletal and connective tissue disorders	0	1 (33.3)	1 (33.3)	0	0	0	1 (33.3)	1 (14.3)	4 (14.3)
Vascular disorders	0	0	1 (33.3)	0	0	0	1 (33.3)	2 (28.6)	4 (14.3)
General disorders and administration site conditions	0	0	2 (66.7)	0	0	0	0	1 (14.3)	3 (10.7)
Skin and subcutaneous tissue disorders	1 (33.3)	1 (33.3)	0	0	0	0	1 (33.3)	0	3 (10.7)
Cardiac disorders	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
Renal and urinary disorders	0	0	0	0	0	0	1 (33.3)	0	1 (3.6)

Brief summary of adverse events (Safety analysis set)

	Cohort 1 LNA043 0.2mg/Joint N=3 nE, nS (%)	Cohort 2 LNA043 2mg/Joint N=3 nE, nS (%)	Cohort 3 LNA043 10mg/Joint N=3 nE, nS (%)	Cohort 4 LNA043 20mg/Joint N=3 nE, nS (%)	Cohort 5 LNA043 20mg/Joint N=3 nE, nS (%)	Cohort 6 LNA043 20mg/Joint N=3 nE, nS (%)	Cohort 7 LNA043 40mg/Joint N=3 nE, nS (%)	Placebo N=7 nE, nS (%)	Total N=28 nE, nS (%)
AEs, Patients with AEs	3, 1 (33.3)	22, 3 (100.0)	20, 3 (100.0)	2, 2 (66.7)	6, 2 (66.7)	0	18, 3 (100.0)	24, 5 (71.4)	95, 19 (67.9)
AEs of Grade 1 (mild)	3, 1 (33.3)	5, 1 (33.3)	4, 1 (33.3)	2, 2 (66.7)	0	0	8, 0	15, 1 (14.3)	37, 6 (21.4)
AEs of Grade 2 (moderate)	0	14, 0	13, 1 (33.3)	0	4, 1 (33.3)	0	7, 2 (66.7)	6, 2 (28.6)	44, 6 (21.4)
AEs of Grade 3 (severe)	0	3, 2 (66.7)	3, 1 (33.3)	0	2, 1 (33.3)	0	3, 1 (33.3)	1, 1 (14.3)	12, 6 (21.4)
AEs of Grade 4 (life-threatening)	0	0	0	0	0	0	0	2, 1 (14.3)	2, 1 (3.6)
Study drug-related AEs	0	0	0	0	0	0	2, 1 (33.3)	0	2, 1 (3.6)
Serious AEs	0	1, 1 (33.3)	4, 1 (33.3)	0	0	0	2, 1 (33.3)	3, 2 (28.6)	10, 5 (17.9)
AEs leading to discontinuation of study treatment	0	0	0	0	0	0	0	0	0
Study-drug related AEs leading to discontinuation of study treatment	0	0	0	0	0	0	0	0	0

Incidence of clinical laboratory measurements outside normal range - n (percent) of subjects (Safety analysis set)

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo N=7 n (%)	Total N=28 n (%)
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)		
ABSBAS	EOS	50	High	0	0	0	0	0	1 (33.3)	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
ABSEOS	EOS	36	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
ABSLYM	D8	9	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
ABSMON	SCR	-8	High	0	0	0	0	0	1 (33.3)	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
ABSNEU	D8	9	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
	EOS	36	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo	Total
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)		
			Low	0	0	0	0	0	0	0	0	0
ALB	D1	1	High	0	1 (33.3)	0	0	0	0	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
ALKPHS	D8	7	High	0	0	0	0	0	0	1 (33.3)	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
	D15	17	High	0	0	0	0	1 (33.3)	0	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
	EOS	32	High	0	0	0	0	0	0	1 (33.3)	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
APTT	SCR	-9	High	0	0	0	0	1 (33.3)	0	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
		-7	High	0	0	0	0	1 (33.3)	0	0	0	1 (3.6)

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo	Total
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)		
			Low	0	0	0	0	0	0	0	0	0
		-6	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
		-5	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
	D1	1	High	0	0	0	0	2 (66.7)	0	0	1 (14.3)	3 (10.7)
			Low	0	0	0	0	0	0	0	0	0
	D15	16	High	0	0	0	0	1 (33.3)	0	0	1 (14.3)	2 (7.1)
			Low	0	0	0	0	0	0	0	0	0
		18	High	0	0	0	0	1 (33.3)	0	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
	EOS	24	High	0	0	0	0	1 (33.3)	0	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
		30	High	0	0	0	0	1 (33.3)	0	0	1 (14.3)	2 (7.1)

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo	Total
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)		
			Low	0	0	0	0	0	0	0	0	0
CALC	SCR	-1	High	0	0	1 (33.3)	0	0	0	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
CHLOR	D4	3	High	0	0	0	0	0	0	0	0	0
			Low	1 (33.3)	0	0	0	0	0	0	0	1 (3.6)
	EOS	36	High	0	0	0	0	0	0	0	0	0
			Low	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
CK	SCR	-6	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
	D1	1	High	0	0	0	0	0	2 (66.7)	0	2 (28.6)	4 (14.3)
			Low	0	0	0	0	0	0	0	0	0

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo N=7 n (%)	Total N=28 n (%)
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)		
	D4	3	High	0	0	0	1 (33.3)	0	0	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
	4	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)	
		Low	0	0	0	0	0	0	0	0	0	
D8	7	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)	
		Low	0	0	0	0	0	0	0	0	0	
EOS	28	High	0	0	0	0	0	0	0	0	0	
		Low	0	0	0	0	1 (33.3)	0	0	0	1 (3.6)	
	32	High	0	0	0	0	0	0	0	0	0	
		Low	0	0	0	0	0	0	1 (33.3)	0	1 (3.6)	
	34	High	0	0	0	0	0	0	0	0	0	
		Low	0	1 (33.3)	0	0	0	0	0	0	1 (3.6)	
DPLCNT	SCR	-1	High	0	0	1 (33.3)	0	0	0	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo	Total
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)		
D15	16	High	0	0	0	0	1 (33.3)	0	0	1 (14.3)	2 (7.1)	
		Low	0	0	0	0	0	0	0	0	0	
	17	High	0	0	0	0	1 (33.3)	0	0	0	1 (3.6)	
		Low	0	0	0	0	0	0	0	0	0	
	18	High	0	0	0	0	1 (33.3)	0	0	0	1 (3.6)	
		Low	0	0	0	0	0	0	0	0	0	
EOS	24	High	0	0	0	0	1 (33.3)	0	0	0	1 (3.6)	
		Low	0	0	0	0	0	0	0	0	0	
	28	High	0	0	0	0	1 (33.3)	0	0	0	1 (3.6)	
		Low	0	0	0	0	0	0	0	0	0	
	36	High	0	0	0	0	0	0	0	2 (28.6)	2 (7.1)	
		Low	0	0	0	0	0	0	0	0	0	
	39	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)	
		Low	0	0	0	0	0	0	0	0	0	

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo	Total
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)		
GGT	SCR	-4	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
		-3	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
	D1	1	High	0	0	0	0	0	0	0	2 (28.6)	2 (7.1)
			Low	0	0	0	0	0	0	0	0	0
	D4	4	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
		7	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
	D8	7	High	0	0	0	0	0	0	0	0	0
			Low	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
		8	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo N=7 n (%)	Total N=28 n (%)
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)		
		9	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
	EOS	36	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
		39	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
GLUC	SCR	-11	High	0	0	0	0	0	0	1 (33.3)	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
		-9	High	0	0	0	0	1 (33.3)	0	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
		-7	High	0	0	0	0	1 (33.3)	0	2 (66.7)	0	3 (10.7)
			Low	0	0	0	0	0	0	0	0	0
		-6	High	0	0	1 (33.3)	0	0	0	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
		-4	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo	Total
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)		
			Low	0	0	0	0	0	0	0	0	0
		-3	High	0	0	0	0	0	1 (33.3)	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
		-1	High	1 (33.3)	0	1 (33.3)	1 (33.3)	0	0	0	1 (14.3)	4 (14.3)
			Low	0	0	0	0	0	0	0	0	0
	D1	1	High	2 (66.7)	0	1 (33.3)	1 (33.3)	2 (66.7)	0	1 (33.3)	3 (42.9)	10 (35.7)
			Low	0	0	0	1 (33.3)	0	0	0	0	1 (3.6)
	D4	3	High	0	1 (33.3)	0	1 (33.3)	0	1 (33.3)	0	0	3 (10.7)
			Low	0	0	0	0	0	0	0	0	0
		4	High	2 (66.7)	0	0	0	0	2 (66.7)	1 (33.3)	1 (14.3)	6 (21.4)
			Low	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
		5	High	0	0	1 (33.3)	1 (33.3)	0	0	1 (33.3)	1 (14.3)	4 (14.3)
			Low	0	0	0	0	0	0	0	0	0
		7	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo	Total
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)		
D8	7	High	1 (33.3)	0	0	1 (33.3)	0	0	1 (33.3)	2 (28.6)	5 (17.9)	
		Low	0	0	0	0	0	0	0	0	0	
	9	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)	
		Low	0	0	0	0	0	0	0	0	0	
	12	High	0	0	1 (33.3)	0	0	0	0	0	1 (3.6)	
		Low	0	0	0	0	0	0	0	0	0	
D15	16	High	0	0	0	0	1 (33.3)	0	0	1 (14.3)	2 (7.1)	
		Low	0	0	0	0	0	0	0	0	0	
	17	High	0	0	0	0	1 (33.3)	0	0	0	1 (3.6)	
		Low	0	0	0	0	0	0	0	0	0	
	18	High	0	0	0	0	1 (33.3)	0	0	0	1 (3.6)	
		Low	0	0	0	0	0	0	0	0	0	
EOS	24	High	0	0	0	0	1 (33.3)	0	0	0	1 (3.6)	
		Low	0	0	0	0	0	0	0	0	0	

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo N=7 n (%)	Total N=28 n (%)
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)		
HCT	SCR	28	High	0	0	0	0	1 (33.3)	0	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
		36	High	0	0	0	1 (33.3)	0	0	0	4 (57.1)	5 (17.9)
			Low	0	0	0	0	0	0	0	0	0
		37	High	1 (33.3)	0	0	0	0	0	1 (33.3)	0	2 (7.1)
			Low	0	0	0	0	0	0	0	0	0
	39	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)	
		Low	0	0	0	0	0	0	0	0	0	
	D1	-7	High	0	0	0	0	0	0	0	0	0
			Low	0	0	0	0	0	0	1 (33.3)	0	1 (3.6)
		-2	High	0	0	0	1 (33.3)	0	0	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
1		High	0	0	0	0	0	0	0	0	0	
		Low	0	0	0	0	0	0	1 (33.3)	0	1 (3.6)	

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo	Total
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)		
D4	4	High	0	0	0	0	0	0	0	0	0	0
		Low	0	0	0	0	0	0	1 (33.3)	0	1 (3.6)	
	5	High	0	0	0	1 (33.3)	0	0	0	0	0	1 (3.6)
		Low	0	0	0	0	0	0	0	0	0	0
D8	7	High	0	0	0	0	0	0	0	0	0	0
		Low	0	0	0	0	0	0	2 (66.7)	0	2 (7.1)	
	9	High	0	0	0	1 (33.3)	0	0	0	0	0	1 (3.6)
		Low	0	0	0	0	0	0	0	0	0	0
D15	16	High	0	0	0	0	0	0	0	0	0	0
		Low	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)	
	17	High	0	0	0	0	0	0	0	0	0	0
		Low	0	0	0	0	1 (33.3)	0	0	0	0	1 (3.6)
D22	21	High	0	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
		Low	0	0	0	0	0	0	0	0	0	0

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo	Total
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)		
EOS	28	High	0	0	0	0	0	0	0	0	0	0
		Low	0	0	0	0	1 (33.3)	0	0	0	0	1 (3.6)
	32	High	0	0	0	0	0	0	0	0	0	0
		Low	0	0	0	0	0	0	1 (33.3)	0	0	1 (3.6)
	36	High	0	0	0	0	0	0	0	0	0	0
		Low	0	1 (33.3)	0	0	0	0	0	0	1 (14.3)	2 (7.1)
	37	High	0	0	0	0	0	0	0	0	0	0
		Low	1 (33.3)	0	0	0	0	0	0	0	0	1 (3.6)
	56	High	0	0	0	0	0	0	0	0	0	0
Low		0	0	0	0	0	0	1 (33.3)	0	0	1 (3.6)	
HDL	SCR	-7	High	0	0	0	0	0	0	0	0	0
		Low	0	0	0	0	0	0	1 (33.3)	0	1 (3.6)	
	-1	High	0	0	0	0	0	0	0	0	0	
		Low	1 (33.3)	0	0	1 (33.3)	0	0	0	0	2 (7.1)	

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo	Total
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)		
D1	1		High	0	0	0	0	0	0	0	0	0
			Low	1 (33.3)	0	0	1 (33.3)	0	0	1 (33.3)	0	3 (10.7)
D4	3		High	0	0	0	0	0	0	0	0	0
			Low	0	0	0	1 (33.3)	0	0	0	0	1 (3.6)
	4	High	0	0	0	0	0	0	0	0	0	
		Low	1 (33.3)	0	0	0	0	1 (33.3)	1 (33.3)	0	3 (10.7)	
D8	7		High	0	0	0	0	0	0	0	0	0
			Low	1 (33.3)	0	0	0	0	0	1 (33.3)	1 (14.3)	3 (10.7)
	8	High	0	0	0	0	0	0	0	0	0	
		Low	0	0	0	1 (33.3)	0	0	0	0	1 (3.6)	
D15	16		High	0	0	0	0	0	0	0	0	0
			Low	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
	18	High	0	0	0	0	0	0	0	0	0	
		Low	0	0	0	0	1 (33.3)	0	0	0	1 (3.6)	

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo	Total
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)		
D22	28	High	0	0	0	0	0	0	0	0	0	0
			Low	0	0	0	0	0	1 (33.3)	0	0	1 (3.6)
	EOS	36	High	0	0	0	0	0	0	0	0	0
			Low	0	0	0	1 (33.3)	0	0	0	3 (42.9)	4 (14.3)
	37	High	0	0	0	0	0	0	0	0	0	0
		Low	1 (33.3)	0	0	0	0	0	0	1 (33.3)	0	2 (7.1)
56	High	0	0	0	0	0	0	0	0	0	0	
	Low	0	0	0	0	0	0	1 (33.3)	0	0	1 (3.6)	
HGB	SCR	-7	High	0	0	0	0	0	0	0	0	0
		Low	0	0	0	0	0	0	0	1 (33.3)	0	1 (3.6)
D1	1	High	0	0	0	0	0	0	0	0	0	0
		Low	0	0	0	0	0	0	0	1 (33.3)	0	1 (3.6)

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo N=7 n (%)	Total N=28 n (%)
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)		
	D4	4	High	0	0	0	0	0	0	0	0	0
			Low	0	0	0	0	0	0	1 (33.3)	0	1 (3.6)
	D8	7	High	0	0	0	0	0	0	0	0	0
			Low	0	0	0	0	0	0	2 (66.7)	0	2 (7.1)
	D15	16	High	0	0	0	0	0	0	0	0	0
			Low	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
		17	High	0	0	0	0	0	0	0	0	0
			Low	0	0	0	0	1 (33.3)	0	0	0	1 (3.6)
	EOS	28	High	0	0	0	0	0	0	0	0	0
			Low	0	0	0	0	1 (33.3)	0	0	0	1 (3.6)
		32	High	0	0	0	0	0	0	0	0	0
			Low	0	0	0	0	0	0	1 (33.3)	0	1 (3.6)
		34	High	0	0	0	0	0	0	0	0	0
			Low	0	1 (33.3)	0	0	0	0	0	0	1 (3.6)

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo	Total
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)		
		36	High	0	0	0	0	0	0	0	0	0
			Low	0	0	0	1 (33.3)	0	0	0	2 (28.6)	3 (10.7)
		37	High	0	0	0	0	0	0	0	0	0
			Low	1 (33.3)	0	0	0	0	0	0	0	1 (3.6)
		56	High	0	0	0	0	0	0	0	0	0
			Low	0	0	0	0	0	1 (33.3)	0	0	1 (3.6)
IBIL	D1	1	High	0	0	0	1 (33.3)	0	1 (33.3)	0	0	2 (7.1)
			Low	0	0	0	0	0	0	0	0	0
	D4	3	High	0	0	0	1 (33.3)	0	0	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
LDH	D8	7	High	0	0	0	0	0	0	1 (33.3)	1 (14.3)	2 (7.1)
			Low	0	0	0	0	0	0	0	0	0
	9		High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo	Total	
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)			
	D15	16	High	0	0	0	0	1 (33.3)	0	0	1 (14.3)	2 (7.1)	
			Low	0	0	0	0	0	0	0	0	0	
		17	High	0	0	0	0	1 (33.3)	0	0	0	1 (3.6)	
			Low	0	0	0	0	0	0	0	0	0	
EOS	35	High	0	0	1 (33.3)	0	0	0	0	0	0	1 (3.6)	
		Low	0	0	0	0	0	0	0	0	0	0	
		36	High	1 (33.3)	0	0	0	0	0	0	0	1 (14.3)	2 (7.1)
			Low	0	0	0	0	0	0	0	0	0	0
LDL	SCR	-11	High	0	0	0	0	0	0	1 (33.3)	0	1 (3.6)	
			Low	0	0	0	0	0	0	0	0	0	
		-9	High	0	0	0	0	1 (33.3)	0	0	0	1 (3.6)	
			Low	0	0	0	0	0	0	0	0	0	
		-6	High	0	1 (33.3)	0	0	0	0	0	0	1 (14.3)	2 (7.1)
			Low	0	0	0	0	0	0	0	0	0	0

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo N=7 n (%)	Total N=28 n (%)
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)		
		-3	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
		-2	High	0	1 (33.3)	0	1 (33.3)	0	0	0	0	2 (7.1)
			Low	0	0	0	0	0	0	0	0	0
		-1	High	0	0	2 (66.7)	0	0	0	0	0	2 (7.1)
			Low	0	0	0	0	0	0	0	0	0
	D1	1	High	0	1 (33.3)	2 (66.7)	0	1 (33.3)	0	0	2 (28.6)	6 (21.4)
			Low	0	0	0	0	0	0	0	0	0
	D4	3	High	0	1 (33.3)	1 (33.3)	1 (33.3)	0	0	0	0	3 (10.7)
			Low	0	0	0	0	0	0	0	0	0
		4	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
		5	High	0	0	1 (33.3)	0	0	0	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo N=7 n (%)	Total N=28 n (%)
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)		
D8	7	High	0	0	1 (33.3)	0	0	0	0	0	0	1 (3.6)
		Low	0	0	0	0	0	0	0	0	0	0
	8	High	0	1 (33.3)	0	1 (33.3)	0	0	0	0	1 (14.3)	3 (10.7)
		Low	0	0	0	0	0	0	0	0	0	0
	9	High	0	0	0	1 (33.3)	0	0	0	0	0	1 (3.6)
		Low	0	0	0	0	0	0	0	0	0	0
	12	High	0	0	1 (33.3)	0	0	0	0	0	0	1 (3.6)
		Low	0	0	0	0	0	0	0	0	0	0
EOS	30	High	0	0	0	0	1 (33.3)	0	0	0	0	1 (3.6)
		Low	0	0	0	0	0	0	0	0	0	0
	34	High	0	1 (33.3)	0	0	0	0	0	0	0	1 (3.6)
		Low	0	0	0	0	0	0	0	0	0	0
	35	High	0	0	1 (33.3)	0	0	0	0	0	0	1 (3.6)
		Low	0	0	0	0	0	0	0	0	0	0
	36	High	0	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
		Low	0	0	0	0	0	0	0	0	0	0

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo	Total	
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)			N=7 n (%)
POT	SCR	39	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)	
			Low	0	0	0	0	0	0	0	0	0	
		41	High	0	0	1 (33.3)	0	0	0	0	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0	0
		-4	High	0	0	0	0	0	0	0	0	0	0
			Low	0	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
	D1	1	High	0	0	0	0	0	0	0	0	0	0
			Low	0	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
	D4	7	High	0	0	0	0	0	0	0	0	0	0
			Low	0	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
	D8	9	High	0	0	0	0	0	0	0	0	0	0
			Low	0	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo N=7 n (%)	Total N=28 n (%)
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)		
PTINR	SCR	-2	High	0	0	0	1 (33.3)	0	0	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
	D1	1	High	0	0	0	1 (33.3)	0	0	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
	D4	5	High	0	0	0	1 (33.3)	0	0	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
	D8	9	High	0	0	0	1 (33.3)	0	0	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
	D15	17	High	0	0	0	0	1 (33.3)	0	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
	EOS	35	High	0	0	1 (33.3)	0	0	0	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo	Total	
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)			N=7 n (%)
RBC		36	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)	
			Low	0	0	0	0	0	0	0	0	0	
		41	High	0	0	0	1 (33.3)	0	0	0	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0	0
	SCR	-7	High	0	0	0	0	0	0	0	0	0	0
			Low	0	0	0	0	0	0	1 (33.3)	0	1 (3.6)	
	D1	1	High	0	0	0	0	0	0	0	0	0	0
			Low	0	0	0	0	0	0	1 (33.3)	0	1 (3.6)	
	D4	4	High	0	0	0	0	0	0	0	0	0	0
			Low	0	0	0	0	0	0	1 (33.3)	0	1 (3.6)	
	D8	7	High	0	0	0	0	0	0	0	0	0	0
			Low	0	0	0	0	0	0	2 (66.7)	0	2 (7.1)	

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo	Total	
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)			N=7 n (%)
	D15	16	High	0	0	0	0	0	0	0	0	0	
			Low	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)	
	17	High	0	0	0	0	0	0	0	0	0	0	
		Low	0	0	0	0	1 (33.3)	0	0	0	0	1 (3.6)	
	EOS	28	High	0	0	0	0	0	0	0	0	0	0
			Low	0	0	0	0	1 (33.3)	0	0	0	0	1 (3.6)
32		High	0	0	0	0	0	0	0	0	0	0	
		Low	0	0	0	0	0	0	0	1 (33.3)	0	1 (3.6)	
36		High	0	0	0	0	0	0	0	0	0	0	
		Low	0	1 (33.3)	0	1 (33.3)	0	0	0	0	2 (28.6)	4 (14.3)	
SGOT	D4	7	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)	
			Low	0	0	0	0	0	0	0	0	0	
EOS	36	High	0	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)	
		Low	0	0	0	0	0	0	0	0	0	0	

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo	Total	
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)			N=7 n (%)
SGPT	SCR	-7	High	0	0	0	0	0	0	1 (33.3)	0	1 (3.6)	
			Low	0	0	0	0	0	0	0	0	0	
		-2	High	0	0	0	1 (33.3)	0	0	0	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0	0
		-1	High	1 (33.3)	0	0	0	0	0	0	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0	0
	D1	1	High	1 (33.3)	0	0	0	0	0	0	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0	0
	D4	7	High	0	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0	0
SOD	D1	1	High	0	0	0	1 (33.3)	0	0	0	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0	0

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo	Total
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)		
TBIL	D8	8	High	0	1 (33.3)	0	1 (33.3)	0	0	0	0	2 (7.1)
			Low	0	0	0	0	0	0	0	0	0
	D22	28	High	0	0	0	0	0	1 (33.3)	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
	EOS	36	High	0	0	0	1 (33.3)	0	0	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
	SCR	-1	High	0	0	0	1 (33.3)	0	0	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
	D1	1	High	0	1 (33.3)	0	1 (33.3)	0	0	0	0	2 (7.1)
			Low	0	0	0	0	0	0	0	0	0
	D4	3	High	0	0	0	1 (33.3)	0	0	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo	Total
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)		
	D8	8	High	0	0	0	1 (33.3)	0	0	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
EOS	36		High	0	0	0	1 (33.3)	0	0	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
	37	High	0	0	0	0	0	0	0	0	0	0
		Low	0	0	0	0	0	0	0	1 (33.3)	0	1 (3.6)
TCHOL	SCR	-11	High	0	0	0	0	0	0	1 (33.3)	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
	-9	High	0	0	0	0	1 (33.3)	0	0	0	0	1 (3.6)
		Low	0	0	0	0	0	0	0	0	0	0
	-6	High	0	1 (33.3)	0	0	0	0	0	0	1 (14.3)	2 (7.1)
		Low	0	0	0	0	0	0	0	0	0	0
	-5	High	0	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
		Low	0	0	0	0	0	0	0	0	0	0

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo	Total
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)		
		-3	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
		-2	High	0	1 (33.3)	0	1 (33.3)	0	0	0	0	2 (7.1)
			Low	0	0	0	0	0	0	0	0	0
		-1	High	1 (33.3)	0	2 (66.7)	0	0	0	0	1 (14.3)	4 (14.3)
			Low	0	0	0	0	0	0	0	0	0
	D1	1	High	0	2 (66.7)	2 (66.7)	1 (33.3)	2 (66.7)	0	0	2 (28.6)	9 (32.1)
			Low	0	0	0	0	0	0	0	0	0
	D4	3	High	0	1 (33.3)	1 (33.3)	0	0	0	1 (33.3)	0	3 (10.7)
			Low	0	0	0	0	0	0	0	0	0
		4	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
		5	High	0	0	1 (33.3)	1 (33.3)	0	0	0	0	2 (7.1)
			Low	0	0	0	0	0	0	0	0	0

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo	Total
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)		
D8	7	High	1 (33.3)	0	1 (33.3)	0	0	0	0	0	0	2 (7.1)
		Low	0	0	0	0	0	0	0	0	0	0
	8	High	0	1 (33.3)	0	0	0	0	0	0	1 (14.3)	2 (7.1)
		Low	0	0	0	0	0	0	0	0	0	0
	9	High	0	0	0	1 (33.3)	0	0	0	0	0	1 (3.6)
		Low	0	0	0	0	0	0	0	0	0	0
	12	High	0	0	1 (33.3)	0	0	0	0	0	0	1 (3.6)
		Low	0	0	0	0	0	0	0	0	0	0
D15	16	High	0	0	0	0	1 (33.3)	0	0	0	0	1 (3.6)
		Low	0	0	0	0	0	0	0	0	0	0
EOS	30	High	0	0	0	0	1 (33.3)	0	0	0	0	1 (3.6)
		Low	0	0	0	0	0	0	0	0	0	0
	34	High	0	1 (33.3)	0	0	0	0	0	0	0	1 (3.6)
		Low	0	0	0	0	0	0	0	0	0	0
	35	High	0	0	1 (33.3)	0	0	0	0	0	0	1 (3.6)
		Low	0	0	0	0	0	0	0	0	0	0

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo	Total
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)		
			Low	0	0	0	0	0	0	0	0	0
		37	High	0	0	0	0	0	0	1 (33.3)	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
		39	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
		41	High	0	0	1 (33.3)	1 (33.3)	0	0	0	0	2 (7.1)
			Low	0	0	0	0	0	0	0	0	0
TRIGLY	SCR	-11	High	0	0	0	0	0	0	1 (33.3)	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
		-9	High	0	0	0	0	1 (33.3)	0	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
		-7	High	0	0	0	0	1 (33.3)	0	1 (33.3)	0	2 (7.1)
			Low	0	0	0	0	0	0	0	0	0
		-6	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
		-5	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo	Total
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)		
			Low	0	0	0	0	0	0	0	0	0
		-4	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
		-2	High	0	0	0	1 (33.3)	0	0	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
		-1	High	2 (66.7)	0	1 (33.3)	0	0	0	0	1 (14.3)	4 (14.3)
			Low	0	0	0	0	0	0	0	0	0
	D1	1	High	1 (33.3)	0	1 (33.3)	0	1 (33.3)	0	0	1 (14.3)	4 (14.3)
			Low	0	0	0	0	0	0	0	0	0
	D4	4	High	2 (66.7)	0	0	0	0	0	0	0	2 (7.1)
			Low	0	0	0	0	0	0	0	0	0
		5	High	0	0	0	1 (33.3)	0	0	1 (33.3)	0	2 (7.1)
			Low	0	0	0	0	0	0	0	0	0
		7	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo	Total
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)		
D8	7	High	1 (33.3)	0	0	1 (33.3)	0	0	1 (33.3)	0	3 (10.7)	
		Low	0	0	0	0	0	0	0	0	0	
	8	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)	
		Low	0	0	0	0	0	0	0	0	0	
	9	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)	
		Low	0	0	0	0	0	0	0	0	0	
12	High	0	0	1 (33.3)	0	0	0	0	0	1 (3.6)		
	Low	0	0	0	0	0	0	0	0	0		
D15	16	High	0	0	0	0	1 (33.3)	0	0	1 (14.3)	2 (7.1)	
		Low	0	0	0	0	0	0	0	0	0	
	18	High	0	0	0	0	1 (33.3)	0	0	0	1 (3.6)	
		Low	0	0	0	0	0	0	0	0	0	
EOS	28	High	0	0	0	0	1 (33.3)	0	0	0	1 (3.6)	
		Low	0	0	0	0	0	0	0	0	0	

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo N=7 n (%)	Total N=28 n (%)	
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)			
		30	High	0	0	0	0	1 (33.3)	0	0	0	1 (3.6)	
			Low	0	0	0	0	0	0	0	0	0	
		35	High	0	0	0	1 (33.3)	0	0	0	0	1 (3.6)	
			Low	0	0	0	0	0	0	0	0	0	
		36	High	1 (33.3)	0	0	0	0	0	0	2 (28.6)	3 (10.7)	
			Low	0	0	0	0	0	0	0	0	0	
		37	High	1 (33.3)	0	0	0	0	0	2 (66.7)	0	3 (10.7)	
			Low	0	0	0	0	0	0	0	0	0	
UACID	SCR	-7	High	0	0	0	0	0	0	1 (33.3)	0	1 (3.6)	
			Low	0	0	0	0	0	0	0	0	0	
		-2	High	0	0	0	1 (33.3)	0	0	0	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0	0
		-1	High	0	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0	0
	D1	1	High	1 (33.3)	0	0	0	0	0	1 (33.3)	0	2 (7.1)	

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo	Total
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)		
			Low	0	0	0	0	0	0	0	0	0
	D4	4	High	0	0	0	0	0	0	1 (33.3)	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
		5	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
	D8	7	High	1 (33.3)	0	0	0	0	0	2 (66.7)	0	3 (10.7)
			Low	0	0	0	0	0	0	0	0	0
UBLOST	SCR	-11	High	0	0	0	0	0	0	1 (33.3)	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
		-6	High	0	0	0	0	0	1 (33.3)	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
		-3	High	0	0	0	0	0	1 (33.3)	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo	Total
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)		
D1	1		High	0	0	0	1 (33.3)	0	0	1 (33.3)	1 (14.3)	3 (10.7)
			Low	0	0	0	0	0	0	0	0	0
D4	3		High	0	0	0	1 (33.3)	0	0	1 (33.3)	0	2 (7.1)
			Low	0	0	0	0	0	0	0	0	0
	4	High	0	0	0	0	0	1 (33.3)	0	0	1 (3.6)	
		Low	0	0	0	0	0	0	0	0	0	
	5	High	0	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
		Low	0	0	0	0	0	0	0	0	0	0
D8	8	High	0	0	0	1 (33.3)	0	0	0	0	0	1 (3.6)
		Low	0	0	0	0	0	0	0	0	0	0
EOS	35	High	0	0	0	1 (33.3)	0	0	0	0	0	1 (3.6)
		Low	0	0	0	0	0	0	0	0	0	0
	57	High	0	0	0	0	0	1 (33.3)	0	0	0	1 (3.6)
		Low	0	0	0	0	0	0	0	0	0	0

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo	Total	
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)			N=7 n (%)
UKETST	D1	1	High	1 (33.3)	0	0	0	0	0	0	0	1 (3.6)	
			Low	0	0	0	0	0	0	0	0	0	
	D8	8	High	0	1 (33.3)	0	0	0	0	0	0	1 (3.6)	
			Low	0	0	0	0	0	0	0	0	0	
ULEUKST	SCR	-9	High	0	0	0	0	1 (33.3)	0	0	0	1 (3.6)	
			Low	0	0	0	0	0	0	0	0	0	
		-6	High	0	0	0	0	0	1 (33.3)	0	0	1 (3.6)	
			Low	0	0	0	0	0	0	0	0	0	
		-3	High	0	0	0	0	0	1 (33.3)	0	0	1 (3.6)	
			Low	0	0	0	0	0	0	0	0	0	
		-1	High	0	0	2 (66.7)	0	0	0	0	0	0	2 (7.1)
			Low	0	0	0	0	0	0	0	0	0	0
	D1	1	High	0	0	1 (33.3)	1 (33.3)	0	0	1 (33.3)	0	3 (10.7)	

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo	Total
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)		
			Low	0	0	0	0	0	0	0	0	0
	D4	3	High	0	0	0	0	0	0	1 (33.3)	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
		4	High	0	0	0	0	0	1 (33.3)	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
		5	High	0	0	0	1 (33.3)	0	0	0	1 (14.3)	2 (7.1)
			Low	0	0	0	0	0	0	0	0	0
	EOS	35	High	0	0	0	1 (33.3)	0	0	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
UPROTST	SCR	-6	High	0	0	0	0	0	1 (33.3)	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
		-1	High	0	0	1 (33.3)	0	0	0	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo	Total
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)		
	D4	5	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
EOS	35		High	0	0	0	1 (33.3)	0	0	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
	41	High	0	0	1 (33.3)	0	0	0	0	0	0	1 (3.6)
		Low	0	0	0	0	0	0	0	0	0	0
UREA	SCR	-7	High	0	0	0	0	0	0	2 (66.7)	0	2 (7.1)
			Low	0	0	0	0	0	0	0	0	0
	-1	High	0	1 (33.3)	0	0	0	0	0	0	0	1 (3.6)
		Low	0	0	0	0	0	0	0	0	0	0
D1	1		High	0	0	0	0	0	0	1 (33.3)	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
D4	4		High	0	0	0	0	0	0	1 (33.3)	0	1 (3.6)

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo N=7 n (%)	Total N=28 n (%)
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)		
			Low	0	0	0	0	0	0	0	0	0
	D8	7	High	0	0	1 (33.3)	0	0	0	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
	EOS	36	High	0	0	1 (33.3)	0	0	0	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
		37	High	0	0	0	0	0	0	1 (33.3)	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
UUROST	EOS	34	High	0	1 (33.3)	0	0	0	0	0	0	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
WBC	SCR	-4	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
	D4	3	High	0	0	0	0	0	0	0	0	0

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo N=7 n (%)	Total N=28 n (%)
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)		
			Low	0	0	0	0	0	1 (33.3)	0	0	1 (3.6)
		7	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
	D8	9	High	0	0	0	0	0	0	0	1 (14.3)	1 (3.6)
			Low	0	0	0	0	0	0	0	0	0
	EOS	36	High	0	0	0	0	0	0	0	2 (28.6)	2 (7.1)
			Low	0	0	0	0	0	0	0	0	0
		57	High	0	0	0	0	0	0	0	0	0
			Low	0	0	0	0	0	1 (33.3)	0	0	1 (3.6)

n: number of unique subjects with measurement outside normal range; * Unscheduled visits are not included

Incidence of vital signs measurements outside normal range - n (percent) of subjects (Safety analysis set)

There were no observations which met the report criteria

Incidence of clinically significant abnormalities in ECG interpretation - n (percent) of subjects (Safety analysis set)

Lab test code	Visit*	Study Day	High/Low	Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 5	Cohort 6	Cohort 7	Placebo	Total
				LNA043 0.2mg/ Joint N=3 n (%)	LNA043 2mg/ Joint N=3 n (%)	LNA043 10mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 20mg/ Joint N=3 n (%)	LNA043 40mg/ Joint N=3 n (%)		
ECG Interpretation	SCR	-7	ABN	0	0	0	0	0	0	1 (33.3)	0	1 (3.6)
	D1	1	ABN	0	0	0	0	0	0	1 (33.3)	0	1 (3.6)

n: number of unique subjects with measurement outside normal range; * Unscheduled visits are not included

Summary of KOOS questionnaire score “Pain and discomfort” (Safety analysis set)

Analysis part: Part 1 – injection 7 days pre-TKR surgery
 Category: Pain and discomfort
 Parameter: Normalized score

Visit		Cohort 1	Cohort 2	Cohort 3	Cohort 4	Cohort 7	Cohort 1-4 & 7
		LNA043 0.2mg/Joint N=3	LNA043 2mg/Joint N=3	LNA043 10mg/Joint N=3	LNA043 20mg/Joint N=3	LNA043 40mg/Joint N=3	Placebo N=5
BAS	n	3 (3)	3 (3)	3 (3)	3 (3)	3 (3)	5 (5)
	mean	38.89 (0.00)	51.85 (0.00)	45.37 (0.00)	49.77 (0.00)	50.00 (0.00)	38.61 (0.00)
	SD	10.015 (0.000)	5.782 (0.000)	30.598 (0.000)	5.906 (0.000)	14.699 (0.000)	30.907 (0.000)
	minimum	30.6 (0.0)	47.2 (0.0)	13.9 (0.0)	43.8 (0.0)	38.9 (0.0)	11.1 (0.0)
	median	36.11 (0.00)	50.00 (0.00)	47.22 (0.00)	50.00 (0.00)	44.44 (0.00)	27.78 (0.00)
	maximum	50.0 (0.0)	58.3 (0.0)	75.0 (0.0)	55.6 (0.0)	66.7 (0.0)	80.6 (0.0)
D4	n	3 (3)	3 (3)	3 (3)	3 (3)	3 (3)	5 (5)
	mean	38.89 (0.00)	49.07 (-2.78)	41.67 (-3.70)	52.43 (2.66)	35.19 (-14.81)	33.61 (-5.00)
	SD	11.111 (2.778)	11.226 (7.349)	7.349 (23.625)	13.190 (7.482)	13.981 (8.486)	28.941 (14.353)
	minimum	27.8 (-2.8)	38.9 (-11.1)	33.3 (-27.8)	40.6 (-3.1)	22.2 (-22.2)	12.5 (-30.6)
	median	38.89 (0.00)	47.22 (0.00)	44.44 (-2.78)	50.00 (0.00)	33.33 (-16.67)	27.78 (0.00)
	maximum	50.0 (2.8)	61.1 (2.8)	47.2 (19.4)	66.7 (11.1)	50.0 (-5.6)	83.3 (2.8)
EOS	n	3 (3)	3 (3)	3 (3)	3 (3)	3 (3)	5 (5)
	mean	42.48 (3.59)	46.18 (-5.67)	60.19 (14.81)	67.11 (17.34)	62.04 (12.04)	50.35 (11.74)
	SD	15.041 (24.207)	18.066 (14.634)	27.824 (35.825)	7.258 (12.047)	30.974 (40.286)	18.766 (36.075)

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Analysis part: Part 1 – injection 7 days pre-TKR surgery
 Category: Pain and discomfort
 Parameter: Normalized score

Visit	Cohort 1 LNA043 0.2mg/Joint N=3	Cohort 2 LNA043 2mg/Joint N=3	Cohort 3 LNA043 10mg/Joint N=3	Cohort 4 LNA043 20mg/Joint N=3	Cohort 7 LNA043 40mg/Joint N=3	Cohort 1-4 & 7 Placebo N=5
minimum	30.6 (-19.4)	27.8 (-22.2)	38.9 (-25.0)	60.7 (10.1)	38.9 (-27.8)	25.0 (-44.4)
median	37.50 (1.39)	46.88 (-0.35)	50.00 (25.00)	65.63 (10.71)	50.00 (11.11)	58.33 (12.50)
maximum	59.4 (28.8)	63.9 (5.6)	91.7 (44.4)	75.0 (31.3)	97.2 (52.8)	66.7 (47.2)

Analysis part: Part 2 – injection 2 hours pre-TKR surgery
 Category: Pain and discomfort
 Parameter: Normalized score

Visit		Cohort 5 LNA043 20mg/Joint N=3	Cohort 5 Placebo N=1
BAS	n	3 (3)	1 (1)
	mean	42.59 (0.00)	27.78 (0.00)
	SD	5.782 (0.000)	
	minimum	36.1 (0.0)	27.8 (0.0)
	median	44.44 (0.00)	27.78 (0.00)
	maximum	47.2 (0.0)	27.8 (0.0)

Analysis part: Part 2 – injection 2 hours pre-TKR surgery
 Category: Pain and discomfort
 Parameter: Normalized score

Visit		Cohort 5 LNA043 20mg/Joint N=3	Cohort 5 Placebo N=1
EOS	n	3 (3)	1 (1)
	mean	69.84 (27.25)	44.44 (16.67)
	SD	4.507 (6.785)	
	minimum	66.7 (19.4)	44.4 (16.7)
	median	67.86 (30.56)	44.44 (16.67)
	maximum	75.0 (31.7)	44.4 (16.7)

Analysis part: Part 3 – injection 21 days pre-TKR surgery
 Category: Pain and discomfort
 Parameter: Normalized score

Visit		Cohort 6 LNA043 20mg/Joint N=3	Cohort 6 Placebo N=1
BAS	n	3 (3)	1 (1)
	mean	59.26 (0.00)	33.33 (0.00)
	SD	8.929 (0.000)	

Analysis part: Part 3 – injection 21 days pre-TKR surgery
 Category: Pain and discomfort
 Parameter: Normalized score

Visit	Cohort 6 LNA043 20mg/Joint N=3	Cohort 6 Placebo N=1
	minimum 52.8 (0.0)	33.3 (0.0)
	median 55.56 (0.00)	33.33 (0.00)
	maximum 69.4 (0.0)	33.3 (0.0)
D4	n 3 (3)	1 (1)
	mean 66.67 (7.41)	41.67 (8.33)
	SD 10.015 (1.604)	
	minimum 58.3 (5.6)	41.7 (8.3)
	median 63.89 (8.33)	41.67 (8.33)
	maximum 77.8 (8.3)	41.7 (8.3)
EOS	n 3 (3)	1 (1)
	mean 70.24 (10.98)	33.33 (0.00)
	SD 18.596 (10.073)	
	minimum 58.3 (2.8)	33.3 (0.0)
	median 60.71 (7.94)	33.33 (0.00)
	maximum 91.7 (22.2)	33.3 (0.0)

Secondary Outcome Result(s)
Summary of IHC cartilage matrix staining analysis for ANGPTL analyte on TKR surgery visit/time - comparison with cohort 5 (Biomarker analysis set)

Tissue location		All Placebo N=7	Cohort 1-4, 6 & 7 N=18	Cohort 5 N=3
Cartilage matrix	n	49	123	21
	Mean (SD)	19.3 (26.50)	16.5 (15.39)	55.5 (37.15)
	Median	10.0	10.0	50.0
	Range	0-160	0-80	5-160

Summary statistics for serum LNA043 PK parameters of primary interest per treatment (Pharmacokinetic analysis set)

Treatment	Statistic	AUClast (h*ng/mL)	Cmax (ng/mL)	Tmax (h)
Cohort 1 LNA043 0.2mg/Joint	n	3	3	
	Mean (SD)	0.00 (0.00)	0.00 (0.00)	
	CV% mean			
	Median	0.00	0.00	
	min-max	0.00 - 0.00	0.00 - 0.00	
Cohort 2 LNA043 2mg/Joint	n	3	3	1
	Mean (SD)	106 (183)	89.0 (154)	
	CV% mean	173.2	173.2	
	Median	0.00	0.00	0.233
	min-max	0.00 - 317	0.00 - 267	0.233 - 0.233

Treatment	Statistic	AUClast (h*ng/mL)	Cmax (ng/mL)	Tmax (h)
Cohort 3 LNA043 10mg/Joint	n	3	3	3
	Mean (SD)	243 (60.4)	90.1 (9.85)	
	CV% mean	24.9	10.9	
	Median	274	87.3	2.03
	min-max	173 - 281	81.9 - 101	2.02 - 3.67
Cohort 4 LNA043 20mg/Joint	n	3	3	3
	Mean (SD)	329 (194)	117 (52.2)	
	CV% mean	59.0	44.7	
	Median	339	133	2.07
	min-max	130 - 518	58.4 - 159	2.03 - 3.73
Cohort 5 LNA043 20mg/Joint	n	3	3	3
	Mean (SD)	126 (60.4)	47.1 (19.9)	
	CV% mean	48.0	42.2	
	Median	99.8	46.8	1.90
	min-max	83.0 - 195	27.4 - 67.2	1.87 - 2.00
Cohort 6 LNA043 20mg/Joint	n	3	3	3
	Mean (SD)	209 (39.6)	88.1 (10.6)	
	CV% mean	18.9	12.1	
	Median	213	84.9	3.58
	min-max	168 - 247	79.5 - 100	2.05 - 3.72
Cohort 7 LNA043 40mg/Joint	n	3	3	3
	Mean (SD)	1460 (191)	259 (39.3)	
	CV% mean	13.1	15.2	

Treatment	Statistic	AUClast (h*ng/mL)	Cmax (ng/mL)	Tmax (h)
	Median	1530	274	4.25
	min-max	1240 - 1600	214 - 288	3.75 - 7.30

Summary statistics for serum ANGPTL PK parameters of primary interest per treatment (Pharmacokinetic analysis set)

Treatment	Statistic	AUClast (h*ng/mL)	Cmax (ng/mL)	Tmax (h)
Cohort 1 LNA043 0.2mg/Joint	n	3	3	3
	Mean (SD)	14500 (5620)	19.8 (7.01)	
	CV% mean	38.9	35.4	
	Geo-mean	13700	18.9	
	CV% geo-mean	42.5	39.2	
	Median	14200	20.2	839
	min-max	8970 - 20200	12.6 - 26.6	74.4 - 861
Cohort 2 LNA043 2mg/Joint	n	3	3	3
	Mean (SD)	19100 (3710)	26.2 (7.53)	
	CV% mean	19.4	28.7	
	Geo-mean	18900	25.5	
	CV% geo-mean	20.4	28.9	
	Median	19900	24.6	789
	min-max	15100 - 22400	19.6 - 34.4	170 - 837
Cohort 3 LNA043 10mg/Joint	n	3	3	3
	Mean (SD)	13900 (1760)	19.7 (3.45)	
	CV% mean	12.7	17.5	

Treatment	Statistic	AUClast (h*ng/mL)	Cmax (ng/mL)	Tmax (h)
	Geo-mean	13800	19.5	
	CV% geo-mean	13.0	16.9	
	Median	14100	18.1	0.250
	min-max	12000 - 15500	17.4 - 23.7	0.00 - 965
Cohort 4 LNA043 20mg/Joint	n	3	3	3
	Mean (SD)	31400 (17300)	46.3 (17.8)	
	CV% mean	55.2	38.5	
	Geo-mean	28700	44.2	
	CV% geo-mean	54.1	38.8	
	Median	21800	41.4	814
	min-max	21000 - 51400	31.5 - 66.1	0.00 - 959
Cohort 5 LNA043 20mg/Joint	n	3	3	3
	Mean (SD)	17900 (6720)	45.2 (9.84)	
	CV% mean	37.6	21.7	
	Median	15700	49.4	0.283
	min-max	12500 - 25400	34.0 - 52.3	0.00 - 389
Cohort 6 LNA043 20mg/Joint	n	3	3	3
	Mean (SD)	37400 (12800)	37.0 (4.41)	
	CV% mean	34.3	11.9	
	Median	44200	38.9	2.00
	min-max	22600 - 45400	32.0 - 40.2	0.267 - 644

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Treatment	Statistic	AUClast (h*ng/mL)	Cmax (ng/mL)	Tmax (h)
Cohort 7 LNA043 40mg/Joint	n	3	3	3
	Mean (SD)	28200 (21200)	43.6 (35.2)	
	CV% mean	75.0	80.7	
	Median	23300	30.3	142
	min-max	9960 - 51400	17.0 - 83.5	73.2 - 870
Placebo	n	7	7	7
	Mean (SD)	19900 (3350)	29.8 (7.36)	
	CV% mean	16.9	24.7	
	Median	20400	30.6	171
	min-max	13100 - 24300	17.5 - 38.9	0.00 - 842

Immunogenicity (Safety analysis set)

	Anti LNA043 antibodies	Cohort 1 LNA043 0.2mg/Joint N=3 n (%)	Cohort 2 LNA043 2mg/Joint N=3 n (%)	Cohort 3 LNA043 10mg/Joint N=3 n (%)	Cohort 4 LNA043 20mg/Joint N=3 n (%)	Cohort 5 LNA043 20mg/Joint N=3 n (%)	Cohort 6 LNA043 20mg/Joint N=3 n (%)	Cohort 7 LNA043 40mg/Joint N=3 n (%)	Placebo N=7 n (%)	Total N=28 n (%)
D1	Negative	3 (100)	3 (100)	3 (100)	3 (100)	3 (100)	3 (100)	3 (100)	7 (100)	28 (100)
D8	Negative	3 (100)	3 (100)	3 (100)	3 (100)	3 (100)	3 (100)	3 (100)	7 (100)	28 (100)
EOS	Negative	3 (100)	3 (100)	3 (100)	3 (100)	3 (100)	3 (100)	3 (100)	7 (100)	28 (100)

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Summary of Safety

Safety Results

See Primary Outcome Results.

Other Relevant Findings

N/A

Conclusion:

In this study, LNA043 displayed a favorable safety profile with no significant drug related safety signals and no immunogenicity. In addition, LNA043 penetrated transiently the target tissue and was quickly cleared locally and systemically.

Date of Clinical Trial Report

03-Dec-2018